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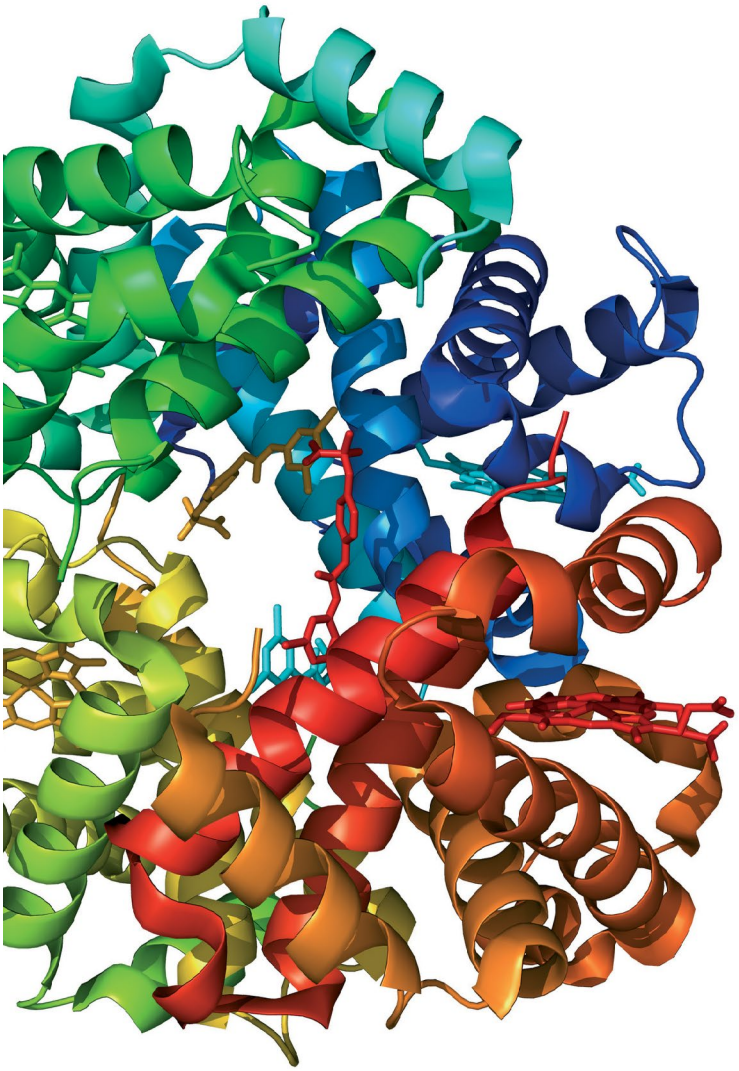

2021 Guidelines on the management of patients with diabetes

A position of Diabetes Poland

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2021 Guidelines on the management of patients with diabetes

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The 2021 Diabetes Poland guidelines — summary of the most important changes

Since 2005, the Diabetes Poland (Polskie Towarzystwo Diabetologiczne, PTD) prepares and publishes annually its guidelines on the management of diabetic patients. The idea of guideline development was first suggested in 2004 by Prof. Jacek Sieradzki who was the president of PTD at that time. The first chairperson of the PTD Guideline Writing Group was Prof. Władysław Grzeszczak who acted in this capacity in 2005––2011, followed by the next president of PTD, Prof. Leszek Czupryniak, in 2011–2015. In 2015–2019, the coordinator of the Recommendations Team was prof. Dorota Zozulińska-Ziółkiewicz, plenipotentiary of the Main Board of the Diabetes Poland for Clinical Guidelines. The guidelines are a product of a team of about 50 experts representing numerous medical specialties. They cover multiple key aspects of clinical diabetes care. Guideline chapters were prepared by teams coordinated by their leaders. The goal of this expert teamwork is to improve prevention, diagnosis, and management of diabetes and its complications in Poland. The Diabetes Poland guidelines reflect advances in diabetology, including new clinical and experimental study findings, epidemiological observations, and registry data. Thus, some modifications and novel aspects appear every year. However, as the guidelines have always been based on the principles of evidence-based medicine, only minor changes are required, related to new knowledge from reliable research with major implications for clinical practice.

Summary of the most important changes to the 2021 Diabetes Poland guidelines

In Chapter 1, a new recommendation is the use of hemoglobin A1c (HbA_{1c}) measurements in the diagnosis of dysglycemia. Introduction of that parameter to the diagnosis of diabetes was possible with an improved standardization of HbA_{1c} measurements in Poland. Diabetes may be diagnosed based on HbA_{1c} level of $\geq$ 6.5% (48 mmol/mol). It has been highlighted that HbA_{1c} level measurements should be performed in a laboratory using analytic methods certified by the National Glycohemoglobin Standardization Program (NGSP), while point-of-care testing for HbA_{1c} should not be used for diagnostic purposes, even if using methods and analyzers certified by NGSP. For the diagnosis of diabetes, HbA_{1c} level measurements should not be used in individuals with conditions interfering with the relationship between HbA_{1c} level and average blood glucose level, such as anemia, pregnancy and postpartum period, treatment with hemodialysis, use of erythropoietin, HIV infection and use of antiretroviral drugs; in these individuals, the diagnostic criteria based on plasma glucose level should be used.

In Chapter 2, it has been highlighted that screening for diabetes type 2 should be undertaken with fasting blood glucose measurements or oral glucose tolerance test. Patients with prediabetes should receive advice regarding healthy lifestyle (weight reduction by at least 7% in those with overweight or obesity and maintaining reduced body weight by physical activity adjusted to the patient's level of fitness, at least 150 minutes per week, along with appropriate diet) with information on the effectiveness of this approach in reducing the risk of incident diabetes. If behavioral therapy of obesity does not lead to adequate body weight reduction, pharmacological treatment or bariatric surgery should be initiated.

In Chapter 5, an information has been added on telemedicine visits as a part of diabetes care. It has been highlighted that each diabetes clinics should be equipped with appropriate equipment (computers with dedicated software), and the personnel should have appropriate knowledge and skills. Individuals with diabetes should be encouraged to use technologies and apps facilitating telemedicine visits. Telemedicine visits in individuals with diabetes may be either a part of regular diabetes care or may be used in the epidemic settings.

In Chapter 6, it has been highlighted that one priority of behavioral therapy of diabetes, regardless of its type, should be to maintain normal body weight in the patient. Continuous and flash glucose monitoring systems are effective tools to facilitate evaluation of the quantity, quality, and proportion of macronutrients on blood glucose levels. Periprandial control of blood glucose levels may be also facilitated by dedicated mobile phone apps; when choosing between them, one should primarily consult the guidance and recommendations by major diabetes societies. It has been highlighted that diabetic individuals should maintain the recommended level of physical activity regardless of the epidemiological situation.

The 2021 Diabetes Poland guidelines include a new chapter that is thematically related to Chapter 6, and thus the chapter numbering in the 2021 Diabetes Poland guidelines has been updated to reflect this inclusion. In the **new Chapter 7**, entitled "Engaging in physical activity and participating in sports by diabetic individuals", it has been highlighted that individuals with diabetes type 1 without clinically significant chronic complications of diabetes may engage in any type of physical activity, including maximal exercise. Aerobic exercise until panting is safe and may be recommended in all diabetic individuals without contraindications. Individuals with diabetes type 2 are recommended to combine aerobic exercise with elements of resistance training. Severe hypoglycemia is a contraindication for exercise for 24 hours.

In Chapter 8, it has been highlighted that psychological and social care should be integrated with the approach focused on cooperation with the diabetic individual and available for all diabetic individuals to allow optimization of treatment outcomes and the quality of life.

In Chapter 9, it has been highlighted that nursing, dietician, and psychologic care with definitions of the basic norms, guidance, and organizational and technical set-tings for the provision of diabetic therapeutic education is provided by the employer. The employer's responsibility is to create and improve conditions for position training, increasing professional qualifications, and self-education for the members of diabetes therapeutic team, including those serving as diabetes educators. It has also been highlighted that it is recommended to perform periodic (annual) verification of the patient knowledge. Further verification and reeducation should be undertaken once new risk factors/complications develop. A description of diabetes management procedures, in particular therapeutic education procedures, must be available and conformed to at the site where education is provided.

In Chapters 10 and 11, it has been highlighted that all therapeutic decisions in the management of diabetes type 1 and 2 should be undertaken in cooperation with the patient and should be accepted by the patient.

In Chapter 10, it has been reiterated that in all individuals with diabetes type 1, the therapeutic team cooperating with the patient should aim to develop a system that allows effective telemedicine visits.

In Chapter 11, a recommendation has been added regarding early use of two-drug combination treatment in diabetes type 2 that should be considered in newly diagnosed diabetes in case of documented atherosclerotic cardiovascular disease, systolic heart failure, chronic kidney disease, or the presence of multiple cardiovascular disease risk factors. In such cases, metformin should be combined with drugs that reduce the risk of progression of the above conditions. Initiation of combined treatment in newly diagnosed diabetes type 2 should also be considered in case of severe hyperglycemia. In patients with chronic kidney disease and systolic heart failure, sodium-glucose cotransporter 2 (SGLT-2) inhibitors should be preferred, and glucagon-like peptide 1 (GLP-1) receptor agonist should be used if SGLT-2 inhibitors are contraindicated. In patients with established atherosclerotic cardiovascular disease, drugs from both these groups should be considered, and GLP-1 receptor agonist should be considered first in patients with multiple cardiovascular disease risk factors. The algorithm for drug treatment in diabetes type 2 has been summarized in two figures developed, respectively, for drug treatment-naive individuals and those previously treated with metformin.

In Chapter 13, it has been added that among antidiabetic medications, SGLT-2 inhibitors and GLP-1 receptor agonists exert a blood pressure lowering effect and may be recommended for the treatment of diabetes also for that reason.

The therapeutic goals for the treatment of dyslipidemia in **Chapter 14** have been unified with the 2019 European Society of Cardiology (ESC) and European Association for the Study of Diabetes guidelines and the 2019 ESC and European Atherosclerosis Society guidelines. In diabetic subjects at very high cardiovascular risk, the target low-density lipoprotein (LDL) cholesterol level < 55 mg/dL (< 1.4 mmol/L) and LDL cholesterol level reduction by at least 50% compared to baseline are recommended. In diabetic subjects at high cardiovascular risk, the target LDL cholesterol level < 70 mg/dL (< 1.0 mmol/L) and LDL cholesterol level reduction by at least 50% compared to baseline are recommended. Information about apolipoprotein B and its target levels has also been added, as has been the information that in acute conditions, rapid triglyceride level reduction may be achieved by plasmapheresis.

In Chapter 15, it has been noted that a thorough evaluation of patient's habits and the current treatment of diabetes and other conditions is necessary in case of recurrent hypoglycemia episodes and hypoglycemia unawareness.

In Chapter 16, an information has been added that in patients with a subcutaneous insulin deposit following previous drug injections, intravenous insulin therapy may be initiated with an insulin infusion without the initial bolus. If serum potassium is > 5.5 mmol/L when potassium is not supplemented, serum potassium should be measured after 2 hours, and if serum potassium is < 5.5 mmol/L and potassium is supplemented – every 4 hours.

In Chapter 17, an information has been added that drugs with an established cardioprotective effect (SGLT2 inhibitors, GLP-1 receptor agonists) should be initiated after myocardial infarction.

In Chapter 18, it has been highlighted that hypoglycemia should be avoided when treating stroke in a diabetic individual.

In Chapter 19, a table has been added on dosing of oral antidiabetic drugs and GLP-1 receptor agonists in relation to the severity of renal dysfunction.

In Chapter 20, a section on the screening for and the treatment of diabetic eye disease has been updated. An information has been added that screening may also be performed by telemedicine using a fundus camera, with evaluation of photographs by skilled personnel or using dedicated image-analysis software. It must be noted, however, that photography of the retina cannot replace the comprehensive ophthalmologic examination which should be performed at least at the onset of the disease, and then as recommended by the ophthalmologist. In women with diabetes type 1 and 2, ophthalmologic examination should be performed before pregnancy or in the first trimester, and then repeated in each trimester and for a year after the delivery to evaluate the degree of retinopathy. Regular follow-up eye fundus examinations and appropriate treatment allow reduction of vision loss due to diabetic retinopathy by 98%.

An information has also been added about subthreshold (mostly micropulse) retinal laser photocoagulation – without tissue coagulation, used in macular edema without its significant thickening and vision loss. In diabetic macular edema with foveal involvement and vision loss, the recommended first-line treatment are intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents. Grid-type retinal laser photocoagulation is used in diffuse diabetic macular edema, when the first-line treatment was not effective. Intravitreal or periocular injections of steroids exerting an antiangiogenic and antiedematous effect are used if contraindications to anti-VEGF agents are present or the monthly visit regimen cannot be maintained. A new indication for vitrectomy are vitreomacular tractions running vertically towards the macula.

In Chapter 21, it has been highlighted that neuropathy may develop already in prediabetes. In painful neuropathy, physical examination may be normal, and thus in case of typical complaints, neuropathy may be diagnosed even with normal physical examination findings. The recommendations regarding the evaluation for autonomic neuropathy have been defined more clearly. It has been highlighted that autonomic neuropathy mostly manifests with hypoglycemia unawareness, resting tachycardia, orthostatic hypotension, gastroparesis, constipation or diarrhea, erectile dysfunction, neurogenic bladder, or sudomotor dysfunction. It should be remembered that diabetic neuropathy is asymptomatic in about 50% of cases. It has been highlighted that the causal treatment for diabetic neuropathy is blood glucose control. In patients with neuropathic pain, treatment of the latter is absolutely necessary as pain impairs the quality of life and patient functioning, and may lead to depression. An algorithm for symptomatic drug treatment of neuropathic pain in somatic diabetic neuropathy has been added.

In Chapter 22, it has been highlighted that in many patients (particularly with the loss of preventive pain sensation, ischemia, and existing deformations), it is recommended to use appropriate footwear insoles to prevent ulcerations or their recurrences by correcting excessive pressure acting on the foot sole. It has been stressed that in acute neuropathic osteoarthropathy (Charcot foot), off-loading should be maintained until stabilization of the process – transition to an inactive phase. The return to full limb loading should be very slow.

In Chapter 23, it has been noted that the presence of a high titer of one type of antibody or elevated titers of two types of antibodies indicates an active autoimmune process involving apoptosis of pancreatic beta cells and is consistent with the diagnosis of preclinical stage 1 diabetes. If impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) develops, preclinical stage 2 diabetes may be diagnosed. Stage 3 is the development of clinically apparent type 1 diabetes. It has also been highlighted that use of continu-

ous glucose monitoring (CGM) is indicated in all children since the disease onset. Each increase of the time in range (TIR) by 5% is associated with cardiovascular risk reduction in adults). In diabetes type 2 in children, addition of a GLP-1 receptor agonist should be considered if blood glucose levels have not been adequately controlled and body weight has not been normalized. Children and adolescents with diabetes should be encouraged to engage in daily moderate or intensive physical activity, and may engage in sport similarly to children without diabetes. The biochemical criteria for the diagnosis of acute hyperglycemic conditions in children and adolescents have been added. Some changes have been made to the algorithm for the management of ketoacidosis in children.

In Chapter 24, it has been highlighted that women with a history of gestational diabetes mellitus (GDM) should be consider at high risk of diabetes and cardiovascular disease. For that reason, annual investigations for dysglycemia are required in this group above 40 years of age. It has also been noted that metformin is secreted to the breast milk at a very low level and thus it seems that metformin may be safely used during lactation by patients with diabetes type 2. A table summarizing the recommendations regarding body weight increase during pregnancy has been added. In all types of diabetes during pregnancy, the recommended target self-measured blood glucose values between 2 and 4 AM are 70–90 mg/dL (3.9–5.0 mmol/L). Patients with a history of GDM should be tested for diabetes before the next pregnancy and if diabetes is diagnosed, these patients should be treated to reduce the risk of congenital anomalies in the offspring.

In Chapter 27, an information has been added about vaccinations before traveling to endemic areas. In addition, all children in Poland born after Jan 01, 2017 should be routinely vaccinated against *Streptococcus pneumoniae*. Diabetic children born before Feb 01, 2017 should receive compulsory vaccination against *Streptococcus pneumoniae*. Due to their at-risk status, the vaccination should be performed before 5 years of age. For vaccination against influenza, both quadrivalent vaccines available in Poland may be used for that purpose, administered intramuscularly (inactivated virus) or intranasally (live attenuated influenza vaccine). In addition, due to the COVID-19 pandemic ongoing for nearly a year, vaccination using available vaccines is recommended in diabetic individuals.

In Appendix 6, an information has been added that the personnel in a center initiating and/or providing treatment with a personal insulin pump in diabetic patients should include physicians with board certification in pediatric endocrinology and diabetology, physicians with board certification in diabetology skilled in the treatment with personal insulin pumps (Polish Society of Diabetes certification), and nurses/educators trained in the treatment with personal insulin pumps. During visits, it is necessary to regularly retrieve and analyze data from personal insulin pumps, glucose meters, and CGM systems. Another responsibility of the center initiating is to a perform a verification visit to evaluate the patient skills and the achieved metabolic control of diabetes. Acceptance of this form of insulin therapy by children and/or their parents has been added to the indications for insulin pump therapy. In children with newly diagnosed diabetes, the initial patient selection for the treatment with a personal insulin pump is performed by a diabetologist or pediatric endocrinologist and diabetologist working in a pediatric diabetes ward. The training should continue until the patient/caregiver is well versed with practical aspects of personal insulin pump use.

Like every year, we hereby present to you the new edition of the Diabetes Poland guidelines. Despite many difficulties related to the COVID-19 pandemic and the need to adjust the working conditions in our diabetes wards and clinics accordingly, we tried to incorporate the most recent research findings in the recommendations included in this year's guideline edition, and to reflect these new working conditions for the whole diabetic team in the context of the current epidemiologic threats. By making the above changes, as usual suggested in part by the users of these guidelines, the 2021 Diabetes Poland guidelines Writing Group hopes that they will serve for improvement of medical care for diabetic patients in our country.

We sincerely thank everybody who has contributed to the development of the new edition of the Diabetes Poland guidelines.

Prof. Irina Kowalska
Plenipotentiary of the Board
of the Diabetes Poland for Clinical Guidelines

Prof. Dorota Zozulińska-Ziółkiewicz
President of the Diabetes Poland

Table 1. American Diabetes Association evidence-grading system for "Standards of Medical Care in Diabetes"

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted multicentre trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis Compelling nonexperimental evidence, i.e., "all or none" rule developed by the Centre for Evidence--Based Medicine at the University of Oxford Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted trial at one or more institutions • Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Supportive evidence from well-conducted cohort studies • Evidence from a well-conducted prospective cohort study or registry • Evidence from a meta-analysis of cohort studies Supportive evidence from well-conducted case-control study
C	Supportive evidence from poorly or incontrolled studies • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

1. Approach to the evaluation of dysglycemia

Most important recommendations

- Blood glucose measurements to allow early diagnosis of prediabetes/diabetes type 2 should be performed in all subjects > 45 years of age and younger overweight or obese subjects with at least one additional risk factor for diabetes. [**B**]
- Women without a prior diagnosis of diabetes should be evaluated for gestational diabetes with oral glucose tolerance test with 75 g of glucose performed between 24 and 28 weeks of gestation. [**A**]
- The diagnosis of diabetes in children during the first 9 months of life requires genetic testing for neonatal diabetes. [**A**]
- In patients with cystic fibrosis, annual oral glucose tolerance test should be performed beyond 10 years of age to diagnose diabetes. [**A**]

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia due to defective secretion and/or action of insulin. Chronic hyperglycemia is associated with damage, dysfunction, and failure of various organs, in particular eyes, kidneys, nerves, heart, and blood vessels.

I. **Symptoms suggesting the presence of diabetes:**
   — Polyuria;
   — Increased thirst;
   — Weight loss that cannot be explained by intended weight reduction;
   — Other, less typical symptoms and signs: fatigue and somnolence, purulent skin lesions, and inflammatory conditions of the genitourinary tract.

II. **Approach to the evaluation of dysglycemia (Table 1.1):**
   — If symptoms of hyperglycemia are present, random venous plasma glucose level measurement should be performed — values ≥ 200 mg/dL (≥ 11.1 mmol/L) are consistent with the diagnosis of diabetes;
   — If no symptoms are present or when symptoms are present and random blood glucose is < 200 mg/dL (< 11.1 mmol/L), diabetes may be diagnosed based on:
   — Morning fasting blood glucose measurement performed twice on separate days — diabetes is diagnosed if fasting blood glucose on both these occasions is ≥ 126 mg/dL (≥ 7.0 mmol/L);
   — Single measurement of hemoglobin A_{1c} (HbA_{1c}) level — diabetes is diagnosed if HbA_{1c} level is ≥ 6.5% (≥ 48 mmol/mol);

Table 1.1. Diagnostic criteria for dysglycemia

Venous plasma glucose level determined in a laboratory			HbA_{1c} level determined in a laboratory using a NSGP-certified method
Random blood glucose — measured in a blood sample collected at any time of the day, regardless of the timing of the last meal	Fasting blood glucose — measured in a blood sample collected 8–14 hours after the last meal	Blood glucose at 120 minutes during an oral glucose tolerance test (OGTT) according to WHO	
≥ 200 mg/dL (≥ 11.1 mmol/L) → diabetes* (if symptoms of hyperglycemia are present, such as increased thirst, polyuria, fatigue)	70–99 mg/dL (3.9–5.5 mmol/L) → normal glucose tolerance (NGT)	< 140 mg/dL (7.8 mmol/L) → normal glucose tolerance (NGT)	
	100–125 mg/dL (5.6–6.9 mmol/L) → impaired fasting glucose (IFG)	140–199 mg/dL (7.8–11.0 mmol/L) → impaired glucose tolerance (IGT)	
	≥ 126 mg/dL (≥ 7.0 mmol/L) → diabetes*	≥ 200 mg/dL (≥ 11.1 mmol/L) → diabetes*	≥ 6.5% (48 mmol/mol) → diabetes*

NSGP — National Glycohemoglobin Standardization Program; WHO — World Health Organization

*Diagnosis of diabetes requires abnormal findings as described in the text

Diagnosis of diabetes requires one abnormal reading except for fasting blood glucose which requires two abnormal readings. A potential effect of factors not related to testing itself should be taken into account when measuring blood glucose (timing of the last meal, exercise, time of the day)

— If fasting blood glucose on one or two occasions is 100–125 mg/dL (5.6–6.9 mmol/L), or fasting blood glucose is < 100 mg/dL (5.6 mmol/L) or HbA_{1c} level is < 6.5% (< 48 mmol/mol) in an individual with a reasonable suspicion of impaired glucose tolerance (IGT) or diabetes), an oral glucose tolerance test (OGTT) should be performed – diabetes is diagnosed if blood glucose level at 120 minutes of OGTT is ≥ 200 mg/dL (≥ 11.1 mmol/L).

In general, fasting blood glucose, blood glucose level at 120 minutes of OGTT, and HbA_{1c} level may be all considered equally useful for the diagnostic purposes, although these parameters identify diabetes in different indivduals. Compared to fasting blood glucose and HbA_{1c} level, blood glucose level at 120 minutes of OGTT identifies a higher number of indviduals with diabetes and prediabetes.

III. Principles of diagnostic testing

— An OGTT should be performed without prior limitations of carbohydrate intake in a fasting, rested subject after an overnight sleep; the subject should remain resting at the site of testing for the 2-hour period before ingestion of 75 g glucose solution and blood sampling, with all blood glucose level measurements performed in venous blood plasma in a laboratory;
— If OGTT is to be performed in a subject with prediabetes treated with metformin for that reason, the drug should be withdrawn at least one week before OGTT;
— Blood glucose measurements for diagnostic purposes should be performed in a laboratory; it is unacceptable to replace them with measurements using glucose meters;
— HbA_{1c} level measurements should be performed in a laboratory using analytic methods certified by the National Glycohemoglobin Standardization Program (NGSP) (http://www.ngsp.org); point-of-care testing (POCT) for HbA_{1c} should not be used for diagnostic purposes, even if using methods and analyzers certified by NGSP;
— For the diagnosis of diabetes, HbA_{1c} level measurements should not be used in individuals with conditions interfering with the relationship between HbA_{1c} level and average blood glucose level, such as anemia, pregnancy and postpartum period, treatment wth hemodialysis, use of erythropoietin, HIV infection and use of antiretroviral drugs; in these individuals, the diagnostic criteria based on plasma glucose level should be used.

IV. Nomenclature of hyperglycemic states according to the World Health Organization (WHO):

— Normal fasting blood glucose: 70–99 mg/dL (3.9––5.5 mmol/L);
— Impaired fasting glucose (IFG): 100–125 mg/dL (5.6–6.9 mmol/L);
— Impaired glucose tolerance (IGT): 120-minute blood glucose at 120 minutes of OGTT 140–199 mg/dL (7.8–11 mmol/L);
— Prediabetes: IFG and/or IGT;
— Diabetes — one of the following criteria:
  • Symptoms of hyperglycemia and random blood glucose level ≥ 200 mg/dL (≥ 11.1 mmol/L);
  • Fasting blood glucose ≥ 126 mg/dL (≥ 7.0 mmol/L) on two occasions;
  • Blood glucose at 120 minutes of OGTT ≥ 200 mg/dL (≥ 11.1 mmol/L);
  • HbA_{1c} level ≥ 6.5% (≥ 48 mmol/mol).

V. Subjects at risk require screening for diabetes, as symptoms of hyperglycemia are absent in more than half of them. Testing for diabetes should be performed every three years in all subjects > 45 years of age. In addition, the following risk groups should be tested annually regardless of age:

— Overweight or obese subjects [body mass index (BMI) ≥ 25 kg/m^2 and/or waist circumference > 80 cm (women) or > 94 cm (men)];
— Subjects with a family history of diabetes (in parents or siblings);
— Physically inactive subjects;
— Members of community or ethnic groups characterized by increased rates of diabetes;
— Those with prediabetes identified during previous testing;
— Women with a history of gestational diabetes;
— Women who gave birth to an infant with a birth weight > 4 kg;
— Subjects with hypertension (≥ 140/90 mm Hg);
— Subjects with dyslipidemia [high-density lipoprotein (HDL) cholesterol < 40 mg/dL (< 1.0 mmol/L) and/or triglycerides > 150 mg/dL (> 1.7 mmol/L)];
— Women with polycystic ovary syndrome;
— Subjects with cardiovascular disease.

VI. Etiologic classification of diabetes:

1. **Diabetes type 1** — autoimmune destruction of pancreatic beta cells, usually leading to absolute insulin deficiency.
2. **Diabetes type 2** — progressive loss of the ability of pancreatic beta cells to secrete insulin appropriately, with concomitant insulin resistance.
3. **Other specific forms of diabetes:**

— Genetic defects of beta cell function;
— Genetic defects of insulin function;
— Exocrine pancreatic diseases;
— Endocrinopathies;
— Drugs and chemicals;

— Infections;
— Rare immunologic forms of diabetes;
— Other genetic syndromes associated with diabetes.

4. Hyperglycemia identified for the first time during pregnancy:

— Diabetes during pregnancy;
— Gestational diabetes.

The category of autoimmune diabetes type 1 includes slowly progressing diabetes caused by autoaggression. Latent autoimmune diabetes in adults (LADA) is a late manifesting autoimmune form of diabetes in adults, most commonly diagnosed in patients above 35 years of age, characterized by clinical insulin independence in the first months after the diagnosis, with the presence of serum antibodies against glutamic acid decarboxylase (anti-GAD65) and/or other anti-islet antibodies and a low serum peptide C level. LADA is a form of diabetes type 1 with slowly progressive autoimmune-mediated destruction of beta cells. This diabetes subtype is present in 5–10% of subjects with diabetes diagnosed after 35 years of age and categorized as diabetes type 2. Clinical manifestations of LADA do not always allow a definite diagnosis, presenting diagnostic challenges when differentiating with diabetes type 2.

A definite diagnosis of LADA requires identification of autoantibodies typical for diabetes type 1, mostly anti-GAD65, and/or a low serum peptide C level.

Monogenic diabetes

Monogenic diabetes amounts to 1–2% of all diabetes cases. It is caused by single gene mutations. Most forms are associated with a defect of insulin secretion, and the most common ones are maturity-onset diabetes of the young (MODY), mitochondrial diabetes, and neonatal diabetes. Taking into account the monogenic forms in the differential diagnosis of diabetes may contribute to treatment optimization and proper evaluation of prognosis in the patient and his family members. A definite diagnosis of monogenic diabetes is a result of genetic testing. Patient selection for genetic testing for monogenic diabetes and any therapeutic decisions resulting from such a diagnosis should be made in centers with a large experience in this area.

Persistent neonatal diabetes is defined as the disease onset before 9 months of age. Genetic testing should be performed in all patients with persistent neonatal diabetes. This should include testing for mutations in the KCNJ11 gene which codes for Kir6.2 protein. Mutations in this gene are the most common cause of persistent neonatal diabetes. Regardless of age, most patients with KCNJ11 gene mutations may be treated with sulfonylureas which are effective and safe in this group and thus may be used as an alternative to insulin. Further targets for genetic testing include mutation in the insulin genes, the ABCC8 gene coding for SUR1 protein, and the glucokinase gene. If a mutation in the ABCC8 gene is identified, sulfonylurea treatment may be attempted. Carriers of mutations in the insulin gene and a double mutation in the glucokinase gene need to be treated with insulin. Decisions regarding search for mutations in other genes should be made individually by diabetes specialists (diabetologists) with an appropriate experience in the genetics of diabetes.

In families with autosomal dominant early-onset diabetes caused by impaired insulin secretion, in most cases without obesity, the differential diagnosis should include MODY and mutations in the responsible genes should be searched for. The most common form of MODY is associated with *HNF1A* and glucokinase gene mutations.

Typical clinical presentation of MODY due to a *HNF1A* gene mutation includes:

— Early onset of diabetes (typically before 25 years of age);
— No insulin dependence and ketoacidosis, low insulin requirement, detectable peptide C levels despite the disease being present for several years or even longer;
— Family history of diabetes over at least 2 generations, with early-onset diabetes in at least two family members. OGTT performed at an early stage of diabetes usually shows high postprandial glucose level elevation with often normal fasting blood glucose;
— Absence of autoantibodies typical for diabetes type 1;
— Glycosuria higher than expected based on blood glucose levels.

Chronic complications of diabetes develop in a large proportion of patients with MODY due to a HNF1A gene mutation, and thus optimal disease control should be actively pursued early after the disease onset. Sulfonylureas are the drugs of choice (except for pregnancy or the presence of typical contraindications to these drugs). If these are not effective, combined therapy with insulin, metformin or dipeptidyl peptidase-4 (DPP-4) inhibitors, or insulin monotherapy should be considered.

Testing for glucokinase gene mutations is indicated in the following situations:

— Persistently elevated fasting blood glucose in the range of 99–144 mg/dL (5.5–8.0 mmol/L);
— An increase in blood glucose during OGTT lower than 83 mg/dL (4.6 mmol/L);
— A family history of diabetes in one of the parents, but negative family history does not exclude this form of diabetes.

Healthy nutrition with elimination of simple sugars is the treatment of choice in glucokinase defects due to a single gene mutation; drugs are usually ineffective. HbA_{1c}

value characteristic for glucokinase defect is not higher than 7.5%.

Decisions regarding testing for mutations in other genes associated with MODY should be made individually in centers experienced in such testing.

The most common cause of mitochondrial diabetes is the A3243G mutation of the gene coding for leucine tRNA. Testing for this mutation should be performed in case of maternal transmission of early-onset diabetes associated with deafness in some family members. The therapeutic approach in mitochondrial diabetes may include diet and treatment with sulfonylureas or insulin depending on the degree of defective insulin secretion. Metformin use should be avoided in mitochondrial diabetes.

Cystic fibrosis-related diabetes (CFRD)

Diabetes is present in about 20% of adolescents and 40–50% adults with cystic fibrosis. Diabetes associated with cystic fibrosis is classified as other specific type of diabetes associated with exocrine pancreatic disease, characterized by a slow progression and usually remains asymptomatic for many years. Diabetic ketoacidosis occurs rarely, most likely due to preserved endogenous insulin secretion or concomitant impairment of glucagon secretion. Initially, hyperglycemia is usually seen in circumstances that exacerbate insulin resistance, such as acute and chronic infections, glucocorticoid therapy, and ingestion of large amounts of carbohydrates (intake by oral or intravenous route, gastric tube or percutaneous gastrostomy). Insulin therapy is the treatment of choice.

Routine annual testing for diabetes should be performed in generally healthy subjects with cystic fibrosis aged > 10 years.

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2. Preventing and delaying development of diabetes

Most important recommendations

- Patients with prediabetes should receive recommendations on healthy lifestyle (weight reduction and maintenance, physical activity at least 150 minutes per week) and information regarding the effectiveness of these methods in preventing overt diabetes. [**A**]
- In patients with prediabetes, particularly those with body mass index (BMI) ≥ 35 kg/m^2 and below 60 years of age, and in women with a history of gestational diabetes mellitus (GDM), pharmacological prevention of diabetes with metformin should be considered along with lifestyle modifications. [**A**]
- Screening should be performed with fasting blood glucose measurements and oral glucose tolerance test. [**C**]

Diabetes type 1

Currently, no effective and clinically useful methods exist to prevent diabetes type 1 both in the general population and in subjects at risk.

Diabetes type 2

I. Screening should be undertaken with fasting blood glucose measurements or oral glucose tolerance test [C].

II. Risk factors for diabetes type 2 (see Chapter 1).

III. Overview of recommendations regarding prevention and delaying development of diabetes:

— Subjects at a high risk of developing diabetes type 2 should receive appropriate education regarding the role of healthy lifestyle in the prevention of diabetes type 2;

— Subjects with prediabetes should receive advice regarding healthy lifestyle [weight reduction by at least 7% in those with overweight or obesity and maintaining reduced body weight by physical activity (at least 150 minutes per week) adjusted to the patient's level of fitness along with appropriate diet]

with information on the effectiveness of this approach in reducing the risk of incident diabetes; [A]
— In individuals with prediabetes, particularly with concomitant IFG and IGT and/or body mass index ≥ 35 kg/m^2 and/or below 60 years of age, and in women with a history of gestational diabetes mellitus (GDM), pharmacological prevention of diabetes type 2 by using metformin should be considered along with lifestyle modifications.
— If behavioral treatment of obesity does not lead to adequate body wight reduction, pharmacological treatment or bariatric surgery should be considered; [A]
— All individuals benefit from increased physical activity, regardless of their age; however, it should be emphasized that this intervention is most effective in people over 60;
— Repeating advice regarding lifestyle changes during each patient visit is of a paramount importance for the effectiveness of preventing glucose metabolism disturbances;
— It is recommended to monitor patients regularly for other cardiovascular disease risk factors (e.g., obesity, tobacco smoking, hypertension, dyslipidemia) and to institute appropriate treatment if these are present. The goals of treating concomitant diseases for people with pre-diabetes are the same as for the general population;
— Prescription of diabetogenic drugs should be avoided.

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3. Blood glucose monitoring

Most important recommendations

- Most individuals treated with intensive insulin therapy should perform self-monitoring of blood glucose (SMBG) before and after meals, before bedtime, before planned physical activity, whenever hypoglycemia is suspected, and before activities associated with particular dangers of hypoglycemia (e.g., driving). [**B**]
- Within a comprehensive education program, SMBG may guide self-management decisions in individuals receiving less intensive insulin therapy [B] and diabetic individuals not treated with insulin. [**E**]
- Continuous patient education and periodic assessment of proper measurement technique, interpretation of the measurement results, and their effect on therapeutic decisions are important when ordering SMBG. [**E**]
- Continuous glucose monitoring (CGM) combined with intensive insulin therapy is a useful tool to reduce HbA_{1c} levels in adult individuals (≥ 25 years of age) with diabetes type 1. [**A**]
- Although the evidence for a reduction in HbA_{1c} level in children and young adults are less robust, CGM may be helpful also in these groups of patients, The therapeutic success depends on the adherence to regular measurements. [**B**]
- CGM may be a useful tool in individuals with hypoglycemia unawareness and individuals with recurrent episodes of hypoglycemia. [**C**]

Table 3.1. Recommended frequency of self-monitoring of blood glucose

Treatment regimen	Frequency of self-monitoring of blood glucose
Multiple (i.e., at least 3 times daily) insulin injections Intensive insulin therapy, regardless of the diabetes type	Multiple (i.e., at least 4 times daily) readings during the day according to the treatment regimen and patient needs
Oral hypoglycemic drugs and/or GLP-1 receptor agonists	4-point blood glucose profile (fasting and 2 hours post main meals) once a week, once daily at various times of the day
Diabetes type 2 treated with fixed insulin doses	1–2 readings daily plus 4-point blood glucose profile (fasting and 2 hours post main meals) once a week plus 7-point blood glucose profile once a month

GLP — glucagon-like peptide

Current monitoring and retrospective evaluation of blood glucose levels are integral parts of adequate diabetes treatment. Appropriate self-monitoring of blood glucose (SMBG) requires regular patient education in this regard, including evaluation of the ability to use a glucose meter and interpret SMBG results, i.e., using them for day-to-day modifications of nutrition, exercise, and medication doses. Regular HbA_{1c} level measurements are another necessary component of diabetes treatment monitoring.

I. Self-monitoring of blood glucose

Blood glucose self-monitoring is an integral part of diabetes treatment.

Diabetic individuals treated with multiple daily insulin injections or continuous subcutaneous insulin infusion (CSII) should perform a daily blood glucose profile that includes readings at morning fast, before and 60–120 minutes after each main meal, and before bedtime. Frequency and timing of additional measurements should be set individually.

Use of blood glucose monitoring systems including real-time continuous glucose monitoring (rtCGM) and intermittently scanned continuous glucose monitoring (isCGM)/flash glucose monitoring (FGM) to supplement blood glucose self-monitoring is particularly indicated in individuals with labile diabetes type 1 with frequent hypoglycemia episodes and hypoglycemia unawareness, as it improves treatment safety and effectiveness.

Self-monitoring of blood glucose is also indicated to reach therapeutic targets in patients treated with single insulin injections, oral antidiabetic agents, and/or GLP-1 receptor agonists (Table 3.1). Regardless of the treatment used, all patients should check blood glucose levels more frequently in case of feeling unwell or a sudden illness.

Proper SMBG requires patient education regarding glucose meter use, interpretation of readings, and further management steps. For SMBG, it is recommended to use glucose meters that display plasma glucose level with the declared margin of error of up to 15% for glucose levels ≥ 100 mg/dL (5.6 mmol/L) and 15 mg/dL (0.8 mmol/l) for glucose levels < 100 mg/dL (5.6 mmol/L). Analysis of glucose readings using dedicated computer software may be useful in patients performing ≥ 4 measurements daily. Glucose meters and the technique of their use by the patients should be checked in case of suspected measurement errors and at least once a year at the facility where the diabetic individual receives outpatient treatment. This assessment should involve measuring glucose level in the same material with a glucose meter using a comparative method (laboratory method or point of care testing (POCT) consistent with the laboratory method) — the difference in results obtained should not exceed the above-defined margins of error.

II. Hemoglobin A_{1c} (HbA_{1c})

Hemoglobin A_{1c} level reflects average blood glucose levels during the period of approximately 3 last months, with about 50% of HbA_{1c} currently present in blood being formed during the last month before the measurement.

Hemoglobin A_{1c} level measurements should be performed annually in individuals with stable disease in whom the therapeutic targets have been met. In those in whom the therapeutic targets have not been met or the treatment has been modified, HbA_{1c} level should be measured at least every 3 months.

Hemoglobin A_{1c} level measurements should be performed using analytic methods certified by the National Glycohemoglobin Standardization Program (NGSP) (http://www.ngsp.org). Point-of-care testing for HbA_{1c} is also possible when using methods and analyzers certified by NGSP. It has been suggested that diagnostic laboratories report HbA_{1c} levels in SI units (mmol/mol) in addition to traditional units.

When interpreting HbA_{1c} levels, interfering factors should be taken into account, such as changes in the erythrocyte survival time, hemoglobinopathies, and chemical hemoglobin modifications which may render use of these measurements difficult or impossible.

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4. Setting therapeutic targets in diabetes

Most important recommendations

- In diabetic patients, the overall goal of diabetes control is HbA_{1c} level ≤ 7.0% (53 mmol/mol). [**A**]
- Low-density lipoprotein cholesterol (LDL-C) level < 55 mg/dL (1.4 mmol/L) and reduction by at least 50% in diabetic subjects at very high cardiovascular risk. [**B**]
- LDL-C level < 70 mg/dL (1.8 mmol/L) and reduction by at least 50% in diabetic subjects at high cardiovascular risk. [**A**]
- LDL-C level < 100 mg/dL (2.6 mmol/L) in diabetic subjects at moderate cardiovascular risk (young patients < 35 years of age with diabetes type 1 but without chronic complications and other cardiovascular risk factors) or patients with type 2 diabetes < 50 years of age, with duration of diabetes < 10 years, without other risk factors. [**A**]
- The recommended blood pressure goal is < 130/80 mm Hg. [**A**]

I. General considerations

1. Therapeutic targets in diabetes include target blood glucose levels, blood pressure values, lipid profile, and body weight.
2. In older patients and those with comorbidities, who are expected to survive for less than 10 years, therapeutic targets should be relaxed so as to not compromise patient's quality of life.
3. Generally, therapeutic targets and treatment intensification should be largely individualized. In all diabetic patients, and particularly those with diabetes type 2, the following factors should be taken into account when setting therapeutic targets: patient's attitude towards treatment and the expected engagement in the treatment process (including that of patient's family members, caretakers etc.), the risk of hypoglycemia and its possible consequences (more severe in the elderly, and in those with preexisting cardiovascular or nervous system damage), duration of diabetes, expected survival, presence of major vascular diabetic complications and significant comorbidities, the degree of patient's education, and the risk-to-benefit ratio associated with specific therapeutic targets. In some circumstances (e.g., in those with advanced complications and in the elderly), the therapeutic targets should be attained gradually, within several (2 to 6) months.

II. Targets of the metabolic control of diabetes (taking into account the above considerations)

A general target: HbA_{1c} ≤ 7% (≤ 53 mmol/mol)

Individual targets:

1. HbA_{1c} ≤ 6.5% (≤ 48 mmol/mol):

— Diabetes type 1 if this target is not associated with an increased risk of hypoglycemia and impaired quality of life [fasting and preprandial blood glucose, including SMBG: 70–110 mg/dL (3.9––6.1 mmol/L); 2-hour post-prandial SMBG < 140 mg/dL (7.8 mmol/L)];

— Diabetes type 2 of a short duration;

— In children and adolescents, regardless of the diabetes type.

When evaluating blood glucose profile in relation to target HbA_{1c}, values given in Table 4.1 should be consulted, showing mean daily blood glucose values and blood glucose ranges corresponding to specific HbA_{1c} levels.

Table 4.1. Relation between HbA_{1c} levels and average plasma glucose levels

HbA_{1c}	Average plasma glucose levels		Average fasting blood glucose	Average preprandial blood glucose	Average postprandial blood glucose
	[mg/dL]	[mmol/L]	[mg/dL]	[mg/dL]	[mg/dL]
6	126	7.0			
< 6.5			122	118	144
6.5–6.99			142	139	164
7	154	8.6			
7.0–7.49			152	152	176
7.5–7.99			167	155	189
8	183	10.2			
8–8.5			178	179	206
9	212	11.8			
10	240	13.4			
11	269	14.9			
12	298	16.5			

Correlation between HbA_{1c} and average plasma glucose levels 0.92 (according to *Diabetes Care* 2015; 28: 35)

Table 4.2. Glycemic targets in patients with type 1 and type 2 diabetes and in pregnant women using CGM/FGM on a regular basis

	Time-in-Range — TIR		Time below range — TBR		Time above range — TAR	
	% of readings; time per day	Target range	% of readings; time per day	Below target range	% of readings; time per day	Above target range
Type 1 diabetes/type 2 diabetes	> 70%; > 16 h, 48 min	70–180 mg/dL (3.9–10.0 mmol/L)	< 4%; < 1 h < 1%; < 15 min	< 70 mg/dL (< 3.9 mmol/L) < 54 mg/dL (< 3.0 mmol/L)	< 25%; < 6 h < 5%; < 1 h, 12 min	> 180 mg/dL (> 10.0 mmol/L) > 250 mg/dL (> 13.9 mmol/L)
Elderly/ /individuals with a high risk of hypoglycemia	> 50%; > 12 h	70–180 mg/dl (3.9–10 mmol/L)	< 1%; < 15 min	< 70 mg/dL (< 3.9 mmol/L)	< 10%; < 2 h, 24 min	> 250 mg/dL (> 13.9 mmol/L)
Pregnant women with type 1 diabetes	> 70%; > 16 h, 48 min	63–140 mg/dL (3.5–7.8 mmol/L)	< 4%; < 1 h < 1%; < 15 min	< 63 mg/dL (< 3.5 mmol/L) < 54 mg/dL (< 3.0 mmol/L)	< 25%; < 6 h	> 140 mg/dL (> 7.8 mmol/L)

Modified from Battelino T et al. Diabetes Care 2019; 42: 1593–1603

2. $HbA_{1c} \leq 8.0\%$ (≤ 64 mmol/mol):
   — n patients at an advanced age with long-standing diabetes and major macroangiopathic complications (previous myocardial infarction and/or stroke) and/or multiple comorbidities;
3. HbA_{1c} level < 6.5% (48 mmol/mol) in women with pre-pregnancy diabetes contemplating pregnancy, < 6.0 % (42 mmol/mol) in the second and third trimester, if it is not associated with an increased rate of hypoglycemia.

If a diabetic patient aged > 65 years is expected to survive for more than 10 years, gradual attainment of general therapeutic targets should be aimed for, with target HbA_{1c} level $\leq 7\%$.

In patients using continuous glucose monitoring (CGM) or intermittently scanned continuous glucose monitoring (isCGM)/flash glucose monitoring (FGM), the time in range (TIR) should be one of major parameters of diabetes control. Detailed recommendation regarding TIR in relation to diabetes type are shown in Table 4.2.

III. Criteria of adequate lipid profile control:

— LDL-C level < 55 mg/dL (1.4 mmol/L) and reduction by at least 50% in diabetic subjects at very high cardiovascular risk;

— LDL-C level < 70 mg/dL (1.8 mmol/L) and reduction by at least 50% in diabetic subjects at high cardiovascular risk;

— LDL-C level < 100 mg/dL (2.6 mmol/L) in diabetic subjects at moderate cardiovascular risk (young patients < 35 years of age with type 1 diabetes but without chronic complications and other cardiovascular risk factors) or patients with type 2 diabetes < 50 years of age, with duration of diabetes < 10 years, without other risk factors);

— Non-HDL cholesterol level < 85 mg/dL (2.2 mmol/L) in diabetic subjects at very high cardiovascular risk;

— Non-HDL cholesterol level < 100 mg/dL (2.6 mmol/L) in diabetic subjects at high cardiovascular risk;

— HDL cholesterol > 40 mg/dL (> 1.0 mmol/L) [in women, higher by 10 mg/dL (0.275 mmol/L)];

— Triglyceride level < 150 mg/dL (< 1.7 mmol/L);

IV. Criteria of adequate blood pressure control:

— Systolic blood pressure < 130 mm Hg;

— Diastolic blood pressure < 80 mm Hg.

It is recommended that in patients aged < 65 years, systolic blood pressure should be maintained in the range of 120–129 mm Hg.

It is recommended that in patients aged ≥ 65 years, systolic blood pressure should be maintained in the range of 130–140 mm Hg.

Details — see Chapter 13.

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5. Organization of care for patients with diabetes

Most important recommendations

- Contemporary comprehensive diabetes care requires an input of adequately competent physicians, nurses engaged in diabetic education or diabetes educators, and dietitians. Care should be patient-centered, taking into account individual patient situation, needs, and preferences. Due to multidisciplinary nature of late diabetic complications and concomitant conditions, cooperation with other specialists is also necessary. [**B**]

I. Outpatient care

Modern diabetes treatment requires competencies regarding treatment, monitoring, and patient education to convey appropriate knowledge and motivation to comply with treatment recommendations. Cooperation between primary care physicians and specialists is also required.

II. Goals of primary care

Health promotion, identification of risk factors, prevention of carbohydrate disorders, education about pre-diabetes and type 2 diabetes.

1. Diagnosing carbohydrate metabolism disorders.
2. Referring patients to a diabetes clinic for chronic treatment in case of:

Table 5.1. Recommendations regarding monitoring in adult diabetic patients

Parameter	Comments
Nutritional and therapeutic education	At each visit
HbA_{1c} level	Once a year, more frequently if doubts regarding maintenance of normoglycemia or need to verify treatment effectiveness following its modifications
Serum total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides	Once a year, more frequently if dyslipidemia
Albuminuria	Once a year in patients not receiving an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker (beginning at 5 years after the diagnosis in diabetes type 1)
Urinalysis (with urine sediment)	Once a year
Serum creatinine + calculation of eGFR	Once a year (beginning at 5 years after the diagnosis in diabetes type 1)
Serum creatinine, Na^+, K^+, Ca^{2+}, PO_4^{3-}	Every six months in patients with elevated serum creatinine
Fundoscopy (with mydriasis)	At 5 years after the diagnosis in diabetes type 1, at the time of the diagnosis in diabetes type 2 (details see Chapter 20)

eGFR — estimated glomerular filtration rate; HbA_{1c} — hemoglobin A_{1c}; HDL — high-density lipoprotein; LDL — low-density lipoprotein

- Type 1 diabetes;
- Other specific types of diabetes;
- Difficulties in determining the type of diabetes;
- Any type of diabetes in children and adolescents, and in women who are pregnant or planning to become pregnant.

3. Treatment of pre-diabetes.
4. Treatment of type 2 diabetes, including simple insulin therapy.
5. Referring patients for diabetologist consultations (less frequently for chronic treatment) in case of:
   - Failure to achieve therapeutic goals; patients should be referred primarily to intensify insulin therapy;
   - Comorbidities that interfere with treatment;
   - Complications of diabetes;
   - Complications of pharmacotherapy;
   - Other special situations.

III. Goals of specialist care (Table 5.1)

- Evaluation of treatment effects and setting therapeutic targets during annual check-ups in diabetic patients managed in the primary care setting;
- Managing diabetic patients treated with injected agents [insulin, glucagon-like peptide 1 (GLP-1) receptor agonists];
- Managing diabetic patients treated with continuous subcutaneous insulin infusion (CSII);
- Performing the differential diagnosis of diabetes types, including monogenic diabetes and diabetes combined with other diseases;
- Diagnosing, preventing and treating long-term complications;
- Diabetes education;
- Investigating and managing diabetes in pregnant women;
- Investigating and managing concomitant conditions;
- Performing annual check-ups according to the current Diabetes Poland guidelines.

IV. Goals of specialist inpatient care

- Cases of newly detected diabetes type 1 and diabetes type 2 with symptomatic hyperglycemia, when appropriate treatment cannot be provided on an outpatient basis;
- Acute diabetic complications (hypo- and hyperglycemia, diabetic ketosis and coma);
- Exacerbation of chronic complications;
- Modifications of the treatment regimen in patients in whom therapeutic targets cannot be met during outpatient therapy;
- Initiation of intensive insulin therapy using a personal insulin pump and/or continuous glucose monitoring system (CGM), when appropriate treatment cannot be provided on an outpatient basis;
- Initiation of insulin therapy in gestational diabetes and preexisting diabetes previously not treated with insulin, when appropriate treatment cannot be provided on an outpatient basis;
- Difficulties with obtaining normoglycemia in pregnant patients with preexisting diabetes, when appropriate treatment cannot be provided on an outpatient basis.

V. Organizational requirements

Specialist diabetes hospital units

1. Physician personnel

— two full-time diabetologists, alternatively, in addition to one diabetologist, an internist with a mi-

nimum one-year experience in a diabetes ward or clinic, or a 2nd year fellow in diabetology.

2. **Nursing staff**:
   — a nurse specialized in diabetes care or internal medicine or who completed a "Diabetes Educator" course or a qualification course for diabetes nurses or with a minimum 2-year experience in a diabetes ward/clinic;
   — one nurse per 10 diabetic beds with duties limited to education and care for diabetic patients.
3. **Dietician** — a full-time dietician, with duties limited to diabetes care.
4. **Access to psychologist consultations.**
5. **Access to specialist consultations**.
6. **Equipment**:
   — At least two beds for patients with acute metabolic conditions equipped with an ECG monitor, a blood pressure monitor, a pulse oximeter, an infusion pump, and access to oxygen therapy;
   — Education room;
   — Intravenous infusion pumps;
   — Equipment for the diagnosis and treatment of diabetic foot syndrome;
   — Access to cardiac [exercise testing, electrocardiography (ECG), echocardiography, ECG Holter monitoring, ambulatory blood pressure monitoring] and vascular (Doppler ultrasonography) investigations.

Specialist diabetes clinics

1. **The team providing Outpatient Specialist Care to diabetic patients includes:**
   — A diabetologist or an internist with a minimum two-year experience in a diabetes ward or clinic, or a 2nd year fellow in diabetology;
   — In pediatric diabetology clinic — a diabetologist, or pediatric endocrinologist and diabetologist, or a pediatrician with a minimum two-year experience in a pediatric diabetes ward or clinic, or a 2nd year fellow in diabetology or pediatric endocrinology and diabetology;
   — A nurse specialized in diabetes care or who completed a "Diabetes Educator" course, or a nurse specialized in internal medicine or who completed a qualification course for diabetes nurses or with a minimum 2-year experience in a hospital diabetes ward or a specialist diabetes clinic.
   — A full-time dietician with duties limited to diabetes education.
   — Access to psychological care as warranted in individual clinical cases.

Children and adolescents, pregnant women — see relevant chapters.

2. **Equipment in specialist diabetes clinics:**
   — Doctors' offices;
   — A treatment room with a separate part for sampling and performing tests;
   — A nurse's office also intended for patient education, with a dietary education section;
   — Computer equipment that allows retrieval and analysis of data from insulin pumps and continuous glucose monitoring systems;
   — Instruments to screen for diabetic foot syndrome (thermos-tip, 128 Hz tuning fork, 10 g monofilaments, reflex hammer);
   — A Doppler ultrasound device for the assessment of vascular flow.

In addition, access to specialist consultations should be provided to periodically assess the diabetes complication status.

VI. Organization of care for patients with diabetic foot syndrome

Referral diabetes foot outpatients clinics

1. Personnel requirements:
   — Physicians: equivalent of at least 2 full-time positions — diabetes specialist with at least one year of documented experience in the management of patients with diabetic foot syndrome;
   — Nurses: equivalent of at least 2 full-time positions — at least one year of documented experience in the management and care of patients with diabetic foot syndrome or chronic wounds.
2. An established organizational pathway allowing patient hospitalizations in a unit within the same facility (medical center) that has a contract for diabetology or internal medicine services signed with the Polish National Health Fund (NFZ, *Narodowy Fundusz Zdrowia*).
3. Access to multidisciplinary care, including surgeon, vascular surgeon, or angiology specialist consultations.
4. Ability to provide intravenous antibiotic therapy.
5. Access to basic imaging modalities, i.e., X-ray, ultrasound (including Doppler studies) and CT and/or MRI.
6. Access to laboratory and microbiologic testing performed in a medical diagnostic laboratory listed in the register of the National Chamber of Laboratory Diagnosticians (KRDL, *Krajowa Rada Diagnostów Laboratoryjnych*).

Basic care outpatient clinics

1. The responsibility of these clinics should include the diagnosis and management of diabetes foot syndrome along with prevention of ulcerations, infections, and Charcot neuro-osteoarthropathy complicating the diabetes foot syndrome. These clinics should cooperate with referral clinics where more severe cases are consulted and offered further treatment.

VII. Telemedicine visits as part of diabetes care

Each diabetes clinic should be able to provide effective telemedicine visits. For this purpose, diabetes clinics should be equipped with appropriate equipement (computers with dedicated software), and the personnel should have appropriate knowledge and skills. Individuals with diabetes should be encouraged to use technologies and apps facilitating telemedicine visits. It should be noted that telemedicine visits are more effective if more patient treatment data (e.g., data from glucose meter memory, CGM system, or personal insulin pump) are available to the physician performing the telemedicine visit.

Telemedicine visits in individuals with diabetes may be either a part of regular diabetes care or may be used in the epidemic settings.

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6. Behavioral therapy (lifestyle changes)

Most important recommendations

- All individuals with diabetes should be offered education regarding the general principles of proper diabetes nutrition by appropriately trained personnel (physician, dietician, diabetes nurse, diabetes educator) and using various methods and techniques, including telemedicine. Detailed nutritional recommendations should be tailored to the needs and capabilities of the patient. [**A**]
- The major macronutrient determining periprandial insulin requirement are carbohydrates. Instruction how to estimate carbohydrate content of a meal to optimize insulin dosing should be a key component of dietary education in individuals with diabetes type 1. Individuals with type 2 diabetes should be educated how to control portion sizes and about the proportion of carbohydrates in individual meals and in the whole diet. [**A**]
- There is no single universal diet that would be appropriate for all diabetic individuals. The optimal proportions of macronutrients for a given patient should be determined individually, taking into account patient's age, physical activity, presence of diabetes complications, concomitant conditions, and patient preferences. [**E**]
- Due to its pleotropic benefits, physical exercise is an integral part of proper comprehensive diabetes management. For optimal effects, exercise should be regular, undertaken at least every 2–3 days but preferably daily. [**A**]
- Diabetic individuals should limit time spent sitting without breaks. [**B**]

Behavioral therapy is an indispensable treatment component in all individuals diagnosed with diabetes (both type 1 and type 2), regardless of age. Proper nutrition and physical activity are important in improving the overall health status and in the prevention and treatment of chronic complications of diabetes. All diabetic individuals should be educated on the general principles of proper nutrition in diabetes by authorized persons (physician, dietician, diabetes nurse, diabetes educator) by using different methods and techniques, including interactive methods and telemedicine. The management of diabetic individuals should include therapeutic lifestyle changes encompassing balanced diet, regular physical activity, avoidance of tobacco smoking and alcohol use, optimal sleep duration, and avoidance of stress. Education for therapeutic lifestyle, adapted to the needs and possibilities of a diabetic individual, allows to achieve the intended therapeutic target and reduces the costs related to the treatment of diabetic complications.

It should be highlighted that one priority of behavioral therapy of diabetes, regardless of its type, should be to mamaintain normal body weight in a diabetic individual.

Dietary recommendations

I. General recommendations

The goals of dietary treatment in diabetic patients are to obtain and to maintain:

— Normal (near normal) blood glucose level to prevent diabetic complications;

— Optimal serum lipid and lipoprotein levels;

— Optimal blood pressure values to reduce the risk of vascular disease; and
— Desired body weight.
— Dietary treatment includes advice on:
— Individually determined energy value of the diet;
— Calorie distribution over individual meals during the day;
— Food sources that will provide necessary calories, vitamins, minerals, and phytochemicals.
— Products that should be limited.

When planning diet, individual nutritional and cultural preferences, patient's age, gender, the level of physical activity, and the economic status should be taken into account. It is important that dietary education provide patients with practical information that facilitates direct application of the acquired knowledge in the everyday life. Eating meals is an important element of the patients' quality of life. Information on the diet provided to the patient should be as positive as possible, indicating that the diabetic diet provides the opportunity to prepare meals according to individual preferences. Negative information provided to patients should be limited and relate only to situations where the need to limit/eliminate some nutrients has been well proven in clinical trials.

The nutritional strategy in diabetic patients should include:

— Evaluation of usual dietary intake;
— Nutritional diagnosis;
— Determination of the goal and plan of the dietary intervention;
— Nutritional intervention (individual or group counseling);
— Monitoring of nutrition and evaluation of its effects;
— Correction of the dietary plan if the therapeutic goal has not been reached.

Diabetic individuals should be encouraged to adhere to the recommendations on healthy nutrition addressed to healthy subjects, and additionally to:

— Control the size of usually consumed portions;
— Monitor carbohydrate intake overall and in individual meals;
— Limit intake of foods containing easily absorbable carbohydrates, including added sugar and free sugars;
— Consume regular meals, including a breakfast.

There is no single universal diet that would be appropriate for all diabetic individuals. Various dietary strategies can be used to treat diabetes, e.g. DASH diet, Mediterranean diet, and plant-based diets.

Individuals with diabetes type 1 should avoid consuming easily absorbable carbohydrates and adhere to an appropriately balanced diet. In all cases, the dietary plan and insulin regimen should be individually tailored. Insulin therapy should be adjusted to the patient's dietary habits, meal composition (carbohydrate, protein, and fat content), lifestyle, and physical activity. When planning diet, a priority should be given to estimation of absorbable carbohydrate content of the meal, e.g. using the carbohydrate exchange system. Glycemic index and glycemic load values may also be useful when making dietary choices.

In diabetic patients in the oldest age groups, dietary education should be particularly careful and individualized to provide appropriate protein intake, and at the same time it should be simple and easily understood by the patients.

Although carbohydrates are the major macronutrient determining periprandial insulin requirement, individuals with diabetes type 1 should also be educated regarding the glycemic effect of protein and fat. Effective tools to facilitate evaluation of the quantity, quality, and proportion of macronutrients on blood glucose levels are continuous and flash glucose monitoring systems.

Periprandial control of blood glucose levels may be also facilitated by dedicated mobile phone apps; when choosing between them, one should primarily consult the guidance and recommendations by major diabetes societies.

In diabetes type 2, the major goals are not only to maintain good metabolic control of the disease but also reduce excess body weight and maintain the desired body weight. Thus, in addition to the above recommendations, a factor of major importance is the total calorie content of the diet which should be adjusted to the patient's age, actual body weight, and the level of physical activity. The energy deficit should be set individually to allow gradual but systematic body weight reduction (by about 0.5–1 kg/ /week). Body weight reduction by at least 5% compared to the baseline result in a measurable improvement in blood glucose control but the optimum weight reduction should be at least 7%. A daily caloric deficit of 500–750 kcal is considered safe.

Body weight reduction may be achieved by using a low-calorie diet with various proportions of macronutrients (protein, fat, carbohydrates). However, chronic use of very low carbohydrate diets and fasting is not recommended. All individuals with diabetes and overweight/ obesity are advised to control portion sizes.

II. Specific recommendations

Diet composition

1. Carbohydrates:

— No sufficient scientific evidence is available to determine single optimal carbohydrate content in the diet of diabetic individuals;

— Carbohydrates should provide about 45% of the total calorie intake; and if they are consumed in the form of low glycemic index and high fiber content products, their share in the total calorie intake may be even higher (up to 60%). High caloric intake from carbohydrates should also be a feature of the diet in subjects who are very active physically. In contrast, a lower carbohydrate share in the total calorie intake (25–45%) may be temporarily recommended in patients with little physical activity if it cannot be significantly increased, e.g., due to concomitant conditions;
— The main source of carbohydrates should be whole grain cereal products, especially with low glycemic index (< 55 IG);
— The major limitation should apply to the intake of simple carbohydrates (mono- and disaccharides) which should be reduced to the minimum. It also recommended to reduce intake of added sugars (during food production and meal preparation) and free sugars, the major sources of which are primarily sugar and sweets, but also honey and fruit juices and drinks;
— Artificial sweeteners may be used in doses recommended by the manufacturers;
— Daily fructose intake should not exceed 50 g. Fructose use as a replacement for sugar is not recommended;
— Minimum daily dietary fiber intake should be 25 g or 15 g/1000 kcal. Dietary fiber intake should be increased by consuming at least 2 portions of whole-grain cereal products and 3 portions of high-fiber vegetables. If the recommended dietary fiber intake cannot be reached, addition of fiber supplements, particularly containing soluble fibers, should be considered. It is reasonable to increase dietary intake of resistant starch.

2. Fats:
— Dietary fat intake should be the same as in healthy subjects, providing 25–40% of the total calorie intake;
— The quality of dietary fat is more important than total amount of fat consumed. Fat composition is particularly important with high dietary fat intake;
— Saturated fats should provide less than 10% of the total calorie intake;
— Monounsaturated fats should provide up to 20% of the total calorie intake;
— Polyunsaturated should provide about 6–10% of the total calorie intake;
— Cholesterol intake should be limited to ≤ 300 mg/day, and < 200 mg/day in patients with dyslipidemia;
— To reduce serum LDL cholesterol level, low glycemic index carbohydrates and/or monounsaturated fats should be substituted for saturated fats;
— In patients with hypercholesterolemia, introduction of foods providing 2–3 g of plant sterols/stanols per day may be beneficial.
— Intake of trans fatty acids should be limited to the minimum.
— Vegetable fats are recommended, with the exception of palm oil and coconut oil.

3. Proteins:
— Dietary protein intake should be individualized. There is no evidence of adverse effects of high-protein diets in diabetic individuals. In most diabetic individuals, similarly to the general population, proteins should provide 15–20% of the total calorie intake (about 1–1.5 g/kg body weight/day). In patients with diabetes type 2 and excessive body weight, a low-calorie diet containing 20–30% of protein provides greater satiety and helps reduce and maintain a healthy body weight. In patients with chronic kidney disease, protein intake should be about 0.8–1 g/kg body weight/day;
— There is no need to limit animal protein intake, although substituting plant protein (e.g., soy protein) for animal protein may be beneficial in some patients.

4. Vitamins and microelements:
— Vitamin or microelement supplementation is not recommended unless their deficiencies have been identified;
— The exceptions are vitamin D3 (supplementation according to the recommendations for the general population), folic acid (supplementation at the dose of 400 μg in pregnant women), and vitamin B12 in patients on long-term metformin therapy with confirmed vitamin B12 deficiency;
— Multivitamin supplementation may be necessary for the elderly, vegetarians, vegans and people on very low calorie diets.

5. Alcohol:
— Alcohol intake is not recommended in diabetic patients;
— Patients should be informed that alcohol inhibits hepatic glucose release and thus its intake (particularly without food) may predispose to hypoglycemia;
— Acceptable levels of alcohol intake are ≤ 20 g/day of ethanol in women and ≤ 30 g/day in men.

Alcohol should not be consumed by individuals with dyslipidemia (hypertriglyceridemia), neuropathy, or a history or pancreatitis.

6. Salt:
— Salt intake from all sources should not exceed 5 g per day (2300 mg sodium/day);
— If reasonable, patients with hypertension may be advised to introduce more strict salt intake limita-

tions according to the DASH diet principles; however, the data on the reduction of sodium intake below 1.500 mg/day in diabetic patients are not clear.

Dietary recommendations for special patient populations (e.g., pregnant women, children and adolescents, patients with established nephropathy etc.) are provided in the relevant chapters. Detailed recommendations on the dietary treatment of diabetes are provided in the Polish Society of Dietetics guidelines (*www.ptd.prg.pl*).

Physical exercise

Due to its pleotropic benefits, physical exercise is an integral part of comprehensive diabetes management. Physical exercise has a beneficial effect on insulin sensitivity, blood glucose control, and lipid profile, promotes body weight reduction, and exerts a beneficial effect on mood, even with subjects with depression.

I. General recommendations regarding physical exercise:

— Initially, moderate physical activity should be recommended, depending on the patient's ability to exercise;
— For optimal effects, exercise should be regular, undertaken at least every 2–3 days, preferably daily;
— Intensive physical activity should be preceded by a 5- to 10-minute warm-up and concluded with cool-down exercises;
— Physical exercise may increase the risk of acute or delayed hypoglycemia;
— Alcohol may increase the risk of hypoglycemia after exercise;
— Dehydration should be prevented when exercising in high ambient temperatures;
— The risk of foot damage during exercise (particularly with coexisting peripheral neuropathy and reduced pain perception) and the need for appropriate foot care and comfortable shoes should be taken into account.

II. Exercise intensity is determined by the physician based on the full clinical picture

Nordic walking is an appropriate form of exercise in overweight/obese subjects at any age.

The most appropriate form of exercise in individuals with diabetes type 2 aged > 65 years and/or overweight is brisk walking (until panting) 3–5 times a week (approx. 150 minutes/week).

Those without significant contraindications, especially in the younger age groups, should be encouraged to engage in high physical activity, including sports. Such individuals require additional education regarding the glycemic effect induced by different types of physical activity (e.g. aerobic exercise, resistance and interval training).

Control of blood glucose levels in the peri-exercise period may be greatly facilitated by continuous and flash glucose monitoring systems, used both in the real time and for retrospective evaluation of the effect of exercise and undertaken therapeutic inteventions on blood glucose levels.

Control of blood glucose levels in the peri-exercise period may be also facilitated by dedicated mobile phone apps; when choosing between them, similarly to the apps used for optimization of periprandial blood glucose control, one should primarily consult the guidance and recommendations by major diabetes societies.

A simple and effective recommendation is that adults, especially those with type 2 diabetes, limit the time spent sitting without breaks. Glycemic benefits can be gained by avoiding sitting continuously for more than 30 minutes.

III. Risks of physical exercise in diabetic patients

Without adequate preventive measures, exercise may result in hypo- or, more rarely, hyperglycemia and metabolic decompensation. The approach to prevent extreme blood glucose level excursions in the peri-exercise period is discussed in Chapter 7.

In some circumstances, strenuous exercise may have a negative effect on the general health status of the patient:

— Diabetic proliferative retinopathy — risk of vitreous body bleeding and retinal detachment;
— Diabetic nephropathy — increase in albuminuria/ /proteinuria;
— Autonomic neuropathy — risk of orthostatic hypotension;
— Risk of myocardial ischemia.

IV. Physical exercise in the era of COVID-19 pandemic

It shoud be noted that diabetic individuals should maintain the recommended level of physical activity regardless of the epidemiological situation. If limitations regarding travelling or use of sports facilities are imposed due to the epidemiological situation, previous forms of physical activity may need to be replaced with alternative activities that may be persued despite the imposed limitations, such as home-based activities. As it may be associated with a different nature of exercise and its glycemic effect, and thus different precautionary measures may be required, these issues should always be consulted with the managing physician.

Tobacco control

In all current or former smokers, determine:

— Age at which the patient began smoking;
— Duration of smoking;

— Number of cigarettes smoked;
— Any attempts to quit smoking and duration of abstinence;
— Duration of current abstinence.

Counselling:
— Explanation of the risks associated with smoking and use of e-cigarettes to non-smoking diabetic individuals;
— Advice to quit smoking and/or discontinue use of e-cigarettes;
— Patient support in the decision to quit smoking;
— Psychological and pharmacological support if needed;
— Discussion regarding smoking during each visit;
— If the patient refuses to quit smoking, this should be documented in the medical records.

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7. Engaging in physical activity and participating in sports by diabetic individuals

Most important recommendations

- Individuals with diabetes type 1 without clinically significant chronic complications of diabetes may engage in any type of physical activity, including maximal exercise. [**E**]
- Aerobic exercise until panting is safe and may be recommended in all diabetic individuals without contraindications. [**B**]
- Individuals with diabetes type 2 are recommended to combine aerobic exercise with elements of resistance training. [**B**]
- Severe hypoglycemia is a contraindication for exercise for 24 hours. [**E**]
- Late hypoglycemias may occur for up to 24 hours after the exercise. [**C**]
- Proliferative retinopathy is contraindication for exercise until stabilization of retinal changes. [**E**]
- Hyperglycemia > 250 mg/dL without ketonemia and/or ketonuria is not a contraindication for exercise, provided that the patient is generally well and knows the reason for hyperglycemia. [**E**]
- Participation in competitive sports differs much from the amateur sport and requires individual solutions. [**E**]

I. Recommended duration and intensity of exercise

Engaging in physical activity by a diabetic individual requires a pre-assessment by a diabetologist, including the degree of planned physical activity (type, duration, and intensity of exercise), possible contraindications, patient expectations, patient knowledge and skills regarding the prevention of hypoglycemia, and the current degree of fitness. In individuals with diabetes typ 2 aged > 65 years and/or overweight, and in patients with a history of a cardiovascular event or with established cardiovascular disease, it is recommended to monitor the heart rate and and to evaluate the intensity of physical exercise using the Borg rating of perceived exertion scale. The target ranges for heart rate and the intensity of physical exercise may be determined during the electrocardiographic stress testing. In this patient group, aerobic exercise (until panting) is safe and should be recommended for at least 150 minutes per week. In obese subjects, 200-300 minutes of exercise per week are recommended, leading to an energy deficit of 500-750 kcal/day. Daily intensive physical activity including participation in sports is recommended in younger diabetic individuals in whom no significant contraindications are present.

II. Contraindications to physical activity

Contraindications to recreational participation in sports are specified in Chapter 6. Decisions made by diabetologists may need to be informed based on consultations of other specialists, such as ophthalmologists, cardiologists, nephrologists, and neurologists.

Contraindications to participations in competetitive sports, including training and competitions, are defined in Appendix 7.

III. Self-monitoring of blood glucose during exercise

Self-monitoring of blood glucose is indicated in individuals in whom the treatment used is associated with a risk of hypoglycemia. Blood glucose level should be measured using a glucose meter within 15 minutes before initiation of exercise and every 60 minutes or less frequenly if CGM or isCGM/FGM is used. Optimal use of CGM requires individual programming of higher thresholds of hypoglycemia alerts and consideration of blood glucose trends. Informing persons accompanying the patient during the exercise about the diagnosis of diabetes in the patient is a major factor facilitating self-monitoring of blood glucose.

IV. Hypoglycemia and hyperglycemia related to exercise

Changes in blood glucose levels during exercise are shown in Figure 7.1.

Severe hypoglycemia is a contraindication for exercise for 24 hours.

In case of a hypoglycemia alert (≤ 70 mg/dL) one should consume simple carbohydrates, optimally as a fluid, and exercise may be continued once the symptoms of hypoglycemia subside.

In case of severe hypoglycemia in an individual with diabetes type 1 the effect of glucagon following strenuous exercise may be weaker but it should always be attempted to administer the drug.

Type of exercise	**Aerobic** Examples: walking, nordic walking, slow cycling, jogging	**Mixed (aerobic-anaerobic)** Examples: team games, more rapid running, swimming, interval cycling	**Anaerobic** Examples: sprint, strength training with maximum load
Intensity			
Heart rate range	< 55 (60)% HR_{max}	60–75 (80)% HR_{max}	> 75 (80)% HR_{max}
Borg rating of perceived exertion scale	7–11	12–15	16–20
Expected change in glucose level	Decrease 	Decrease and/or increase 	Increase 
Risk of hypoglycemia	High	Increased	Low

Figure 7.1. Types of physical exercise and its effect on blood glucose levels

Late hypoglycemias may occur for up to 24 hours after the exercise and their risk is higher in untrained subjects and those irregularly engaging in physical activity. This group of individuals should pay particular attention to the prevention of nocturnal hypoglycemia.

Anaerobic exercise may result in hyperglycemia which should be cautiously corrected with rapid-acting insulin due to a risk of hypoglycemia several hours after the exercise.

If hyperglycemia is present with blood glucose level > 250 mg/dL, accompanied by ketonuria and/or ketonemia ≥ 1.5 mmol/L, exercise is contraindicated.

If hyperglycemia > 250 mg/dL is not accompanied by ketonuria and/or ketonemia and/or the cause of hyperglycemia is known, mild to moderate exercise may be performed.

V. Approach to exercise in individuals with diabetes type 2 who do not require insulin

The risk of hypoglycemia in diabetic individuals who are not treated with insulin or sulphonylureas is very low. Blood glucose levels < 100 mg/dl do not require consuming additional carbohydrate portions. Self-monitoring of blood glucose in relation to exercise needs to performed only occasionally.

Systematic physical activity improves insulin sensitivity and thus inreases the chance of delaying insulin therapy. An important addition to aerobic training are resistance exercises. It is recommened to engage large muscle groups with 8–12 repetitions 2–3 times a week.

VI. Approach to exercise in individuals treated with insulin

Exercise within 2 hours from administration of a rapid-acting insulin analog requires a reduction in insulin dose if physical activity lasts at least 30 minutes.

Bolus may be reduced by 25-75% depending on the duration and intensity of exercise.

Physical activity requires additional carbohydrate consumption:

- 1.0–1.5 g/kg of body weight/hour of intensive exercise at the time of a peak effect of an insulin bolus that was not reduced;
- 0.2–0.5 g/kg of body weight/hour of intensive exercise at the time of a peak effect of an insulin bolus that was reduced or was administered more than 2 hours before initiation of physical activity.

Disconnection of insulin pump during exercise is recommended for up to 3 hours. The prerequisite for disconnecting insulin pump is active insulin, the amount of which should be monitored using a bolus calculator.

Reduction of basal insulin is particularly needed during long endurance exercise. The adjustment must be based not only on the type of exercise but also the type of basal insulin administered using an insulin pen (i.e., insulin NPH/long-acting analog/ultra-long-acting analog).

During treatment with an insulin pump, it is recommended to reduce basal insulin rate by 20–80%, depending on the intensity and duration of exercise, preferably 2 hours before exercise.

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8. Psychological management in diabetes

Most important recommendations

- The mental condition of the diabetic individual should be evaluated at the initiation of diabetes treatment and during each subsequent visit. [**B**]
- Depression often coexists with diabetes and significantly increases the risk of diabetes complications. [**A**]
- Diabetic individuals should be evaluated for anxiety symptoms, addictions, eating disorders, and cognitive dysfunction. These conditions may significantly impair their adaptation to the disease. [**B**]
- Psychological and social care should be integrated with the approach focused on cooperation with the diabetic individual and available for all diabetic individuals to allow optimization of treatment outcomes and the quality of life. [**A**]

The mental state of the patient affects nearly all aspects of the management. Non-compliance to treatment is commonly associated with psychological problems which require identification and appropriate psychotherapeutic interventions. For this reason, education limited to providing the patient with information regarding prescribed therapy and other therapeutic recommendations is not very effective. The mental state of the diabetic individual should be evaluated at the treatment initiation and during every visit. Use of appropriate questionnaires and tests is recommended.

I. Psychological support should include:

— Adequate communication with the patient;
— Continuous evaluation (monitoring) of the mental state and compliance to treatment, along with psychological interventions.

II. The goals of individualized approach to the patient include:

— Consideration of the patient's psychosocial status and planning treatment which in the patient's opinion may be realistically undertaken in his or her current life situation (which is of major importance for setting the therapeutic plan that will be both optimal and realistic);
— Developing motivation to engage in optimal management;
— Avoidance of frightening the patient with adverse consequences of non-compliance to therapeutic recommendations which is ineffective and harmful in most cases;
— Implementation of effective education based on the psychological diagnosis.

III. Evaluation of the psychological/mental state (psychological diagnosis) in diabetic individuals includes the following aspects:

1. Social and psychological situation.
2. Quality of life of the diabetic individual.
3. Attitudes, beliefs, concerns, and duties related to diabetes (unjustified worries and concerns may reduce the ability to cope with the disease). Ask the following question:

— To what degree do you worry about the future and the possibility that severe complications will develop: (0) It is not an issue at all; (1) It is a minor issue; (2) It is a moderately important issue; (3) It is quite an important issue; (4) It is a very important issue. A score of 3 or more indicates a high risk of developing psychosocial problems.

4. Sense of control over the disease. Lacking sense of control over the disease results in choosing approaches to cope with the disease-related stress that are characterized by avoidance of thoughts about the disease and/or reducing emotions provoked by the disease.
5. Evaluation of the ability to cope with the disease (a trend to reduce search for the optimal coping strategy and focus on solving disease-related problems is seen).
6. Evaluation of depressive symptoms (depression often coexists and increases the risk of diabetic complications).

A. Use tools available freely online to screen for depression: the Well-being index WHO-5, www.who-5.org (score < 13 indicates the need to investigate for depression, and score ≤ 7 indicates a high risk of depression) or the Patient Health Questionnai-

re PHQ-9, *www.phqscreeeners.com/overview/aspx* (score < 5 is normal, 5–9 indicates mild depression, 10–14 indicates moderate depression, 15–19 indicates moderately severe depression, and 20–27 indicates severe depression). In the Polish translation, score > 12 indicates a high risk of depression episode (sensitivity 82%, specificity 89%);

OR

B. Ask two questions:

— Did you often feel depressed or hopeless during the last month?

— Did you often lack an interest in undertaking various activities or a feeling of pleasure during these activities?

A positive answer to one of these questions has a **sensitivity of 97%** and a **specificity of 67%** for the diagnosis of depression. In these circumstances, the patient should be referred to a psychiatrist.

Evaluation of anxiety symptoms, addictions, eating disorders, reduced cognition (these may significantly impair adaptation to diabetes).

IV. Psychological interventions in diabetic patients include:

— Developing the sense of control over the disease by:

- Providing the patient with comprehensible information regarding the disease and its treatment;
- Collaborative development of therapeutic goals and plans which are realistic from the patient's perspective;
- Gradual achievement of therapeutic goals (small steps strategy);
- Offering help in case of treatment failures (so the patient knows that the physician will help him determine the cause of failure without any negative attitude);

— Developing and maintaining diabetes coping skills focused on solving disease-related problems.

V. Clinically severe depression (depressive episode, dysthymia) and other mental health problems require psychiatric consultation. In case of maladaptation to the disease, psychotherapeutic intervention may be undertaken by a primary care physician or a specialist. Help of a clinical psychologist is necessary in more complex cases.

VI. Teamwork

Cooperation of the whole therapeutic team is an important prerequisite of treatment success. Effective communication between team members is required. In diabetes clinics, a psychologist is a necessary member of the specialist therapeutic team.

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9. Therapeutic education

Developed in cooperation with Alicja Szewczyk, MA, National Consultant in Diabetes Nursing

Most important recommendations

- Education is the mainstay of effective diabetes care and prevention. [**A**]
- All diabetic individuals and their caregivers should participate in diabetes education to acquire knowledge and skills regarding diabetes self-management and support initiation and maintenance of constant self-control. [**B**]
- The main goals of diabetes education are effective self-care, improved metabolic control and quality of life, and support for the diabetic individual/his or her caregivers. The effectiveness of education and its programs undergo systematic monitoring, evaluation and methodical improvement. [**B**]
- Diabetes education should be focused on the diabetic individual and his or her individual needs. [**B**]
- A coordinated and unified position of the multidisciplinary diabetes team has a beneficial effect on the metabolic control and the psychological aspect of care. [**B**]
- All diabetic individuals and their caregivers should be provided access to institutionalized education. [**B**]

I. General recommendations

1. Education is targeted at subjects at an increased risk of diabetes, subjects with prediabetes, and those treated for diabetes, along with their caregivers and family members. Education is a constant, integral, and necessary component of diabetes management during each visit. In addition, it should be undertaken in a structured way, including education at the time of treatment initiation, followed be reinforcements based on regular evaluation of the patient's educational needs or if requested by the diabetic individual, taking into account the progress in diabetology and organizational and social improvements.
2. The educational program should be developed in cooperation between the diabetic individual and the therapeutic team (physician — in charge of the team, nurse, diabetes educator, dietitian, psychologist) and be closely associated and coordinated with the recommended treatment approach. By performing self-care, the patient is an active member of the therapeutic team.
3. The goal of patient education is to support self-management and lifestyle modifications based on the recommended diet and physical activity. Education on obesity and weight control is a particularly important issue in diabetes type 2. The primary goal is the patient's ability to avoid acute complications of diabetes: hypoglycemia and hyperglycemia.
4. The effectiveness of self-management programs has been documented. They actively engage participants in the learning process, adjusting the content and form to the individual situation and personal experiences of the participants, and motivate them to set personal behavioral treatment targets, developed in cooperation with the physician.
5. Nursing, dietician, and psychologic care with definitions of the basic norms, guidance, and organizational and technical settings for the provition of diabetic therapeutic education (e.g., for a nurse/midwife working as a diabetes educator) is provided by the employer.

II. Specific recommendations

1. Strategies to integrate diabetes therapy and self-care with everyday healthy lifestyle are recommended. Their goals are to increase patients' empowerment by discovering and using their natural and acquired abilities to take responsibility for their own life.
2. It is recommended to provide individualized education along with realization of group educational programs (groups of 6–10 people). Education should be provided by an appropriately trained personnel (physicians, diabetes educators, nurses, dieticians). Other members of the therapeutic team, representing various medical professions, should also participate in the education. Both educational programs for subjects with newly diagnosed diabetes and reinforcement programs for patients with long-standing diabetes are needed. It is necessary to offer education to patients' family members and caretakers particularly of children and elderly with diabetes and also to their probation officers.
3. In the education, modern pedagogical methods for the youth or the elderly should be used. Use of electronic communication, short message service (SMS) systems, teleeducation techniques, webinars, and individual and group teleconferences is

recommended, using reliable websites and mobile applications. The advantages of the online/mobile methods of therapeutic education in diabetes include easy accessibility, practical aspects, individual interactivity, flexible timing, and the fact that single education items may be accessed/repeated at any time. However, the online methods also have some disadvantages, such as the lack of personal contact with the educator and other people with diabetes. Currently, this method can only be a supplementary tool, and knowledge of a diabetic individual must be ultimately verified by a personal contact. Education must be conducted in a particularly clear way due to the issues discussed, the methods used, and the type of trainees.

4. Education should focus on setting individual diabetes management goals, taking into account problems specific for a given person or a given patient group. The educational program should include developing skills to influence the course of the disease, as the knowledge itself is not sufficient for optimal diabetes management.
5. Diabetes education in children and adolescents should be tailored to their intellectual capabilities, age, and needs.
6. Therapeutic education should be offered to all elderly subjects. Its goals, methods, and skill teaching should be adjusted to the intellectual and physical capabilities of the elderly subjects (who may be independent, functionally dependent on caregivers, or at the end of life). Education should also be targeted at patient's caregivers. The extent of blood glucose monitoring should be set at a minimal level. Basic goals of education in the elderly patients and their families are to reduce the risk of acute diabetic complications including hypoglycemia and severe hyperglycemia, and the risk of non-ketotic diabetic coma in daily geriatric care.

III. A framework educational program should include the following components:

1. Support regarding disease acceptance, increasing appropriate motivation for treatment, and increasing patient empowerment.
2. Setting and evaluating individual therapeutic goals based on the disease course, prognosis, recommended treatment, and personal and social situation of the patient.
3. Basic information about the disease and its treatment (causes, clinical characteristics, course and prognosis, action of antidiabetic drugs, insulin action profiles, adjusting insulin doses)
4. Teaching the techniques of systematic self-monitoring of blood glucose using a glucose meter and/or continuous glucose monitoring (CGM) systems, keeping a self-monitoring diary, including a virtual/ /electronic one, measuring ketone bodies, blood pressure etc., and managing acute situations.
5. Teaching the techniques of subcutaneous administration of insulin and other medications (sites of administration, needle length, factors affecting absorption, prevention of insulin-related complications).
6. For patients treated with a personal insulin pump: advantages and disadvantages of and indications and contraindications to insulin pump therapy, principles of programming and modifying basal infusion rate, temporary changes of the basal infusion rate, use of single, delayed, and combination boluses, use of bolus calculator and active insulin functions, setting an infusion system (how to choose the injection site), what to do in case of an insulin pump failure — return to treatment using insulin pens, management of initial symptoms of ketoacidosis, principles of withholding insulin infusion in special situations (e.g., sport), technical aspects of insulin pump use, self-retrieval and interpretation of pump memory data, calculation of dietary carbohydrate, protein and fat content with adequate prandial insulin dosing, maintaining an electronic self-control diary (computer software, cloud-based, smartphone app).
7. Information about the appropriate use of independent and insulin pump-integrated CGM systems, including their functions, setting alerts for hypo- and hyperglycemia, dynamics of trend changes, and self-retrieval and interpretation of CGM data for the current therapy.
8. Information about the diagnosis and treatment of acute and chronic complications along with their risk factors and approaches to prevent complications and diseases related to diabetes.
9. Information about healthy nutrition and its role in the management (including practical information about macronutrient content in foods, their effect on blood glucose levels, meal energy content and composition; and creating a nutritional plan based on individual habits, needs, and therapeutic strategies, etc.).
10. Information about the effect of physical exercise on the regulation of blood glucose (hypo- and hyperglycemia, etc.), and mobilisation of diabetic individuals to initiate/maintain regular physical activity.
11. Information about managing special situations (travel, pregnancy planning and contraception, pregnancy, illness, risky behaviors).
12. Information about social rights of diabetic patients (work, driving license, benefits, insurance, etc.).

13. Principles of healthcare utilization (visit frequency, follow-up evaluations, transition from pediatric to adult care), optimal compliance to treatment recommendations.
14. Discussion of the importance of psychological problems in the management of diabetes (either unrelated or related to diabetes, e.g., diabetes distress) and opportunities for specialist care (psychologist/therapist/psychiatrist).

IV. Organizational recommendations

1. Duration of the initial education (i.e., at the time of the diagnosis) should be at least 5 hours in diabetic individuals treated with diet or diet and oral antidiabetic agents, at least 9 hours in patients treated with insulin, and at least 15 hours in patients treated with a personal insulin pump and using CGM systems, in either outpatient or inpatient settings dependin on the patient situation and facility resources. Diabetes education should be initiated in each patient as early as possible after the diagnosis is made and continued during further follow-up. During subsequent years, duration of education must depend on the knowledge already absorbed by the patient, number of previous errors, and the type of developing complications and concomitant disorders. It is also recommended to perform periodic (annual) verification of the patient knowledge, either by personal contact or electronically with the use of telecommunication techniques. Further verification and reeducation should be undertaken once new risk factors/complications develop.
2. For practical purposes, it may be advisable to organize a "school of diabetes education."
3. Education delivered by physicians, nurses, diabetes educators, and dieticians should be provided in parallel to the drug treatment, taking into the account the above mentioned time constraints, which requires separate funding within specifically defined and contracted services.
4. Every education program should be based on the principle of professional communication between the patient and the therapeutic team. Its goal is to achieve trust, empathy, and motivation for strict compliance with therapeutic recommendations.
5. A description of diabetes management procedures, in particular therapeutic education procedures, must be available and conformed to at the site where education is provided.

V. Standard requirements for an education center

1. Providing an educational room and equipping the workplace with material resources necessary to conduct education at the level enabling achievement of the goals and target effects of diabetes education.
2. Documentation of the educational activities including: framework educational program and training sessions undertaken with each patient, identification of the local education coordinator, and education-related duties of the healthcare personnel and individual patient education charts. **Periodic assessment of patient knowledge (feed-back), optimally annually.**
3. Improving skills of the personnel delivering education by updating their knowledge (participation in education courses, conferences).
4. Providing an opportunity for evaluation of the quality of education by patients and their caregivers, and including this information in the evaluation programs (at least once a year).
5. Determining the way of consulting educational decisions within the therapeutic team and ensuring information sharing about the therapeutic goals and educational progress.
6. The employer's responsibility is to create and improve conditions for position training, increasing professional qualifications, and self-education for the members of diabetes therapeutic team, including those serving as diabetes educators.

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10. General principles of the management of diabetes type 1

Most important recommendations

- The recommended treatment approach is intensive insulin therapy using multiple subcutaneous insulin doses or continuous subcutaneous insulin infusion (CSII) using a personal insulin pump. [**A**]
- A key element of therapy for diabetes type 1 is the patient's ability to modify insulin doses based on carbohydrate meal content, baseline blood glucose level, and planned physical activity. Knowledge of the effect of protein and fat on blood glucose level is also important for optimization of insulin dosage. [**E**]
- In patients with diabetes type 1, use of insulin analogs is preferred due to a lower risk of hypoglycemia and better quality of life. [**A**]
- In patients using continuous glucose monitoring (CGM) or intermittently scanned continuous glucose monitoring (isCGM)/flash glucose monitoring (FGM) systems, one of the basic parameters for assessing diabetes control should be the time spent with blood glucose levels in the target range (time in range), optimally over 70%. [**E**]
- All therapeutic decisions in the management of diabetes type 1 should be undertaken in coooperation with the patient and should be accepted by the patient. **[E]**

Management of diabetes type 1

— Insulin therapy is absolutely required in patients with diabetes type 1. Insulin therapy should be continued even in the remission phase.

— The recommended treatment approach is intensive insulin therapy using multiple subcutaneous insulin doses or continuous subcutaneous insulin infusion (CSII) using a personal insulin pump. A prerequisite for effective treatment is appropriate education (as outlined in Chapter 9), allowing self-adjustments of insulin doses by the patient based on systematic self-monitoring of blood glucose (SMBG) using a glucose meter or other dedicated device (as outlined in Chapter 3). In patients with diabetes type 1, use of insulin analogs is preferred due to a lower risk of hypoglycemia and better quality of life.

— Optimization of insulin dose is important in insulin therapy for diabetes type 1. Long-term use of supraphysiological amounts of insulin without attempts to identify causes of high insulin requirement and treat the underlying problem — except for specific situations (acute illness, medications increasing insulin requirement, stress) — may lead to adverse metabolic consequences including excessive body weight increase.

— A key element of therapy for diabetes type 1 is the patient's ability to modify insulin doses based on meal carbohydrate content, baseline blood glucose level, and planned physical activity. Knowledge of the effect of protein and fat on blood glucose levels is also important for the optimization of insulin doses.

— Use of continuous glucose monitoring (CGM) systems may facilitate the optimization of metabolic control, particularly in patients with frequent hypoglycemia episodes, nocturnal hypoglycemia, severe hypoglycemia, or large circadian variation of

blood glucose levels. The combination of CSII and CGM technologies may be particularly effective in insulin pumps that automatically interrupt insulin administration in case of hypoglycemia or imminent hypoglycemia and in hybrid closed loop (HCL) insulin pumps that can also automatically normalize hyperglycemia to some extent.

— Devices working on a similar principle as HCL are pumps based on open artificial pancreas system (APS) applications, called Do It Yourself (DIY) pumps. Although many patients can significantly improve metabolic control with the use of such systems, it should be emphasized that these are not certified systems, and their use and the associated risks remain in the patient's responsibility.

— Reduction of the risk of hypoglycemia and improved patient quality of life may also be achieved by the use of intermittently scanned continuous glucose monitoring (isCGM) or flash glucose monitoring (FGM).

— Telemedicine is an important tool for the optimization of blood glucose control. It should be noted that in all individuals with diabetes type 1, the therapeutic team cooperating with the patient should aim to develop a system that allows effective telemedicine visits. Developing such a system should be based on patient education and encouraging him or her to use appropriate technological solution. Telemedicine visits in patients with diabetes type 1 may be either a component of regular diabetes care or a backup solution used, e.g., in the settings of an epidemiological risk.

— When combined with insulin therapy, sodium-glucose transport protein 2 (SGLT-2) inhibitors may improve glycemic control and weight reduction in diabetes type 1. It should be emphasized, however, that only some SGLT-2 inhibitors have been approved for adjunct treatment of diabetes type 1. Their use may be associated with the risk of normoglycemic ketoacidosis, especially in case of a significant reduction in the daily insulin dose.

Organization of care for patients with diabetes type 1

— Patients with diabetes type 1 should be cared for by a diabetes specialist since the very diagnosis of diabetes type 1 and afterwards. Such a management approach allows continuous collaboration with an education team (as outlined in Chapter 5) and provides access to necessary consultations.

— New cases of diabetes type 1 and difficult-to-treat acute diabetes complications require admission to a specialist hospital diabetes care unit.

Goals of diabetes type 1 management

— The goal of diabetes type 1 management is to achieve good metabolic control with blood glucose levels as close to normal values as possible. The primary therapeutic goal is to achieve HbA_{1c} level ≤ 7.0%. Aiming for lower HbA_{1c} levels (≤ 6.5%) is warranted unless it is associated with an increased risk of hypoglycemia episodes or reduced quality of life of a diabetic individual.

— Only such a management approach may prevent acute and chronic complications and allow patient to engage in normal, active family, professional, and social life.

— In patients who regularly use CGM or isCGM/FGM, the primary therapeutic goal is to achieve a high (over 70%) percentage of time spent in the target range defined as blood glucose values 70–180 mg/dL. It should be emphasized that one of the treatment priorities should be to avoid hypoglycemia (the maximum acceptable time spent at values lower than 70 and 54 mg/dL is 4% and 1%, respectively). Glucose targets for patients using CGM or isCGM/FGM are summarized in Table 4.2 in Chapter 4 of the present guidelines.

Early diagnosis of chronic diabetes complications

— Early diagnosis of diabetes complications is possible with screening for nephropathy, retinopathy, and neuropathy. Screening for these complications in patients with diabetes type 1 is outlined in Chapters 19–21.

— In patients with long-lasting diabetes type 1, particularly with the disease onset at a young age, diabetic macroangiopathy manifesting as ischemic heart disease, cerebrovascular disease, or peripheral arterial disease may develop earlier compared to the general population. The approach to the diagnosis and treatment of ischemic heart disease is discussed in Chapter 17, and the management of stroke and acute coronary syndrome is outlined in Chapters 18 and 17.1, respectively.

Diagnosis and management of acute complications

— An adequately educated patient with diabetes type 1 must know how to treat acute mild to moderate hyper- and hypoglycemia and should be able to manage these conditions independently. More severe conditions require medical intervention as outlined in Chapters 15 and 16.

Special situations in subjects with diabetes type 1

— Patients with diabetes type 1 and good metabolic control, treated with intensive insulin therapy, may

be subjected to one-day surgery (minor surgical procedures). Other principles of the perioperative management in patients with diabetes type 1 are outlined in Chapter 26.

— Compared to the general population, diabetes type 1 is more commonly accompanied by endocrinopathies, in particular autoimmune disease of the thyroid (Hashimoto disease, Graves disease) and adrenal cortex (Addison disease), celiac disease, vitamin B12 deficiency anemia (Addison-Biermer anemia), and connective tissue disease. These comorbidities may significantly worsen the course of diabetes type 1.

— Development of diseases that complicate the metabolic derangements of diabetes requires admission to a specialist unit.

— Obesity with concomitant insulin resistance may be present in subjects with diabetes type 1, resulting in an increased insulin requirement and worsened metabolic control. The diagnosis and management in these cases require specialist investigations and therapy.

— Eating disorders including bulimia and anorexia are increasingly common in young patients with diabetes type 1. The diagnosis and management of these conditions require specialist psychiatric treatment in close collaboration with a diabetes specialist.

A well-educated patient with diabetes type 1, treated with intensive insulin therapy with good metabolic control, is able to engage in the same physical activity and achieve similar professional goals as non-diabetic subjects of similar age.

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11. Oral antidiabetic agents and GLP-1 receptor agonists in the management of diabetes type 2

Most important recommendations

- Metformin should be the first choice drug when initiating drug therapy of diabetes type 2 unless it is contraindicated or poorly tolerated. [**A**]
- The choice of further drugs should be individualized, taking into account their cardiovascular and renal effect, effectiveness, side effects, the effect on body weight, risk of hypoglycemia, cost, and patient preferences. [**E**]
- If monotherapy using maximum recommended or tolerated doses becomes insufficient to achieve or maintain target HbA_{1c} level, another oral agent, GLP-1 receptor agonist, or basal insulin should be added. This decision should not be postponed by more than 3–6 months. [**A**]
- In justified cases, such as documented atherosclerotic cardiovascular disease, systolic heart failure, chronic kidney disease or presence of multiple cardiovascular disease risk factors, the decision to initiate combined treatment in newly diagnosed diabetes should be considered. In these cases, metformin should be combined with drugs that reduce the risk of progression of the above conditions – SGLT-2 inhibitors or GLP-1 receptor agonists [**A**]. Initiation of combined treatment in newly diagnosed diabetes type 2 should also be considered in case of severe hyperglycemia.
- In patients with atherosclerotic cardiovascular disease, systolic heart failure, chronic kidney disease or multiple cardiovascular disease risk factors, drugs with an established beneficial effect on the risk of progression of these conditions and on total and cardiovascular mortality should be used first. In addition to metformin, such an effect was shown for some SGLT-2 inhibitors and some GLP-1 receptor agonists [**A**].
- In patients with chronic kidney disease and systolic heart failure, SGLT-2 inhibitors should be preferred, and GLP-1 receptor agonists should be used if SGLT-2 inhibitors are contraindicated [**A**].
- In patients with established atherosclerotic cardiovascular disease, drugs from both these groups should be considered, and GLP-1 receptor agonists should be considered first in patients with multiple cardiovascular disease risk factors. Early combination therapy with metformin and SLGT-2 inhibitors and/or GLP-1 receptor agonists should be considered in all patients with the above conditions regardless of whether the therapeutic target has been achieved. [**A**]
- Due to progressive nature of diabetes type 2, insulin therapy is indicated in many patients when the treatment is gradually intensified. [**B**]
- All therapeutic decisions in the management of diabetes type 2 should be undertaken in cooperation with the patient and should be accepted by the patient. [**E**]

Pharmacological lowering of blood glucose levels as a part of the comprehensive management of diabetes type 2 (in addition to treating hypertension and dyslipidemia, lifestyle changes, antiplatelet treatment etc.) is of key importance for preventing and delaying progression of chronic complications of diabetes (both macro- and microvascular).

I. Lowering hyperglycemia occurs by correcting the pathogenetic mechanisms of diabetes type 2 — insulin resistance and impaired insulin secretion. A separate therapeutic mechanism of anti-hyperglycemic drugs is a glucosuric effect. Treatment of diabetes type 2 must be gradual and adapted to the progressive nature of the disease. If the therapy used at a given stage is no longer effective, i.e., target HbA_{1c} level cannot be reached, treatment should proceed to the next step after 3–6 months.

II. Management of diabetes type 2

1. Treatment initiation:

— Lifestyle modification (body weight reduction, increasing physical activity to 30–45 minutes/day), reduction of meal calorie content in combination with metformin monotherapy;

— To minimize the risk of adverse effects of metformin, mostly gastrointestinal complaints, therapy should be started with small doses which are then gradually increased to the maximum tolerated dose;

— If metformin is not tolerated or contraindicated, therapeutic options include sodium-glucose cotransporter 2 (SGLT-2) inhibitors, sulfonylureas, incretin-based therapy (DPP-4 inhibitors and GLP-1 receptor agonists), and peroxisome proliferator activated receptor gamma (PPAR-γ) agonist (pio-

glitazone); in such cases, incretins and SGLT-2 inhibitors should be preferred in obese subjects and those in whom the risks of hypoglycemia are high, and PPAR-γ agonist should not be used in individuals with heart failure;
— Therapeutic effectiveness of the oral therapy used may be assessed only after several weeks of treatment;
— In justified cases, such as documented atherosclerotic cardiovascular disease, systolic heart failure, chronic kidney disease or presence of multiple cardiovascular disease risk factors, the decision to initiate combined treatment in newly diagnosed diabetes should be considered. In these cases, metformin should be combined with drugs that reduce the risk of progression of the above conditions – SGLT-2 inhibitors or GLP-1 receptor agonists. Initiation of combined treatment in newly diagnosed diabetes type 2 should also be considered in case of severe hyperglycemia.

2. Intensification of oral or GLP-1 receptor agonist therapy:
— Lifestyle modification and adding an SGLT-2 inhibitor or incretin-based therapy (DPP-4 inhibitor or GLP-1 receptor agonist), a sulfonylurea or a PPAR-γ agonist to metformin. The choice of the drug in this step should be informed by concomitant diseases, primarily established cardiovascular disease and chronic kidney disease, but also concomitant obesity, the risk of hypoglycemia and the patient's financial capabilities. In patients with atherosclerotic cardiovascular disease, systolic heart failure, chronic kidney disease or multiple cardiovascular disease risk factors, drugs with an established beneficial effect on the risk of progression of these conditions and on total and cardiovascular mortality should be used first. Such an effect was shown for some SGLT-2 inhibitors and some GLP-1 receptor agonists. In patients with chronic kidney disease and systolic heart failure, SGLT-2 inhibitors should be preferred, and GLP-1 receptor agonists should be used if SGLT-2 inhibitors are contraindicated. In patients with established atherosclerotic cardiovascular disease, drugs from both these groups should be considered, and GLP-1 receptor agonists should be considered first in patients with multiple cardiovascular disease risk factors. Early combination therapy with metformin and some SLGT-2 inhibitors and/or GLP-1 receptor agonists should be considered in all patients with the above conditions regardless of whether the therapeutic target has been achieved. Similarly, GLP-1 receptor agonists and SGLT-2 inhibitors are preferred in patients with concomitant obesity. In patients with high risk of hypoglycemia, adding a GLP-1 receptor agonist, a SGLT-2 inhibitor, a DPP-4 inhibitor or a PPAR-γ agonist should be considered. Due to limited reimbursement of novel antihyperglycemic drugs in Poland, sulfonylureas and the PPAR-γ agonist are the most economically available drugs;
— Lifestyle modification and three-drug therapy including metformin (in all cases) and two other agents with different mechanisms of action from the following classes: SGLT-2 inhibitors, GLP-1 receptor agonists, sulfonylureas, DPP-4 inhibitors and PPAR-γ agonist. The choice of drugs in this step should be based on the same premises as in the earlier step and on the general principles of combining antihyperglycemic agents.

It also possible to add basal insulin to metformin, i.e. switching from monotherapy directly to insulin treatment, bypassing the intermediate.

3. Treatment intensification by insulin therapy:
— Lifestyle modification and simple insulin therapy [mostly with basal insulin (long-acting insulin analog, ultralong-acting insulin analog); various regimens — see Chapter 12], with continuation of metformin and other oral drugs or GLP-1 receptor agonist, particularly with persisting overweight or obesity;
— Lifestyle modification and complex insulin therapy, with recommended continuation of metformin and other oral drugs (incretins, pioglitazone, SGLT-2 inhibitors) or GLP-1 receptor agonist, particularly with persisting excessive body weight (see Chapter 12).

III. Agents used for the treatment of diabetes type 2 are listed in Table 11.1. Their effect on non-glycemic parameters (i.e., mortality, cardiovascular, and renal risk, body weight, risk of hypoglycemia, lipid parameters, etc.) should be taken into account when selecting and combining drugs, with due attention paid to treatment individualization (see Chapter 4.I.3). Data from large randomized clinical trials indicate a reduction of total and cardiovascular mortality and cardiovascular and renal endpoints with the use of some GLP-1 receptor agonists and SGLT-2 inhibitors.

IV. Practical drug treatment algorithms for diabetes type 2 are shown in Figures 11.1 and 11.2.

Table 11.1. Drug used for the treatment of diabetes type 2 (insulin — see Chapter 12)

	Metformin	Sulfonylureas	GLP-1 receptor agonists	DPP-4 inhibitors	PPAR-γ agonist	SGLT-2 inhibitors
Effect/mechanism	Decreased hepatic glucose production, increased insulin sensitivity	Increased insulin secretion regardless of the severity of hyperglycemia	Increased hyperglycemia-mediated insulin secretion, decreased appetite	Increased hyperglycemia-mediated insulin secretion	Increased insulin sensitivity	Induction of glucosuria
Hypoglycemic effect	High	High	High	Medium	High	High
Plasma insulin	↓	↑↑	↑↑	↑	↓	↓
LDL cholesterol	↓	↔	↓	↓ or ↔	↔	↔ or ↑
HDL cholesterol	↑	↔	↑	↑	↑	↑
Triglycerides	↓	↔	↓	↔	↓	↔
Body weight	↓ or ↔	↑	↓↓	↔	↑	↓
Risk of hypoglycemia	↔	↑	↔	↔	↔	↔
Adverse effects	Gastrointestinal upset	Hypoglycemia, increase in body weight	Gastrointestinal upset (nausea, vomiting)	No significant	Fluid retention (edema), increase in body weight, increased risk of long bone fractures	Genital fungal infections, increased thirst
Beneficial cardio-vascular effect			Yes**			Yes**[A]
Contraindications	Organ failure (heart, brain, liver, kidneys*, respiratory), alcohol abuse	Heart, liver, kidney failure	Gastrointestinal neuropathy	Liver failure	Heart or liver failure, bladder cancer	Significant reduction of glomerular filtration rate[B]

*See Table 19.3. **Proven for some drugs of this class, according to the recent results from randomized clinical trials
[A]For empagliflozin and canagliflozin, there were no differences in cardiovascular outcome trials between higher and lower doses: 10 mg *vs.* 25 mg and 100 mg *vs* 300 mg, respectively
[B]Use of specific medications according to the current summary of product characteristics wording as related to the estimated glomerular filtration rate.
DPP-4 — dipeptidyl peptidase-4; GLP-1 — glucagon-like peptide 1; HbA_{1c} — hemoglobin A_{1c}; HDL — high-density lipoprotein; LDL — low-density lipoprotein; PPAR-γ — peroxisome proliferator activated receptor gamma; SGLT-2 — sodium-glucose transport protein 2

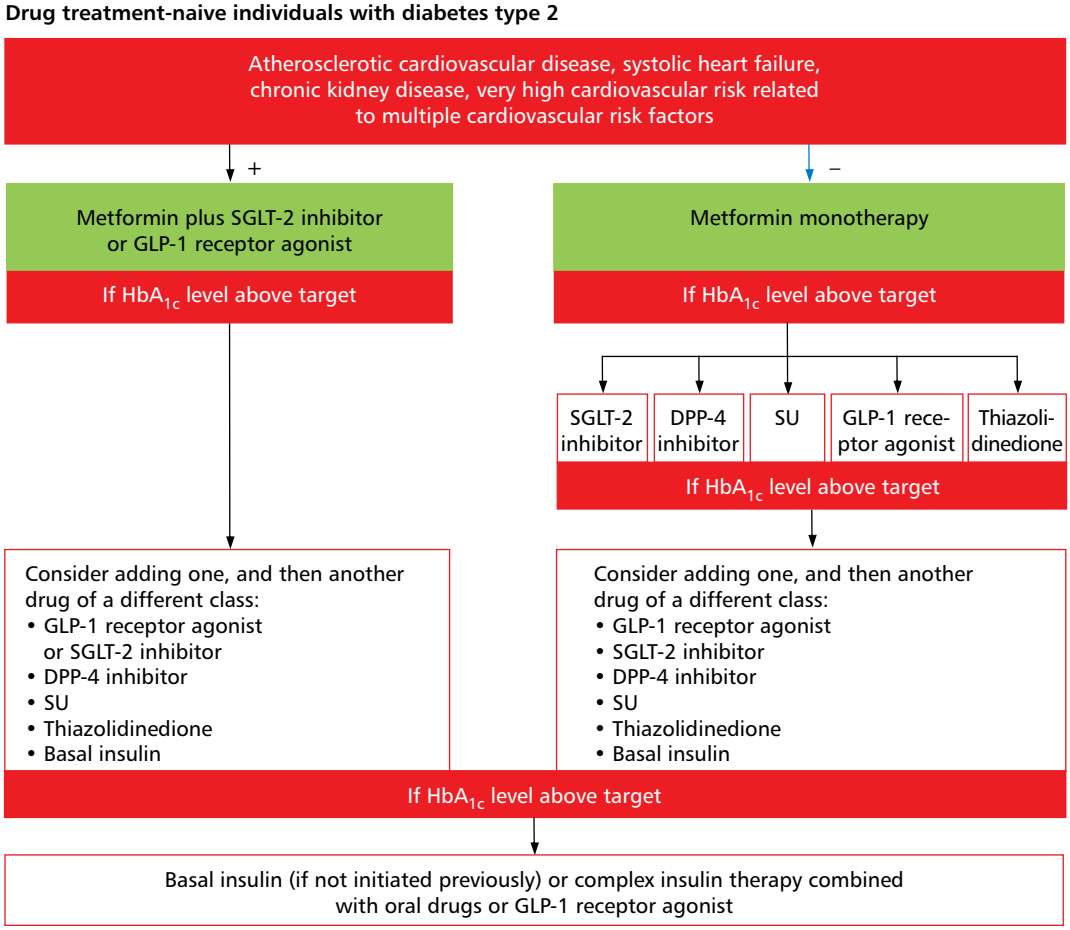

Figure 11.1. Drug treatment algorithm for drug treatment-naive individuals with diabetes type 2

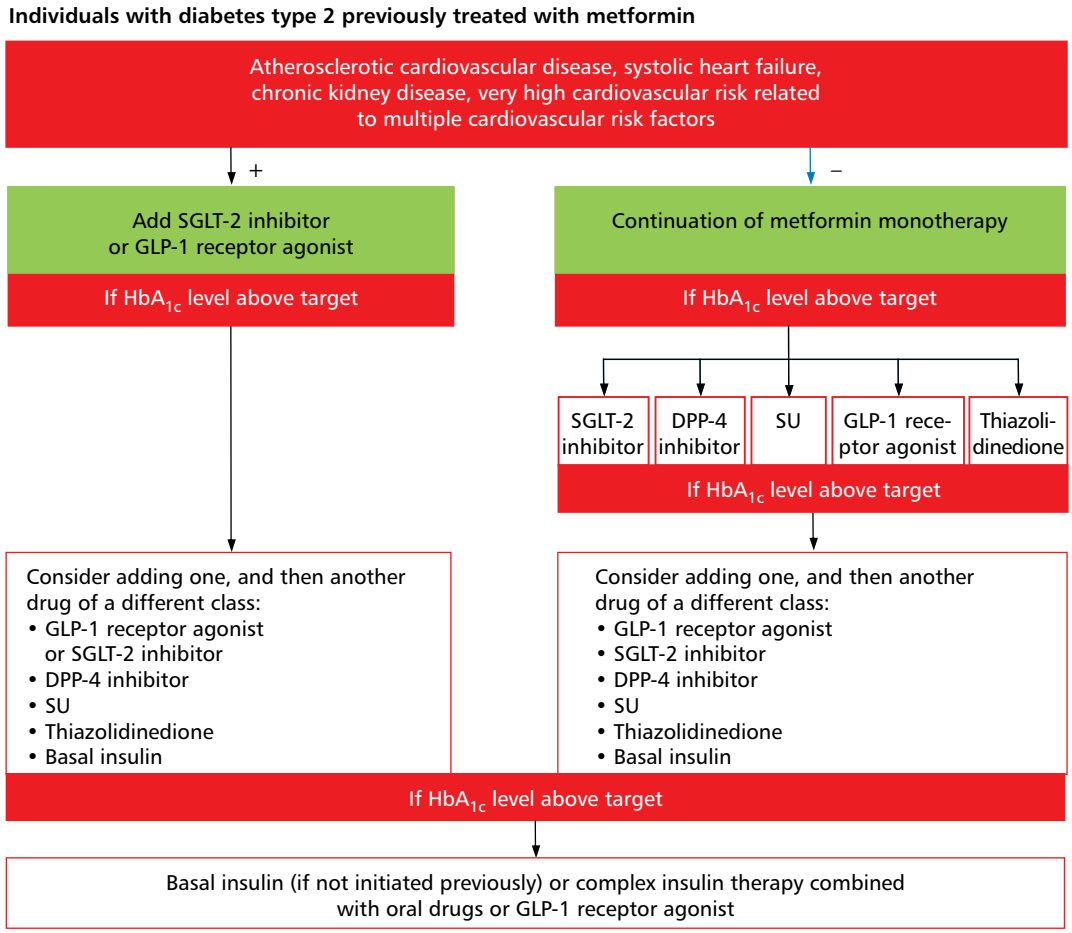

Figure 11.2. Drug treatment algorithm for individuals with diabetes type 2 previously treated with metformin

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12. Insulin therapy

Most important recommendations

- In patients with diabetes type 1, insulin therapy is the only treatment approach. Intensive insulin therapy using insulin pens or personal insulin pump is recommended. [**A**]
- In patients with diabetes type 1, insulin analogs are preferred due to a lower risk of hypoglycemia. [**A**]
- Diabetes type 2 is a progressive disease. Increasing underlying pathophysiologic disturbances, particularly the beta cell defect, result in a need for gradual treatment intensification, including initiation of insulin therapy. [**B**]

I. Indications for initiating insulin therapy in diabetes type 2:

— Newly diagnosed diabetes (with an option to return to the typical treatment algorithm and withdrawal of insulin therapy):
  - Blood glucose ≥ 300 mg/dL (16.7 mmol/L) with concomitant clinical symptoms of hyperglycemia;

— Treatment ineffectiveness without use of insulin (HbA_{1c} above target despite intensified behavioral therapy).

II. **Indications for switching from previous antihyperglycemic therapy (using oral antihyperglycemic agents, in some cases in combination with a GLP-1 receptor agonist) to combined therapy including insulin if blood glucose remains uncontrolled:**

— Continuing hyperglycemia as confirmed on several occasions;

And

— Unsuccessful attempts to eliminate potentially correctable causes of hyperglycemia, such as:
  - Dietary errors;
  - Too low physical activity;
  - Irregular intake of oral antihyperglycemic agents (poor compliance);
  - Infections;
  - Inadequate doses of oral agents.

III. **Indications for initiating insulin therapy regardless of blood glucose levels:**

— Pregnancy;

— Autoimmune-mediated diabetes in adults (type 1/ /latent autoimmune diabetes in adults [LADA]);

— Diabetes associated with cystic fibrosis;

— Reasonable patient's request.

In overweight or obese patients with diabetes type 1, metformin use combined with insulin therapy is beneficial.

IV. Indications for temporary insulin therapy:

— Diabetes decompensation due to transient causes (infection, trauma, glucocorticoid therapy, etc.);

— Surgical procedure (see Chapter 26);

— Stroke (see Chapter 18);

— Percutaneous coronary intervention (PCI);

— Acute coronary syndrome;

— Other acute illness requiring admission to an intensive care unit.

V. Insulin therapy algorithm in diabetes type 2

1. Long-acting insulin (isophane — NPH, long-acting insulin analog, or ultralong-acting insulin analog) in one daily injection:
   — With morning hyperglycemia — in the evening; use of long acting analogues reduces the risk of nocturnal and severe hypoglycemia;
   — With fasting and daytime hyperglycemia — in the morning (consider multiple injections of a short/ /rapid-acting insulin if postprandial hyperglycemia is noticed).

In selected cases, when initiation of insulin therapy was long overdue, resulting in severe hyperglycemia and HbA_{1c} levels much above the therapeutic target, initiation of mixed insulin therapy, treatment with biphasic insulin analog or premixed insulin analogues, or intensive insulin therapy should be considered as the initial treatment option, particularly in relatively young patients with long life expectancy. Currently, no convincing evidence exists for better effectiveness or safety of mixed human insulins or insulin analogs. The choice of a particular insulin preparation should be made individually, taking into account patient's preferences regarding the number of daily meals and costs of treatment.

2. Initial dose is 0.1–0.2 unit/kg or 10 units.
3. Oral antihyperglycemic agents and injectable incretin-based therapies may be used as licensed in subjects treated with insulin:
   — Metformin therapy should be continued in all patients, if tolerated and not contraindicated;
   — In case of concomitant overweight or obesity, combined therapy with metformin and a SGLT-2 inhibitor or an incretin-based therapy (DPP-4 inhibitor or GLP-1 receptor agonist) should be preferred;
   — With normal body weight, combination with a sulfonylurea may be considered.

4. Blood glucose control should be evaluated within 4–5 days, with gradual dose increments by 2–4 units based on SMBG readings until adequate control.
5. If daily basal insulin requirement is > 0.3–0.5 unit/kg body weight and glycemia is poorly controlled, treatment intensification may be considered using mixed insulin, biphasic insulin analog, or premixed insulin analogues; it may also be considered to supplement long-acting insulin (administered once or twice daily) with a short-acting insulin/rapid-acting insulin analog administered at 1–3 meals (basal-plus insulin regimen, intensive insulin therapy). Discontinuation of insulin secretagogues should be considered.
6. If large daily insulin doses are used (> 100 units), indicating insulin resistance, causes of the latter should be considered and the possibility of adverse effects should be taken into account. An attempt to reduce the degree of insulin resistance by a 72- to 96-hour continuous subcutaneous or intravenous insulin infusion is recommended.

Intensive insulin therapy

Intensive insulin therapy is undertaken based on similar principles in all types of diabetes, using multiple daily insulin injections, or by CSII using a personal insulin pump.

I. Principles of intensive insulin therapy:

— Daily SMBG;
— Self-adjustment of insulin doses or administering additional insulin doses depending on blood glucose readings, energy requirement, and physical activity;
— Precise definition of target blood glucose levels;
— Appropriate therapeutic and nutritional education and patient motivation;
— Possibility of a rapid patient contact with the therapeutic team;
— In diabetes type 2, CSII using a personal insulin pump is not a routine treatment approach.

II. Algorithms of multiple insulin injections:

— Short-acting insulin or rapid-acting insulin analog before meals; and
— Izophane insulin (NPH, long-acting insulin analog, or ultralong-acting insulin analog to provide constant basal insulin levels administered before bedtime and/or in the morning.

In some cases of diabetes type 2 with normal fasting blood glucose levels, short-acting insulin injections or insulin analog at mealtimes may be sufficient.

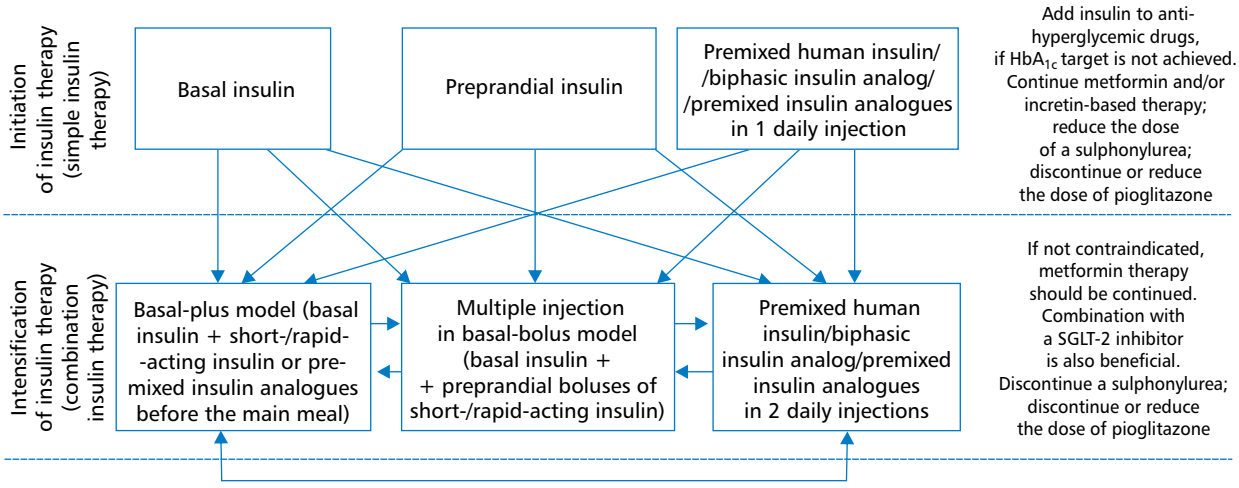
III. Personal insulin pump treatment algorithm

Therapy with personal insulin pumps should be undertaken in centers experienced in such treatment. This approach is used in diabetes type 1 and some other specific diabetes types (e.g. diabetes associated with cystic fibrosis).
Indications:

— Need for small insulin doses (e.g., in children);
— Recurrent, unpredictable hypoglycemia episodes;
— Hypoglycemia unawareness;
— Irregular lifestyle and meals;
— Early-morning hyperglycemia;
— Pregestational diabetes mellitus which is difficult to control with multiple insulin injections;
— Patient preference if costs incurred by this treatment approach are accepted.

Contraindications:

— Low intellectual or educational level of the patient;
— Lack of patient compliance;
— No contact with a specialist clinic.



Each model of insulin therapy requires patient education. In selected cases, the step of simple insulin therapy can be skipped when initiating insulin therapy. In active patients with diabetes type 2 who are motivated and able to learn how to adapt insulin doses, intensive insulin therapy may be recommended.

Figure 12.1. A practical algorithm for insulin therapy in diabetes type 2. Models of initiation and intensification of insulin therapy

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13. General principles of the management of hypertension in patients with diabetes

Most important recommendations

- The general blood pressure target in patients with diabetes is < 130/80 mm Hg (140/80 mm Hg in patients aged > 65 years). [**A**]
- The treatment of hypertension should be initiated with the combination of two drugs: an angiotensin converting enzyme inhibitor (ACEI) or an angiotensin receptor antagonist (ARB) with a calcium antagonist or a thiazide/-thiazide-like diuretic. [**A**]
- Pharmacological treatment of hypertension should be continued indefinitely as it is the only way to reduce cardiovascular risk. [**A**]
- In the treatment of hypertension in individuals with diabetes, the goal should be not only to achieve the target blood pressure but also to maintain or restore normal diurnal blood pressure variation as assessed by 24-hour monitoring, especially in pregnant women with diabetes. [**B**]

In patients with diabetes, initiation of drug treatment is recommended if blood pressure is above 140/90 mm Hg. The goal of treatment is to optimally reduce the global cardiovascular event risk by lowering systolic blood pressure below 140 mm Hg, with the target systolic blood pressure of 130 mm Hg in patients under 65 years of age (and if the treatment is well tolerated — below 130 mm Hg due to benefits associated with stroke risk reduction). The optimal diastolic blood pressure is below 80 mm Hg. Hypertension can be diagnosed based on 24-hour ambulatory blood pressure monitoring (ABPM).

I. Principles of blood pressure measurement

Blood pressure should be measured during each visit, also in the standing position to evaluate orthostatic blood pressure falls. Home blood pressure measurements are recommended in all patients with the diagnosis of hypertension. In patients with systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, measurement should be repeated on another day, and out-of-office blood pressure measurements should be recommended. Systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg during repeated measurements confirms the diagnosis of hypertension. In diabetic individuals, frequent findings include nocturnal hypertension, and masked hypertension (when office blood pressure values are lower than home blood pressure values), and thus 24-hour ambulatory blood pressure measurement is recommended in these individuals, as are home blood pressure measurements.

II. Principles of antihypertensive therapy:

— When striving to achieve the above hypertension treatment goals in diabetic individuals, lowering systolic blood pressure below 120 mm Hg, and below 130 mm Hg in patients with chronic kidney disease should be avoided;
— Diastolic blood pressure should not be lowered below 70 mm Hg;
— Drug treatment should be combined with lifestyle changes in all patients with hypertension;
— As a general rule, treatment should be initiated with the combination of two drugs: an angiotensin converting enzyme inhibitor (ACEI) or an angiotensin receptor antagonist (ARB) with a calcium antagonist or a thiazide/thiazide-like diuretic; however, if specific comorbidities are present (e.g., ischemic heart disease or chronic kidney disease) the combination of two drugs may be different;
— Considering the above recommendation, it is advisable to use single-pill combinations to improve compliance;

— The presence of proteinuria does not change predefined blood pressure goal;
— A combination of an ACEI and a beta-blocker is commonly used in patients with hypertension and cardiac disease (ischemic heart disease, heart failure);
— Combinations of drugs with similar mechanisms of action are of little value, as the blood pressure-lowering effect is less than additive or an increased risk of adverse effects exists;
— A drug from another class should be added if target blood pressure has not been reached despite two-drug treatment (one of the drugs used should be a diuretic);
— In case of a non-dipping nocturnal blood pressure pattern or a morning blood pressure surge, modification of the timing of antihypertensive drug administration should be considered;
— Long-acting antihypertensive drugs which allow 24-hour blood pressure control with once daily dosing should be preferred;
— Serum creatinine, potassium, and glomerular filtration rate (GFR) should be monitored during treatment with ACEI, ARB, renin inhibitors, and diuretics;
— In patients aged > 65 years, blood pressure should be lowered gradually to avoid treatment complications;
— In the very elderly patients (> 80 years) and those with the frailty syndrome, it is reasonable to start antihypertensive therapy with monotherapy.

III. Choice of blood-pressure lowering drugs

An effective treatment resulting in normalization of blood pressure is more important for the prevention of cardiovascular complications than the choice of drugs:

— Antihypertensive drug treatment may be initiated with ACEI, ARB, diuretic, beta-blocker (vasodilating beta-blockers are preferred if there are no specific indications), or calcium antagonist;
— Renin-angiotensin-aldosterone (RAA) system inhibitors should be preferred if albuminuria/proteinuria is present;
— Combined treatment with ACEI and ARB is contraindicated;
— Combined treatment may include drugs from the above listed and other drug classes, taking into account the principles of combining antihypertensive drugs;
— Drug treatment of hypertension in patients with concomitant renal dysfunction — see Chapter 19;
— In patients aged > 55 years with concomitant cardiovascular risk factors, treatment with ACEI should be considered to reduce the cardiovascular risk regardless of blood pressure values;
— ACEI or ARB are not recommended in normotensive subjects with normoalbuminuria for the primary prevention of diabetic kidney disease;
— ACEI or ARB is recommended in normotensive subjects with urinary albumin-to-creatinine ratio ≥ 30 mg/g to prevent and delay progression of diabetic kidney disease;
— In patients with ischemic heart disease, previous myocardial infarction, or heart failure, beta-blockers and ACEI are reasonable as first-choice drugs to reduce mortality risk;
— Use of nonselective beta-blockers should be avoided with concomitant peripheral arterial disease;
— Thiazide/thiazide-like diuretics should be used in patents with GFR ≥ 30 mL/min/1.73 m^2, while a loop diuretic should be used if GFR is < 30 mL/min/1.73 m^2.

Clinical studies indicate that use of at least three different antihypertensive drugs is necessary to reach the therapeutic goals in the majority of patients. Often, this requires use of other drug classes in addition to those listed above (including aldosterone antagonists, beta-blockers, centrally-acting drugs, and vasodilators).

Resistant hypertension, which requires treatment with more than 3 drugs, commonly develops in diabetes. In this situation, use of spironolactone should be considered. Testing for obstructive sleep apnea and secondary hypertension should be considered in diabetic patients with resistant hypertension.

Among antidiabetic medications, SGLT-2 inhibitors and GLP-1 receptor agonists exert a blood pressure lowering effect and may be recommended for the treatment of diabetes also for that reason.

Principles of diabetes management in children and adolescents, pregnant women and those contemplating pregnancy, and individuals above 65 years of age — see Chapters on respective subjects.

IV. Management of hypertension in pregnant women

Target blood pressure values in pregnant women with diabetes are 110–139 mm Hg and 81–85 mm Hg for systolic and diastolic blood pressure, respectively. Blood pressure target below 130/80 mm Hg is recommended for pregnant women with diabetes and vascular complications.

In pregnant women with non-severe hypertension, oral drugs of choice are (in the order given) methyldopa, labetalol, and calcium antagonists. In life-threatening situations, the preferred drugs are labetalol and nitroglycerin (administered parenterally). If these are not available, parenteral hydralazine may be used, although an increase in the rate of adverse effects in the perinatal period has been reported.

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14. Treatment of dyslipidemia

Most important recommendations

- LDL-C level < 55 mg/dL (1.4 mmol/L) and reduction by at least 50% compared to baseline in diabetic subjects at very high cardiovascular risk. [**B**]
- LDL-C level < 70 mg/dL (1.8 mmol/L) and reduction by at least 50% compared to baseline in diabetic subjects at high cardiovascular risk. [**A**]
- LDL-C level < 100 mg/dL (2.6 mmol/L) in diabetic subjects at moderate cardiovascular risk (young patients < 35 years of age with diabetes type 1 without chronic complications and other cardiovascular risk factors or patients with type 2 diabetes < 50 years of age, with duration of diabetes < 10 years, without other risk factors). [**A**]

The main goal is to reduce LDL cholesterol level, while non-HDL cholesterol level is a secondary therapeutic target. Complete normalization of the atherogenic lipid profile after achieving target LDL cholesterol level, i.e. increasing HDL cholesterol level and decreasing triglyceride level, may be associated with beneficial effects.

Diabetic patients with vascular complications (previous myocardial infarction, acute coronary syndrome, coronary revascularization or other revascularization procedures, stroke, transient ischemic attack, aortic aneurysm, and peripheral arterial disease) or other target organ damage (proteinuria or microalbuminuria, impaired renal function — GFR < 30 mL/min/1.73 m^2, left ventricular hypertrophy, retinopathy, neuropathy) or with at least three major risk factors (age, hypertension, dyslipidemia, smoking, obesity) or early onset and long-term of type 1 diabetes (> 20 years) should be considered at very high cardiovascular risk. Patients without chronic diabetes complications who have additional cardiovascular risk factors are at high cardiovascular risk. In young patients with type 1 diabetes < 35 years of age or type 2 diabetes < 50 years of age, with diabetes duration < 10 years and without other cardiovascular risk factors, the risk is moderate. When assessing cardiovascular risk, the following tests are helpful: resting ECG, ultrasound examination of carotid/femoral arteries to detect the presence of atherosclerotic plaques, and ankle-brachial index (ABI). The presence of atherosclerotic plaques in the carotid and/or femoral arteries found by ultrasound examination may be considered a risk-modifying factor.

I. Diagnosis of lipid disorders

History should include:

— Assessment of nutrition and alcohol intake;

— Assessment of physical activity — type and duration of activity;

— Presence of cardiovascular disease: ischemic heart disease, cerebrovascular disease, and peripheral arterial disease;
— Evaluation for thyroid, liver, and kidney disease to exclude secondary hyperlipidemia;
— Family history of lipid disorders, cardiovascular disease, hypertension, and diabetes in first-degree relatives.
— Use of drugs that may increase lipid levels.
— The recommended levels of lipid parameters are presented in Table 14.1.

In patients with diabetes and cardiovascular disease, further decrease in LDL-C level is associated with a greater reduction of the cardiovascular event risk.

LDL cholesterol level may be estimated using the Friedewald formula if triglyceride level is < 400 mg/dL (< 4.5 mmol/L) and LDL cholesterol level cannot be directly measured:

LDL cholesterol [mmol/L] = total cholesterol [mmol/L] – HDL cholesterol [mmol/L] – – triglycerides/2.2 [mmol/L]

HDL-C:
— No target level but values > 1.0 mmol/L (> 40 mg/dL) in men and > 1.2 mmol/L (> 45 mg/dL) in women indicate a lower cardiovascular risk.

Triglycerides:
— No target level but values < 1.7 mmol/L (< 150 mg/dL) indicate a lower cardiovascular risk.

In addition to non-HDL-C level, apolipoprotein B may be measured in subjects with high triglyceride levels, diabetes, obesity, or very low LDL-C levels.

Target apolipoprotein B level (as a secondary therapeutic target) is:
— < 65 mg/dL in the very high cardiovascular risk group;
— < 80 mg/dl in the high cardiovascular risk group;
— < 100 mg/dL in the moderate cardiovascular risk group.

II. Lipid level monitoring

1. Diabetes type 2:
— Lipid parameters should be measured at the time of the diagnosis of diabetes, with follow-up measurements annually or more frequently, depending on the measured levels;
— If lipid parameters are above the normal values, these should be re-checked every 8–12 weeks after treatment initiation until the desired levels are reached;
— If lipid parameters are within the desired range, follow-up measurements should be performed annually.
2. Diabetes type 1:
— If lipid levels indicate moderate risk, lipid parameters should be re-checked every 2–5 years, depending on the presence of other risk factors for cardiovascular disease.

III. Treatment of dyslipidemia in diabetic patients

1. Lifestyle changes:
— Increase in physical activity;
— Body weight reduction in overweight and obese subjects;
— Cessation of tobacco smoking;
— Diet with a reduction of saturated fat intake to < 10% of the total calorie intake, reduced cholesterol intake (< 300 mg/day or < 200 mg/day with increased LDL cholesterol levels), and maximum reduction of trans fat intake; intake of n-6 polyunsaturated fatty acids should be 4–8% of the total calorie intake, and intake of n-3 polyunsaturated fatty acids should be 2 g of linolenic acid and 200 mg/day of very long-chain fatty acids;
— In hypertriglyceridemia, reduction of obesity, reduced alcohol intake, reduced mono- and disaccharide intake (reduction of fructose intake), reduced saturated fat intake, adding monounsaturated fats to diet, and reduction of carbohydrate intake are all of major importance.
2. Tight glycemic control

Tight glycemic control is of major importance for controlling dyslipidemia, in particular hypertriglyceridemia.

3. Drug treatment

Statins are first-line drugs in the treatment of diabetic dyslipidemia.

Drug treatment, mostly with statins, is used in:
— In diabetic patients with concomitant cardiovascular diseases;
— In diabetic patients with chronic kidney disease or other organ damage, or the presence of 3 or more major risk factors;
— In diabetic patients without concomitant cardiovascular disease but with ≥ 1 cardiovascular risk factor.

In type 1 diabetes, statins are recommended in patients at high or very high cardiovascular risk.

Women with diabetes can use statins unless they are planning a pregnancy.

Statin treatment is contraindicated during pregnancy and breastfeeding. Statins should not be recommended for women of childbearing potential unless using effective contraception. In addition, the use of statins is contraindicated in people with transaminase levels greater than 3 times the upper limit of normal and in patients with creatine kinase level greater than 4 times the upper limit of normal.

In diabetic patients with concomitant hypertriglyceridemia > 2.3 mmol/L (> 200 mg/dL) persisting despite attainment of the target LDL cholesterol level using a statin, an increase in statin dose should be considered to reduce non-HDL cholesterol level which is a secondary therapeutic target. Combination treatment with fenofibrate should be considered in selected cases.

4. Combined therapy. Consideration should be given to intensifying statin therapy prior to introducing combination therapy.
   — In statin-treated patients with diabetes type 2 in whom triglyceride level is > 2.3 mmol/L (> 200 mg/dL) and HDL cholesterol level is < 0.9 mmol/L (< 35 mg/dL), adding fenofibrate to a statin is associated with an additional reduction of cardiovascular events;
   — Combined statin and ezetimibe treatment was associated with further LDL cholesterol level lowering and a reduction in the cardiovascular event rate compared to statin monotherapy. Ezetimibe may thus be of use in patients in whom recommended LDL cholesterol lowering has not been attained using a maximum tolerated statin dose or statin treatment is not tolerated.

PCSK9 inhibitors that significantly reduce LDL-C level may be useful in diabetic patients at a very high cardiovascular risk with persisting elevated LDL-C levels despite addition of a second lipid-lowering drug to the maximum tolerated statin dose, or with statin intolerance (IA).

Combined treatment with statins and other lipid-lowering drugs (ezetimibe, PCK9 inhibitors, fenofibrate) may be useful to achieve target lipid parameters in diabetic patients.

Combined therapy (mostly with statin + fenofibrate) is associated with an increased risk of abnormal liver function tests, myositis, and rhabdomyolysis, particularly with concomitant chronic kidney disease and use of high drug doses.

5. Management of severe hypertriglyceridemia

A clinically significant risk of acute pancreatitis occurs with triglyceride levels > 10 mmol/L (> 880 mg/dL). Hypertriglyceridemia underlies about 10% of acute pan-

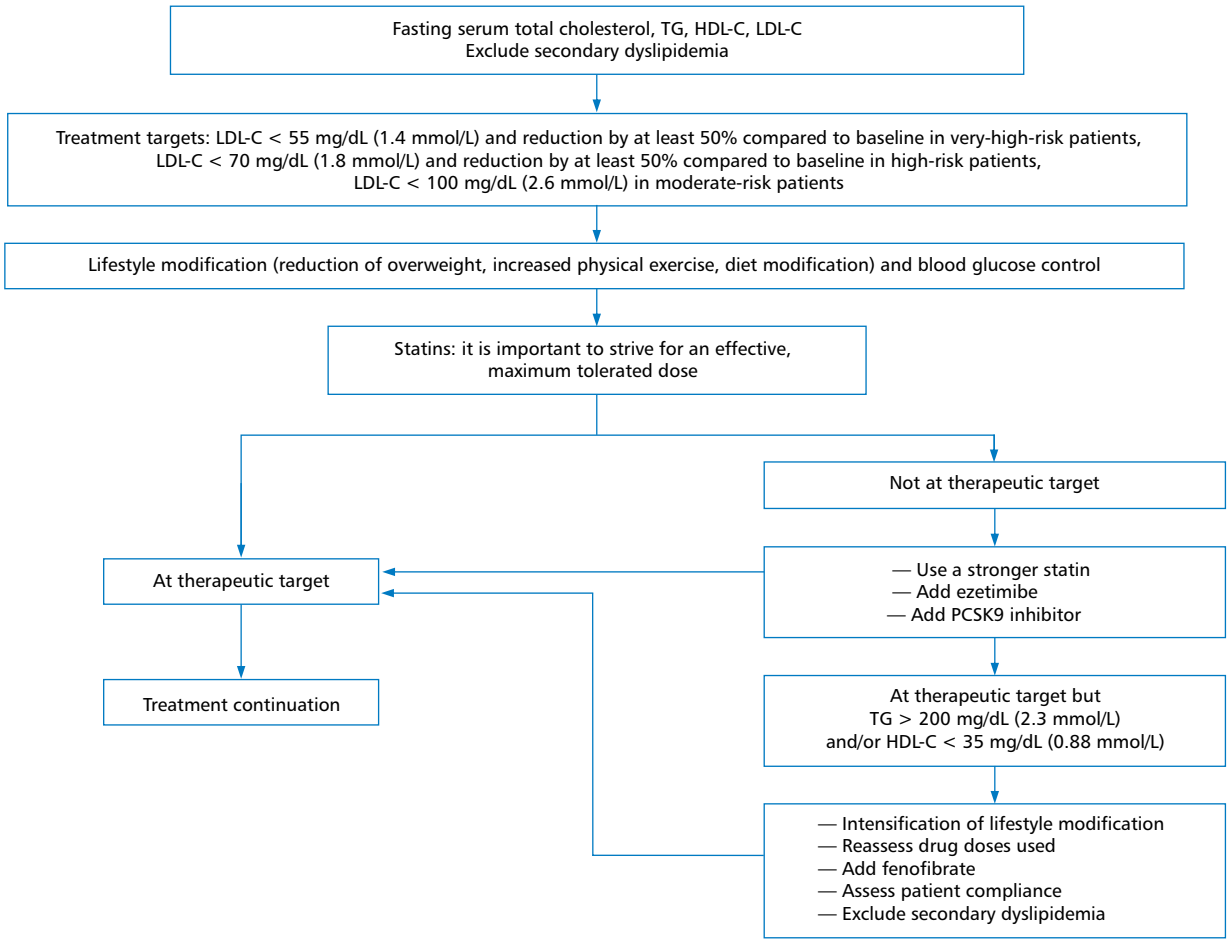

Figure 14.1. An algorithm for managing dyslipidemia in diabetes

Table 14.1. Cardiovascular risk categories and LDL-C and non-HDL-C target levels

Cardiovascular risk categories	Criteria	Target LDL-C and non-HDL-C levels
Very high	Patients with diabetes and cardiovascular disease **OR** target organ damage* **OR** 3 or more major cardiovascular risk factors** **OR** early-onset and long-duration (> 20 years) diabetes type 1	LDL-C < 1.4 mmol/L (55 mg/dL) and 50% reduction in LDL-C (IB) Non-HDL-C < 2.2 mmol/L (85 mg/dL) (IB)
High	Patients with diabetes duration ≥ 10 years, without target organ damage* plus additional risk factors	LDL-C < 1.8 mmol/L (70 mg/dL) and 50% reduction in LDL-C (IA) Non-HDL-C < 2.6 mmol/L (100 mg/dL) (IB)
Moderate	Young patients with type 1 diabetes aged < 35 years or type 2 diabetes aged < 50 years, with diabetes duration < 10 years, without other risk factors	LDL-C < 2.6 mmol/L (100 mg/dL) (IA)

*Target organ damage include: proteinuria or microalbuminuria, impaired renal function (GFR < 30 mL/min/1.73 m^2), left ventricular hypertrophy, retinopathy, and neuropathy

**The major cardiovascular risk factors are: age, hypertension, dyslipidemia, smoking, and obesity

creatitis cases, but pancreatitis may develop already with triglyceride levels > 5 mmol/L (> 440 mg/dL).

The Recommended management includes:

— Hospital admission in case of acute pancreatitis;

— Strict control of triglyceride levels:

- Reduction of the total calorie intake and fat intake (to 10–15% of the total calorie intake);
- Complete abstinence from alcohol;
- Therapy with fenofibrate.

In acute conditions, rapid triglyceride level reduction may be achieved by plasmapheresis.

In diabetic patients who are not treated with insulin, insulin therapy should be started to achieve optimal blood glucose control, most commonly using intravenous insulin pump. This approach allows reduction of triglyceride levels within 2–5 days.

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15. Hypoglycemia

Most important recommendations

- Each diabetic individual diabetes should be asked about the symptoms and frequency of hypoglycemia at each visit. [**C**]
- Each individual at a high risk of clinically significant hypoglycemia (< 54 mg/dL; i.e. < 3.0 mmol/L) should be prescribed glucagon. Family members, caregivers, and teachers involved with diabetic children and adolescents should be aware how to administer glucagon. [**E**]
- Modification of diabetes treatment should be considered if episodes of severe hypoglycemia and hypoglycemia unawareness occur. [**E**]
- When treating hypoglycemia in a conscious patient (with blood glucose level ≤ 70 mg/dL; i.e. 3.9 mmol/L), the key intervention is to administer orally 15 g of glucose or other simple carbohydrates. If repeated blood glucose measurement after 15 minutes still indicates hypoglycemia, the treatment should be repeated. When hypoglycemia resolves, the patient should consume a snack/meal to prevent recurrent hypoglycemia. [**E**]
- In insulin-treated diabetic patients with hypoglycemia unawareness or an episode of severe hypoglycemia, the therapeutic goal should be to maintain somewhat higher blood glucose levels for at least several weeks in order to restore at least partial hypoglycemia awareness and prevent future episodes of hypoglycemia. [**A**]

I. Definition of hypoglycemia. Hypoglycemia is diagnosed when blood glucose level falls below 70 mg/dL (3.9 mmol/L) regardless of clinical symptoms which may occur only with lower blood glucose levels in some patients, particularly those with long-standing diabetes type 1 present for many years. Blood glucose level of 70 mg/dL (3.9 mmol/L) should be considered an alert level that requires carbohydrate consumption or modification of blood glucose-lowering drug doses regardless of the presence or absence of symptoms of hypoglycemia, to prevent further reduction of blood glucose level. This justifies setting the threshold for imminent hypoglycemia at 70 mg/dL (3.9 mmol/L). Clinically significant hypoglycemia should be defined as blood glucose level < 54 mg/dL (3 mmol/L). Symptoms of hypoglycemia may also develop with higher blood glucose levels, even > 100 mg/dL (5.6 mmol/L), if a rapid decrease in blood glucose has occurred. So called hypoglycemia unawareness, defined as unawareness of pathologically low (≤ 70 mg/dL, i.e. ≤ 3.9 mmol/L) blood glucose levels, is a significant complication of frequent hypoglycemia episodes.

Classification of hypoglycemia according to the International Hypoglycemia Study Group (2017) is shown in Table 15.1). Severe hypoglycemia is an episode requiring help of another person to administer carbohydrates, glucagon, or initiate other measures. Exact blood glucose values during the episode may be not available but resolution of symptoms following administration of glucose and/or glucagon is considered a sufficient proof that the episode was caused by low blood glucose levels.

Recurrent severe hypoglycemia: two or more episodes of severe hypoglycemia during last 12 months.

II. General considerations

1. Diabetic subjects should not be automatically considered at risk of hypoglycemia and thus handicapped in terms of employment and the social status.
2. Risk of hypoglycemia is increased in the following situations:
   — Insulin use as monotherapy or in combination with other antidiabetic agents;
   — Sulfonylurea use as monotherapy or in combination with other antidiabetic agents;
   — Inappropriate dosing of the above mentioned agents in the settings of increased physical activity, reduced calorie intake or alcohol consumption;
   — Aiming for rapid HbA_{1c} level normalization;
   — Coexistence of other diseases that promote hypoglycemia (e.g. renal failure, hypothyroidism, adrenal insufficiency, eating disorders, conditions associated with impaired intestinal absorption).
3. Hypoglycemia may be directly life-threatening in some situations (the elderly, patients with ischemic heart disease).

III. Management of recurrent hypoglycemia episodes includes:

— Thorough evaluation of patient's habits and current treatment of diabetes and other conditions;

Table 15.1. Hypoglycemia classification by the International Hypoglycemia Study Group, 2017

Level	Blood glucose level threshold	Comments
Alert glucose level (level 1)	≤ 70 mg/dL (≤ 3.9 mmol/L)	Blood glucose level requiring treatment with simple carbohydrates Indication for an adjustment of blood glucose lowering agent doses
Clinically important hypoglycemia (level 2)	< 54 mg/dL (< 3.0 mmol/L)	Sufficiently low blood glucose level to indicate clinically important hypoglycemia
Severe hypoglycemia (level 3)	No specific value	Hypoglycemia associated with severe cognitive impairment requiring external assistance for recovery

— Education of diabetic individuals regarding the prevention of hypoglycemia (e.g., recommendation to lower insulin dose before the anticipated exercise);
— Modification of diabetes therapy to minimize the risk of hypoglycemia (e.g., by replacing sulfonylurea with another drug associated with a lower risk of hypoglycemia, change of the insulin treatment regimen, switching to another insulin type associated with a lower risk of hypoglycemia, use of an insulin pump, optimally with automatic termination of insulin infusion in case of imminent or incident hypoglycemia, etc.).
— Frequent self-monitoring of blood glucose and use of continuous glucose monitoring (CGM) or intermittently scanned continuous glucose monitoring (isCGM)/flash glucose monitoring (FGM) systems if available for the patient.

IV. Management of hypoglycemia unawareness:

Initiate measures as in recurrent hypoglycemia plus:
— Patient and family member education regarding identification of subtle and atypical prodromes of hypoglycemia (hypoglycemia awareness training);
— Consideration of this problem during professional activities and driving;
— Treatment modifications leading to a significant reduction of hypoglycemia episodes as the only approach to improve hypoglycemia awareness.

V. Acute management of hypoglycemia

1. In a conscious patient:
   — Oral administration of 15 g of glucose and re-evaluation of blood glucose level after 15 minutes. If hypoglycemia persists, another 15 g of carbohydrates should be administered orally and blood glucose level should be measured again after 15 minutes;
   — If there is a risk of recurrent hypoglycemia, e.g. after erroneous administration of an excessive dose of insulin, after alcohol consumption, after prolonged exercise, it is recommended that, in addition to the above described intervention, complex carbohydrates should be consumed and blood glucose level should be monitored.
2. In an unconscious patient or a person with impaired consciousness and unable to swallow:
   — Intravenous administration of 10% or 20% dextrose solution (0.2–0.5 g dextrose/kg body weight); followed by infusion of 10% dextrose with monitoring of blood glucose level if a risk of recurrent hypoglycemia exists;
   — If intravenous access is difficult, administer 1 mg of glucagon intramuscularly or subcutaneously (0.5 mg in children with the body weight of < 25 kg and 1 mg in children with the body weight of > 25 kg); glucagon may also be administered intranasally at 3 mg in subjects > 4 years of age regardless of the body weight;
   — Upon return of consciousness, if there is a risk of recurrent hypoglycemia, oral administration of 10–20 g of carbohydrates and blood glucose monitoring;
   — In patients with diabetes treated with insulin or sulfonylureas, prolonged hypoglycemia may occur that sometimes requires glucose infusion for many hours;
   — If severe hypoglycemia occurs, hospital admission should be considered due to a life-threatening condition associated with a risk of irreversible lesions in the central nervous system, particularly if there is a risk of recurrent hypoglycemia.
3. In patients receiving intensive insulin therapy using insulin analogs or a personal insulin pump, management of hypoglycemia usually includes only administration of 15 g of glucose orally and rechecking blood glucose level after 15 minutes. If blood glucose level continues to be low, glucose should be re-administered and blood glucose level rechecked after further 15 minutes (the 15/15 rule). In case of imminent or incident hypoglycemia in patients treated with a personal insulin pump, interruption of basal insulin infusion and repeated blood glucose measurements are indicated.
4. In patients treated with long-acting insulins (human or insulin analogs) a possibility of delayed recurrent hypoglycemia after initial successful treatment should be taken into consideration.

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16. Management of acute diabetes complications due to hyperglycemia

Most important recommendations

- No large randomized studies are available to support various therapeutic regimens for acute hyperglycemia. Management of diabetic ketoacidosis according to the established regimen is associated with a reduced treatment duration. [**C**]
- In diabetic ketoacidosis, crystalloids are preferred over colloids to replace body fluid deficit. [**C**]
- Continuous intravenous infusion is the preferred method of insulin administration in acute hyperglycemic conditions, and the initial dose (bolus) should be calculated on the basis of the patient's current body mass rather than baseline blood glucose levels. [**C**]
- Acute hyperglycemic conditions, and particularly diabetic ketoacidosis, require potassium supplementation with monitoring of serum potassium level. [**C**]
- Bicarbonate administration is not recommended in diabetic ketoacidosis if blood pH is > 6.9. [**B**]

I. Classification

1. Diabetic ketoacidosis (mortality: 0.2–2%; mortality risk is increased in patients with recurrent episodes of diabetic ketoacidosis).
2. Hyperglycemic hyperosmolar state (mortality — about 15%).
3. Lactic acidosis (mortality — about 50% according to the historical data but currently depends to a large degree on the experience of the treating center, the severity of the underlying disease, and concomitant conditions).

II. Diabetic ketoacidosis

1. Causes:
   — Interruption or errors of insulin therapy;
   — Delayed diagnosis of diabetes type 1;
   — Alcohol abuse, smoking;
   — Acute inflammation (e.g., bacterial, viral, and fungal infections);
   — Pregnancy;
   — Diabetic kidney disease;
   — Other.
2. Diagnosis: see Table 16.1.
3. Differential diagnosis:
   — Fasting ketosis;
   — Alcohol-induced ketoacidosis [blood glucose level rarely > 250 mg/dL (13.9 mmol/L), serum bicarbonate level usually ≥ 18 mmol/L];
   — Metabolic acidosis with anion gap > 20 mEq/L (ethylene glycol, methanol, paraldehyde, or salicylate poisoning);
   — Lactic acidosis (blood lactate level may also increase in ketoacidosis);
   — Other comatose conditions leading to hyperglycemia and ketosis, or the latter accompanied by e.g., stroke or uremic coma.
4. Monitoring of ketoacidosis:
   — Evaluation of blood pressure, heart rate, breathing rate, and the degree of consciousness: every 1–2 hours;
   — Fluid balance: every 1–2 hours;
   — Body temperature measurements: every 8 hours;
   — Blood glucose measurements: every hour;
   — Serum or plasma sodium and potassium measurements: every 4 hours [corrected serum sodium level should be calculated using the formula: measured

Table 16.1 Diagnostic criteria and assessment of the severity diabetic ketoacidosis

	Diabetic ketoacidosis		
	Mild	Moderate	Severe
Plasma blood glucose [mg/dL]*	> 250	> 250	> 250
Blood pH	7.25–7.30	7.00–7.24	< 7.00
Blood $NaHCO_3$ level [mEq/L]	15–18	10–15	< 10
Presence of ketone bodies in urine**	Yes	Yes	Yes
Presence of ketone bodies in serum**	Yes	Yes	Yes
Serum osmolality [mOsm/kg]	Variable	Variable	Variable
Anion gap***	> 10	> 12	> 12
Mental status	Conscious	Conscious/confused	Stupor/coma

*Does not apply to patients treated with SGLT2 inhibitors in whom blood glucose may be lower (euglycemic diabetic ketoacidosis)
**Method using nitroprusside
***According to the formula: Na^+ (mEq/l) – [Cl^- (mEq/l) + HCO3– (mEq/L)]

serum Na^+ + 2.0 mmol/L per each 100 mg/dL (5.6 mmol/L) of blood glucose level above 100 mg/dL (5.6 mmol/L)];
— If serum potassium is > 5.5 mmol/L when potassium is not supplemented: serum potassium measurement after 2 hours; if serum potassium is < 5.5 mmol/L and potassium is supplemented – every 4 hours;
— Blood gases: every 4 hours;
— Baseline blood and/or urine ketones.

5. Management:

A. Patient hydration:
— Water deficit (on average 100 mL/kg body weight) should be corrected intravenously within 24–48 hours with monitoring of the patient's cardiovascular status:
• 1000 mL 0.9% saline within the first hour, followed by:
• 500 mL/h 0.9% saline for 4 hours, followed by:
• 250 mL/h 0.9% saline until normalization of acid-base balance,
• When blood glucose is reduced below 250 mg/dL (13.9 mmol/L), add 5% dextrose infusion at 100 mL/h; if dextrose infusion is added after 24 hours of fluid therapy, decrease the rate of 0.9% saline infusion to 150 mL/h,
• In situations associated with increased energy requirement (e.g., ketoacidosis associated with infection, hyperthyroidism, pregnancy), it is recommended to substitute 10% dextrose for 5% dextrose, administered at the rate of 70 mL/hour;
• In patients with low body weight (< 50 kg), rehydration should be carried out according to pediatric recommendations.

B. Correcting hyperglycemia:
— Intravenous insulin therapy:
• Initial insulin bolus 0.1 unit/kg body weight;
• Followed by intravenous insulin infusion at 0.1 unit/kg body weight/hour with blood glucose monitoring; in patients with a subcutaneous insulin deposit following previous drug injections, intravenous insulin therapy should be initiated with an infusion at 0.1 unit/kg body weight/hour without the initial bolus;
• The rate of infusion should be adjusted depending on current blood glucose level, measured every hour;
• Hourly blood glucose level reduction should be not higher than 100 mg/dL (5.6 mmol/L);
• If plasma glucose level does not fall by 50–70 mg/dL (2.8–3.9 mmol/L) from the baseline value during the first hour, increase (usually double) the rate of intravenous insulin infusion until constant blood glucose level reduction by 50–70 mg/dL (2.8–3.9 mmol/L) per hour is reached.

C. Correction of electrolyte disturbances:
— Potassium deficit in a person with ketoacidosis is 3–5 mmol/kg body weight;
— Potassium supplementation should be carried out according to the following principles:
Serum potassium level:
— K^+ > 5.5 mmol/L → do not administer KCl;
— K^+ 5.0–5.5 mmol/L → 5–10 mmol KCl per hour;
— K^+ 4–5 mmol/L → 10–15 mmol KCl per hour;
— K^+ 3–4 mmol/L → 15–20 mmol KCl per hour;
— K^+ < 3 mmol/L → stop insulin infusion and administer 25 mmol KCl per hour.
Potassium supplementation > 15 mmol/h should be administered via a central venous line or to two peripheral veins.

D. Bicarbonate administration — consider only if arterial blood pH ≤ 6.9 (in small doses, not more than 1 mmol/kg body weight); increased lactate level in ketoacidosis (which is often associated with mild lactate level eleva-

tion due to tissue ischemia) is not an indication for bicarbonate administration.

E. Low-molecular-weight heparin — consider prophylactic dose in patients with severe diabetic ketoacidosis.

6. Treatment adverse effects:
   — Hypokalemia related to insulin administration and correction of acidosis with bicarbonates;
   — Hypernatremia, mostly related to inappropriate administration of sodium bicarbonate (np. pulmonary edema, cerebral edema; intravenous mannitol infusion at 1–2 g/kg body weight during 20 minutes is recommended in case of cerebral edema);
   — Hyperglycemia caused by interruption of intravenous insulin administration following initial improvement, without early initiation of subcutaneous insulin treatment;
   — Hypoglycemia due to overly intensive insulin therapy;
   — Hyperchloremia due to administration of excessive amounts of saline.
7. Complication of diabetic ketoacidosis:
   — Hypovolemic shock;
   — Acute renal failure;
   — Cerebral edema, more commonly in children.
8. Management of acute ketoacidosis in children is shown in Figure 23.1.

III. Hyperglycemic hyperosmolar state

1. Causes:
   — Most commonly develops due to a delayed diagnosis or inadequate treatment of diabetes type 2, in the course of stroke or myocardial infarction, following consumption of large amounts of alcohol, use of some diuretics, in patients with chronic kidney disease, mental health problems, and evidence of infection.
2. Diagnosis

Laboratory diagnostic criteria of a hyperglycemic hyperosmolar state:
   — Blood glucose > 600 mg/dL (> 33.3 mmol/L);
   — pH > 7.30;
   — Serum bicarbonate level > 15.0 mmol/L;
   — Hypernatremia: corrected serum sodium level (calculated using the formula given above) ≥ 150 mmol/L;
   — Serum ketone bodies: absent/trace;
   — Effective plasma osmolality > 320 mOsm/kg H_2O.

Effective plasma osmolality (mOsm/kg H_2O) = 2 [Na^+ (mmol/L)] + blood glucose (mmol/L) {2 [measured Na (mEq/L)] + [blood glucose (mg/dL)]/18}

Normal plasma osmolality is 280–300 mOsm/kg H_2O.

3. Differential diagnosis:
   — Ketoacidotic coma;
   — Comatose states due to central nervous system disease;
   — Uremic coma;
   — Coma due to poisoning.
4. Management

The approach to management is similar to the management of diabetic ketoacidosis:
   — Blood glucose lowering (similar insulin doses as in the management of diabetic ketoacidosis);
   — Normalization of plasma osmolality (with gradual reduction by no more than 3 mOsm/kg H_2O per hour);
   — Subcutaneous administration of a low molecular weight heparin;
   — Correction of water and electrolyte deficits:
     • Water deficit is much larger than in patients with diabetic ketoacidosis;
   — Use of a hypotonic multi-electrolyte solution (0.45% saline or hypotonic multi-electrolyte solution), followed by normal saline when plasma osmolality has been normalized, with monitoring of the patient's cardiovascular status.
     • The rate of saline infusion is determined based on serum sodium level and plasma osmolality;
   — Monitor blood glucose every hour and electrolytes every 4–6 hours.

IV. Lactic acidosis

1. Causes:
   — Type A is due to cardiogenic shock, massive bleeding, septic shock, acute or chronic respiratory failure (it is not characteristic for diabetes) but three fourths of diabetic patients die due to cardiovascular causes; this condition may also occur in diabetic patients;
   — Type B is due to causes other than hypoxemia. It develops in patients with diabetes, liver disease, malignancies, and following ingestion of ethanol, biguanides, salicylates, and methanol.
2. Laboratory diagnostic criteria:
   — Moderately elevated blood glucose (but may also be normal);
   — Reduced blood pH (< 7.30), bicarbonate level < 10 mmol/L, anion gap > 16 mmol/L;
   — Lactate level > 5 mmol/L;
   — Normal serum sodium level (may be reduced in alcohol abuse);
   — Usually increased serum potassium level.
3. Management:
   — Includes the following measures:

- Preventing and counteracting shock (correction of hypovolemia, vasoconstrictors in moderate doses);
- Counteracting hypoxemia and hypoxia;
- Reducing excessive lactate production (glucose and insulin infusion with blood glucose monitoring);
- Alkalization by administration of sodium bicarbonate (requirement: base excess × 0.3 × body mass in kg);
- In some cases, renal replacement therapy may be required (biochemical and/or clinical indications).

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17. Diagnosis and management of ischemic heart disease in patients with diabetes

Most important recommendations

- Acetylsalicylic acid and statin are recommended [**A**], and ACE inhibitor should be considered [**C**] in diabetic patients with ischemic heart disease, if not contraindicated.
- Life-long beta-blocker therapy is recommended after myocardial infarction. [**B**]
- Drugs with an established cardioprotective effect (SGLT2 inhibitors, GLP-1 receptor agonists) should be initiated after myocardial infarction. [**A**]

Ischemic heart disease (IHD) is the major cause of mortality among diabetic patients. Diagnosis and management of IHD and heart failure in this patient population are the same as in subjects without dysglycemia. The dynamic nature of the disease is associated with varying clinical manifestations which may be practically categorized into acute coronary syndromes (ACS) and chronic coronary syndromes (CCS).

The following clinical scenarios are most commonly encountered when CCS are suspected or diagnosed:

— A patient with suspected IHD and "stable" angina and/or dyspnea;
— A patient with newly diagnosed heart failure or left ventricular dysfunction and suspected IHD;
— An asymptomatic or stable patient > 1 year after the diagnosis or revascularization;
— A patient with angina and suspected vasospastic or microvascular angina;
— An asymptomatic patient in whom IHD was diagnosed during screening. All the above scenarios are categorized as CCS but each of them is associated with a different risk of future cardiovascular events which may also change in time.

I. Differences in the clinical course of IHD in diabetic patients indicate the need for follow-up assessment of risk factors in this population at least once a year.

II. Indications for diagnostic, functional, and anatomic investigations to diagnose IHD and stratify risk in diabetic patients (a cardiology consultation) (Figure 17.1):

1. Presence of typical or atypical cardiovascular symptoms or signs.
2. Abnormal resting ECG.
3. Concomitant atherosclerotic lesions in the carotid or peripheral arteries.
4. Planned intensive physical exercise in subjects > 35 years of age who previously lived a sedentary lifestyle.

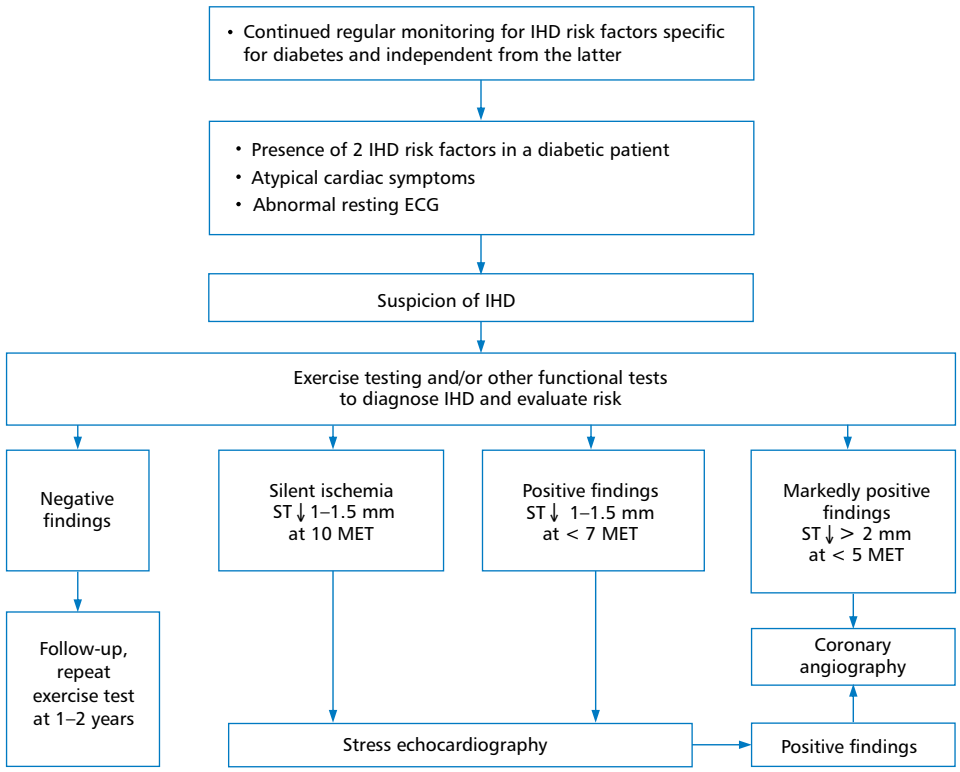

Figure 17.1. An algorithm for the diagnosis of and risk stratification in ischemic heart disease (IHD) in diabetic patients.

5. Diabetes type 1 for > 15 years.
6. Presence of at least two risk factors for IHD in addition to diabetes:
   — Dyslipidemia (see Chapter 4);
   — Hypertension;
   — Smoking;
   — Family history of premature atherosclerosis;
   — Albuminuria;
   — Autonomic neuropathy.

III. Management of stable IHD [chronic coronary syndrome according to the new terminology proposed by the European Society of Cardiology (ESC)] in diabetic patients

1. Initiation of a healthy lifestyle (see Chapter 6).
2. Lipid-lowering therapy to achieve therapeutic targets (see Chapter 4).
3. Reduction or elimination of risk factors for IHD:
   — Blood pressure normalization (see Chapter 13);
   — Treatment of dyslipidemia (see Chapter 14).
4. Drug therapy for IHD in diabetes
   — Antiplatelet therapy — acetylsalicylic acid. Acetylsalicylic acid should be also used in patients > 40 years of age with diabetes type 1 or 2 and an increased cardiovascular event risk (IHD risk > 5% during 10 years). The effectiveness of acetylsalicylic acid in the primary prevention in diabetic patients at low cardiovascular risk has not been established.
   - The recommended acetylsalicylic acid dose is 75–100 mg/day,
   - If acetylsalicylic acid is contraindicated, clopidogrel 75 mg/day may be beneficial although new antiplatelet agents (i.e., prasugrel and ticagrelor) are currently preferred due to their higher effectiveness. If these cannot be used, clopidogrel is recommended,
   - In patients after a percutaneous coronary intervention (PCI), dual antiplatelet therapy with acetylsalicylic acid 75–100 mg/day and clopidogrel 75 mg/day is recommended. In patients after ACS — acetylsalicylic acid 75–100 mg/day and prasugrel 10 mg once daily or ticagrelor 90 mg twice daily as a second drug. If this therapy is not available, clopidogrel 75 mg/day is recommended as the second antiplatelet agent. The duration of dual antiplatelet therapy depends on the presentation of IHD and the type of the implanted stent. Recommended treatment duration is one month after the procedure in stable IHD treated with a bare metal stent (BMS), and 6–12 months after implantation of a drug-eluting stent (DES). In all patients after an acute

coronary syndrome, dual antiplatelet therapy for at least 12 months is recommended;
— Cardioselective beta-blockers or combined alpha$_1$- and beta-adrenergic blockers.
— RAA system inhibitors (ACE inhibitors).

If drug treatment is not effective, coronary revascularization should be considered.

Exercise testing and other functional (stress) tests are used to confirm the diagnosis, document ischemia, stratify risk, and guide selection of the treatment modalities and evaluate their effectiveness. Exercise ECG is still most easily available and thus most commonly performed but its sensitivity and specificity for diagnosing ischemia is limited, particularly in women. Other functional (stress) tests include stress echocardiography, myocardial perfusion scintigraphy, magnetic resonance imaging (MRI), and positron emission tomography (PET). Among anatomical methods, invasive coronary angiography remains the gold standard, although multidetector computed tomography (MDCT) may also be useful. Of note, diabetic patients are usually at high to very high coronary artery disease risk. Functional tests are recommended as first-choice modalities in high-risk patients, while coronary angiography is the major first-choice modality in very high-risk patients. An advantage of MDCT is its high negative predictive value and thus this modality is mostly useful to exclude significant coronary artery disease. However, it is not recommended in high-risk patients, as it results in unnecessary contrast agent and radiation exposure.

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17.1. Management of acute coronary syndromes in patients with diabetes — antihyperglycemic therapy

Most important recommendations

- On admission, blood glucose level should be measured in patients with an acute coronary syndrome, along with HbA_{1c} level in diabetic patients if no current measurement is available. [**A**]
- Intravenous insulin infusion with target blood glucose levels of 100–180 mg/dL is recommended during the first day of an acute coronary syndrome. [**C**]

In acute coronary syndromes, normalization of blood glucose levels using intravenous insulin infusion is recommended in order to maintain relative hyperglycemia, which should be defined as blood glucose level above 140 mg/dL (7.8 mmol/L) in subjects with established diabetes and above 180 mg/dL (10.0 mmol/L) in subjects without a previous diagnosis of diabetes. Intravenous insulin administration is the only approach that allows rapid normalization of blood glucose levels and outcome improvement following an acute coronary syndrome. If possible, a diabetologist should be involved in the management of IHD in patients with dysglycemia.

I. The first day of an acute coronary syndrome

1. Stop oral antidiabetic agents.
2. Measure blood glucose on admission in all patients with an acute coronary syndrome.
3. If blood glucose is above 140 mg/dL (7.8 mmol/L) in subjects with established diabetes or above 180 mg/dL (10.0 mmol/L) in subjects without a previous diagnosis of diabetes, initiate intravenous insulin infusion at the rate shown in Table 17.1.1. Recommended frequencies of blood glucose measurements during daytime: every 1 hour, followed by every 2 hours when blood glucose levels become stabilized. Blood glucose level should be

Table 17.1.1. Approximate insulin infusion rate in relation to blood glucose level

Blood glucose	10% dextrose [ml/hour]	Insulin [unit/hour]
< 100 mg/dL (< 5.5 mmol/L)	50	Stop infusion for 15–30 minutes
100–140 mg/dL (5.5–7.8 mmol/L)	50	0.5–1.0
140–180 mg/dL (6.7–10.0 mmol/L)	50	1.0–2.0
180–250 mg/dL (10.0–13.9 mmol/L)	Stop infusion until blood glucose < 180 mg/dL (10.0 mmol/L) then 50	2.0–4.0
250–300 mg/dL (13.9–17.4 mmol/L)	Stop infusion until blood glucose < 180 mg/dL (10.0 mmol/L) then 50	4.0–6.0

kept at 100–180 mg/dL (5.6–10 mmol/L) by adjusting appropriately the rate of insulin infusion.

4. Serum potassium level should be monitored during insulin infusion.

If blood glucose increases above 180 mg/dL (10 mmol/L), temporarily stop intravenous glucose infusion, restarting it when blood glucose falls to 180 mg/dL (10 mmol/L), and at the same time increase the rate of intravenous insulin infusion.

5. If meals are consumed by the patient, add intravenous boluses of a short-acting insulin.
6. If diabetic ketoacidosis is present, treat accordingly (Chapter 16).

II. From the second day of an acute coronary syndrome until discharge

1. Target blood glucose values during glucose-lowering therapy are 100–180 mg/dL (5.6–10.0 mmol/L) throughout 24 hours. Thus, the treatment must be individualized, preferably in cooperation with a diabetologist.
2. In patients without evidence of acidosis, with dysglycemia diagnosed on the first day of an acute coronary syndrome or with previous successful metformin treatment, appropriate diet may allow adequate metabolic control of diabetes in this period (Chapter 6). In the remaining cases, initiate insulin therapy with multiple injections as described earlier (Chapter 12).
3. In overweight or obese patients with diabetes type 2, metformin may be started before discharge, even as early as on the third day after the coronary intervention, if not contraindicated. A reduction in insulin dose may be possible after 2–3 days of metformin therapy.

III. Following discharge

Metformin should be started in all patients with diabetes type 2 after an acute coronary syndrome, unless contraindicated or not tolerated.

In patients with diabetes type 2 in whom good metabolic control (see II.1 in this chapter) was achieved at the time of discharge and daily insulin requirement does not exceed 30 units, it is possible to return to previous glucose-lowering treatment that was used before the acute coronary syndrome. In overweight or obese patients with diabetes diagnosed during the hospital stay and good metabolic control (see II.1) achieved at the time of discharge, with daily insulin requirement not exceeding 30 units, oral metformin therapy may be used, combined with other agents if needed. If good metabolic control cannot be achieved or daily insulin requirement exceeds 30 units, insulin therapy should be continued. Following an acute coronary syndrome, each patient with dysglycemia should be urgently referred to a diabetologist.

Note 1: In all patients with an acute coronary syndrome, except for those with previously established diabetes, oral glucose tolerance test (see Chapter 1, III, Table 17.1.1.) should be performed before discharge. A consultation with a diabetologist should be conducted if glucose intolerance or diabetes is diagnosed.

Note 2: Metformin should be withdrawn at least 48 hours before elective diagnostic or therapeutic cardiac catheterization/coronary angiography. The drug may be resumed 24 hours after coronary angiography.

Note 3: Randomized trial results indicate an additional cardioprotective effect of SGLT-2 inhibitors and GLP-1 receptor agonists. Addition of these drugs should be considered in patients at high or very high cardiovascular risk.

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18. Stroke in patients with diabetes

Most important recommendations

- Hyperglycemia on admission in the acute phase of stroke is associated with higher mortality, more severe course of stroke, and more severe neurological deficit in both diabetic and non-diabetic subjects. [**A**]
- Available studies do not provide evidence that maintaining normoglycemia in the acute phase of stroke by intravenous insulin therapy improves outcomes. In contrast, such treatment is associated with a higher risk of hypoglycemia. [**A**]
- Current recommendations regarding correction of hyperglycemia in stroke are based only on expert opinion. [**E**]

Diabetes is a strong risk factor for stroke, both ischemic and hemorrhagic. Elevated blood glucose is seen in as many as 60% of patients hospitalized due to an acute stroke. In about 20% of cases, hyperglycemia occurs in subjects with established diabetes, in 16–24% of cases in patients without previous diagnosis of diabetes, and in the remaining cases hyperglycemia is intermittent (stress hyperglycemia).

Hyperglycemia in the acute phase of stroke is an adverse prognostic factor both in diabetic patients and in those without diabetes. Its presence is associated with a risk of a larger ischemic area and its hemorrhagic transformation, a more severe course of the condition, and a worse prognosis (lower degree of patients' independence and increased early and late mortality). Hyperglycemia found on admission often tends to decrease gradually and spontaneously within first several hours to days after the stroke onset.

Few randomized studies performed in the acute phase of stroke (< 72 hours) did not provide evidence that maintaining normoglycemia by intravenous insulin therapy reduced mortality or improved the neurological deficit. Target blood glucose levels in patients with acute stroke are similar to that in other severely ill patients with hyperglycemia. Insulin therapy should be initiated if blood glucose is ≥ 180 mg/dL (10 mmol/L), and blood glucose should be kept at 140–180 mg/dL (7.8–10 mmol/L), avoiding the risk of hypoglycemia.

Insulin should be given intravenously in 0.9% saline using a syringe pump, with strict monitoring of blood glucose levels. The rate of insulin infusion should be modified depending on blood glucose levels measured every 1 hour, and every 2 hours after stable blood glucose values are obtained. A general algorithm for modifying the rate of intravenous insulin infusion depending on blood glucose levels is shown in Table 17.1.1. Serum potassium level should be checked 2–3 times a day during insulin infusion.

It is not recommended to administer insulin as glucose-insulin-potassium (GIK) infusion. Insulin should not be administered subcutaneously during the first two days of stroke or longer in unconscious patients.

Physicians and nursing personnel in the acute stroke care unit should be trained in the treatment of hyperglycemia using a specified intravenous insulin dosing algorithm, with adjustments of the insulin infusion rate in relation to blood glucose levels.

When the patient's condition improves and meals begin to be given orally, intravenous insulin infusion should be stopped and subcutaneous insulin dosing should be initiated. Withdrawal of intravenous insulin should be preceded by subcutaneous administration of a short-acting insulin or rapid-acting insulin analog by about 1 hour before the planned cessation of intravenous insulin infusion. The recommended treatment regimen includes a short-acting insulin or rapid-acting insulin analog before meals and long-acting insulin once or twice daily. In some cases, it is sufficient to give a short-acting insulin or rapid-acting insulin analog before meals. Insulin should be given before food, with dosing based on blood glucose readings immediately before meals.

Due to a high likelihood of diabetes in patients with an acute stroke and no previous diagnosis of diabetes, investigations for diabetes are needed after the patient's condition has stabilized.

The recommendations regarding management of hypertension and other aspects of care for patients with an

ischemic stroke are the same as in non-diabetic patients, as no evidence is available to indicate benefits from any different or specific management of diabetic patients.

Secondary prevention after stroke should be instituted according to the general recommendations in this regard.

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19. Prevention, diagnosis, and treatment of diabetic kidney disease

Most important recommendations

- Screening for increased urinary albumin excretion should be performed annually, beginning at 5 years after the diagnosis in patients with diabetes type 1, since the diagnosis in patients with diabetes type 2, and in all patients with diabetes and concomitant hypertension. [**B**]
- Blood glucose levels, blood pressure values, and lipid parameters should be optimized to decrease the risk of diabetic nephropathy and/or delay its progression. [**A**]
- If an increased urinary albumin excretion is found, therapy with ACEI or ARB should be initiated (unless contraindicated) as these drugs reduce the risk of progression of diabetic nephropathy. [**A**]
- Serum creatinine and potassium should be monitored during treatment with ACEI, ARB, and/or a diuretic. [**E**]

I. In diabetic patients, urinary albumin excretion, serum creatinine, and estimated GFR should be determined to detect and evaluate the severity of diabetic nephropathy. Albuminuria and estimated GFR are independent predictors of cardiovascular and renal risk in diabetic patients.

II. Screening for albuminuria should be performed according to the following principles:

— Testing should be performed annually, beginning at 5 years after the diagnosis of diabetes type 1 and at the time of the diagnosis of diabetes type 2;

To evaluate urinary albumin excretion:

— An albumin/creatinine ratio (ACR) should be determined in a single (spot) urine sample (preferably morning urine sample) — for interpretation of the results see Table 19.1. Increased urinary albumin excretion may be diagnosed when two positive ACR results are obtained.

III. Serum creatinine level in diabetic patients should be measured at least annually regardless of urinary albumin excretion and used for estimation of GFR.

IV. Glomerular filtration rate should be estimated using the CKD-EPI formula:

CKD-EPI formula

$$\text{GFR} = 141 \times \min(\text{SCr}/\kappa, 1)^{\alpha} \times \max(\text{SCr}/\kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018 \text{ (for women)}$$

Where
SCr — serum creatinine
κ = 0.7 for women and 0.9 for men
α = –0.329 for women and –0.411 for men
min = the minimum of SCr/k or 1
max = the maximum of SCr/k or 1

V. Stages of chronic kidney disease are defined in Table 19.2.

VI. If estimated GFR decreases below 60 mL/min/ /1.73 m^2 and non-diabetic nephropathy is suspected, a nephrology consultation should be considered. If estimated GFR decreases below 30 mL/ /min/1.73 m^2, a nephrology consultation should be ordered.

Table 19.1. Definitions of abnormal urinary albumin excretion*

Category	AER [mg/day]	ACR (spot urine sample) [mg/day or mg/g creatinine]*	Albumin excretion [μg/min] in urine collection
A1 normal to slightly increased albuminuria	< 30	< 30	< 20
A2 moderately increased albuminuria	30–300	30–300	20–200
A3 overt proteinuria	> 300	> 300	≥ 200

AER — albumin excretion rate; ACR — albumin/creatinine ratio

*As the amount of albumin excreted with urine per 1 g of creatinine is approximately equal to 24-hour urinary albumin excretion, this approach allows avoiding errors of 24-hour urine collection

Table 19.2. Stages of chronic kidney disease

Category	Description	eGFR [mL/min/1.73 m^2]
G1	Kidney damage* with normal or high eGFR	≥ 90
G2	Kidney damage* with mildly decreased eGFR	60–89
G3a	Moderately decreased eGFR	45–59
G3b	Moderately to severely decreased eGFR	30–44
G4	Severely decreased eGFR	15–29
G5	End-stage renal failure	< 15

eGFR — estimated glomerular filtration rate

*Kidney damage is defined as urinalysis and/or urine sediment abnormalities and/or abnormalities in blood markers of kidney damage and/or imaging studies of the kidneys or urinary tracts persisting for more than 3 months

VII. Recommendations for prevention

1. Blood glucose, blood pressure, and lipid control should be optimized to reduce the risk of nephropathy or delay its progression.
2. Tobacco smoking is an independent risk factor for development and progression of diabetic nephropathy in patients with diabetes type 2.

VIII. Management

1. Therapeutic targets for blood glucose, lipid parameters, and blood pressure as described in Chapter 4 should be aimed for to delay progression of diabetic nephropathy.
2. If albuminuria is found, therapy with ACEI or ARB should be initiated (unless contraindicated) as these drugs reduce the risk of progression of nephropathy.
3. Serum creatinine and potassium should be monitored during treatment with ACEI, ARB, and/or a diuretic.
4. Combining ACEI with ARB is not recommended.
5. Use of a thiazide/thiazide-like diuretic may be considered with estimated GFR ≥ 30 mL/min/1.73 m^2, while a loop diuretic should be used with estimated GFR < 30 mL/min/1.73 m^2.
6. Metformin should not be used in patients with eGFR < 30 mL/min/1.73 m^2. In patients with eGFR 30–59 mL/min/1.73 m^2, metformin doses should be adjusted to renal function (Figure 19.3).
7. In patients with type 2 diabetes mellitus and chronic kidney disease, use of a SGLT2 inhibitor or GLP-1 receptor agonist, the drugs with proven nephroprotective effects, should be considered. These drugs reduce the risk of progression to chronic kidney disease (Figure 19.3).

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Table 19.3. Recommendations regarding the dose of oral antidiabetic drugs and GLP-1 receptor agonists in relation to the severity of renal dysfunction

Stages of chronic kidney disease by KDIGO (eGFR)	Stage G1 and G2 (eGFR > 60 mL/min/1.73m^2)	Stage G3a (eGFR 45–59 mL/ /min/1.73m^2)	Stage G3b (eGFR 30–44 mL/ /min/1.73m^2)	Stage G4 (eGFR 15–30 mL/ /min/1.73m^2)	Stage G5 (eGFR < 15 mL/ /min/1.73m^2)
Metformin			More frequent eGFR measurements if eGFR 30–44. Dose reduced to 500 mg twice daily		
Sulfonylureas		Higher risk of hypoglycemia if eGFR < 60. Consider dose reduction. Gliclazide is the preferred drug due to its hepatic metabolism			
Pioglitazone	Avoid the drug in dialyzed patients				
Alogliptin		Dose reduction to 12.5 mg/day if eGFR < 50		Dose reduction to 6.25 mg/day	
Linagliptin					
Saxagliptin		Dose reduction to 2.5 mg/day. Avoid drug use in dialyzed patients			
Sitagliptin			Dose reduction to 50 mg/day	Dose reduction to 25 mg/day	
Vildagliptin		Dose reduction to 50 mg/day if eGFR < 50			
Canagliflosin (if baseline albuminuria < 30 mg/mmol)	Initial dose 100 mg, gradually increased to 300 mg if needed	Initiate or continue at 100 mg/ /day, discontinue if eGFR < 45			
Canagliflosin (if baseline albuminuria ≥ 30 mg/mmol)		Initiate or continue at 100 mg/day		Continue at 100 mg/day Do not initiate treatment Discontinue in dialyzed patients	
Dapagliflosin	Initiate at 10 mg and discontinue if eGFR < 45, do not initiate if GFR < 60				
Empagliflosin	Initiate at 10 mg/day and gradually increase to 25 mg/day if needed. Do not initiate if GFR < 60	If eGFR decreases to < 60, reduce the dose to 10 mg/day. Discontinue if eGFR < 45			
Dulaglutide					
Exenatide (dosed twice daily)		Increase the dose with caution if creatinine clearance 30–50 mL/min			
Exenatide (dosed once weekly)					
Liraglutide					
Lixisenatide					
Semaglutide	Limited experience in patients with severe kidney dysfunction (eGFR<30)				

No need to adjust the drug dose depending on eGFR

Drug dose adjustment depending on eGFR is recommended

Use of the drug is not recommended with given eGFR values

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20. Diabetic eye disease

Most important recommendations

- Optimization of blood glucose levels, blood pressure values, and lipid parameters reduces the risk of development and progression of diabetic retinopathy. [**A**]
- Fundoscopy after mydriasis should be performed no later than 5 years after the diagnosis in adult patients with diabetes type 1, and at the time of the diagnosis of diabetes type 2. [**B**]
- Retinal laser photocoagulation reduces the risk of vision loss in patients with proliferative retinopathy. [**A**]
- Intravitreal injections of anti-VEGF agents may improve vision in patients with macular edema. [**A**]
- Treatment with acetylsalicylic acid used for cardioprotection is not contraindicated in patients with retinopathy and does not increase the risk of retinal hemorrhage. [**A**]

Diabetic complications involve nearly all anatomic structures of the visual system. The most common and most severe complication, with a threat of vision loss, is diabetic retinopathy and related diabetic macular edema. Retinopathy is a highly specific neurovascular complication of diabetes, both type 1 and type 2. Among extraretinal diabetic complications, clinically the most important are diabetic cataract and secondary (hemorrhagic) glaucoma. The recommendations given below take into account the new classification of diabetic retinopathy.

Prevention, diagnosis, and management of diabetic retinopathy

I. Natural history and classification of diabetic retinopathy

1. No evidence of diabetic retinopathy.
2. Mild non-proliferative diabetic retinopathy (NPDR) — presence of microaneurysms only.
3. Moderate non-proliferative diabetic retinopathy — more advanced changes than in a mild form but less advanced than in a severe form.
4. Severe non-proliferative diabetic retinopathy:
   — Microhemorrhages (> 20) in 4 retinal quadrants; and/or
   — Venous beading in least 2 quadrants; and/or
   — Intraretinal microvascular abnormalities in at least 1 quadrant.
5. Proliferative diabetic retinopathy (PDR) (retinal neovascularization and connective tissue growth) leading to vision loss in the mechanisms of:
   — Recurrent bleeding to the vitreous body from the retinal neovessels;
   — Retinal detachment due to its traction by proliferative membranes;
   — Development of glaucoma.

II. Natural history and classification of diabetic macular edema

1. No evidence of diabetic macular edema.
2. Mild diabetic macular edema — lesions away from the macular center.
3. Moderate diabetic macular edema — lesions close to the macular center.
4. Severe diabetic macular edema — lesions involving the macular center.

III. Risk factors for the development and progression of diabetic retinopathy

1. Duration of diabetes — the strongest prognostic factor for the development and progression of diabetic retinopathy.
2. Poor metabolic control of diabetes:
   — Intensive treatment reduces the risk of the development and progression of retinopathy in patients with diabetes type 1;
   — Intensive treatment of diabetes type 2 reduces the rate of microangiopathic complications and reduction of HbA_{1c} level by 1% is associated with a significantly reduced risk of the development of microangiopathy.
3. Hypertension.
4. Lipid disorders.

5. Diabetic nephropathy.
6. Pregnancy in diabetic women.
7. Period of adolescence.
8. Surgery for cataract.
9. Following kidney and pancreas or kidney transplantation.

IV. Diagnosis of diabetic retinopathy

1. Assessment of visual acuity.
2. Assessment of color identification.
3. Fundoscopy (using an ophthalmoscope, always with mydriasis).
4. Digital color photographs of the eye fundus used mostly for screening (they do not replace complete ophthalmologic examination).
5. Fluorescein angiography of the eye fundus:
   — Indications:
   - Identification of moderate and severe preproliferative retinopathy;
   - Identification of early neovascularization foci in proliferative retinopathy;
   - Evaluation of the effectiveness of laser photocoagulation;
   - Investigation of an unexplained decrease in visual acuity.
6. Wide-angle scanning laser ophthalmoscopy.
7. Optical coherent tomography — the major method for the diagnosis and monitoring of macular edema.
8. Ultrasound — particularly in patients with vitreous body hemorrhage.
9. Confocal microscopy (evaluation of corneal lesions as an early indicator of neuropathy).

V. Indications for ophthalmologic examination in diabetic patients

1. Initial examination
   — In diabetes type 1 — should be performed within 5 years after the diagnosis;
   — In diabetes type 2 — should be performed at the time of the diagnosis or shortly after the diagnosis.
2. Follow-up examinations and management:
   — Indicated due to an initially asymptomatic nature of retinopathy.
   — Frequency should depend on the degree of severity of diabetic retinopathy:
   - No retinopathy at baseline — every 1–2 years;
   - Early non-proliferative retinopathy — every 6––12 months;
   - More severe non-proliferative retinopathy — every 3 months;
   - Severe non-proliferative retinopathy — urgent laser therapy;
   - Proliferative retinopathy — urgent laser therapy or consideration of other ophthalmologic procedures (e.g. vitrectomy);
   - Diabetic macular edema — urgent laser therapy in extrafoveal disease; intravitreal anti-VEGF injections and possibly laser therapy in foveal disease;
   - Following retinal laser treatment — one month after the procedure;
   - Following vitrectomy — individualized follow-up depending on the condition of the eye fundus;
   - In pregnant diabetic women — every 1–3 months throughout the pregnancy depending on the condition of the eye fundus;
   - In women contemplating pregnancy — before conception, with retinal laser treatment at that time if needed.
3. Urgent indications for ophthalmologic examination:
   — Risk of vision loss:
   - Presence of proliferative retinopathy;
   - Presence of advanced eye complications (retinal neovascularization, vitreous body hemorrhage, acute retinal detachment).
   — Presence of changes potentially associated with a risk of vision loss:
   - Severe non-proliferative retinopathy;
   - Non-proliferative retinopathy with diabetic macular edema;
   - Other difficult-to-interpret abnormalities in the eye fundus or an unexplained decrease in visual acuity;
   - Pregnancy.

The recommended frequency of ophthalmologic examination in specific patient groups is summarized in Table 20.1.

VI. Screening

Screening for diabetic retinopathy may be performed under mydriasis by an ophthalmologist using an ophthalmoscope or a trained personnel using a fundus camera based on color photographs of the eye fundus. Screening may also be performed by telemedicine using a fundus camera, with evaluation of photographs by skilled personnel or using dedicated image-analysis software. Color eye photographs have a great potential for follow-up services at the areas where the access to skilled specialists is limited. Photography of the retina may thus serve as a screening tool in retinopathy but it cannot replace the comprehensive ophthalmologic examination which should be performed at least at the onset of the disease, and then as recommended by the ophthalmologist.

If no retinal changes are found during the first two years in patients with diabetes type 1, the eye fundus may be subsequently assessed every 2 years. In patients with diabetes

Table 20.1. Recommended frequency of ophthalmologic examinations in various patient groups

Initial examination	
Diabetes type 1	**Diabetes type 2**
Initial 5 years after the diagnosis (when diagnosed during puberty — shortly after the diagnosis)	At the time of the diagnosis
Follow-up examinations and treatment	
Severity of retinopathy	**Frequency of examinations and treatment**
No retinopathy	Every 1–2 years
Non-proliferative mild or moderate	Every 6–12 months
Non-proliferative severe	At least every 3–6 months
Proliferative	Urgent laser therapy
Diabetic macular edema:	
• extrafoveal	Urgent laser therapy
• intrafoveal	Intravitreal anti-VEGF injections + optionally laser therapy
Follow-up after ophthalmologic procedures in special situations	
After laser treatment	Depending on fundoscopy findings
After vitrectomy	Depending on fundoscopy findings
Pregnant women	Every 1–3 months depending on fundoscopy findings
Women planning pregnancy	Before conception; laser therapy at that time
Uncontrolled diabetes, hypertension or proteinuria	Every 1–6 months depending on fundoscopy findings

type 2 and good metabolic control, if no retinal changes are present, the eye fundus may be assessed every 2–3 years.

In women with diabetes type 1 and 2, ophthalmologic examination should be performed before pregnancy or in the first trimester, and then repeated in each trimester and for a year after the delivery to evaluate the degree of retinopathy.

Regular follow-up eye fundus examinations and appropriate treatment allow reduction of vision loss due to diabetic retinopathy by 98%.

The screening strategies developed allow for a significant, several-fold reduction of the risk of blindness and reduce treatment costs in patient with diabetic eye complications.

VII. Management of diabetic retinopathy

1. Treatment intensification in patients with poor metabolic control of diabetes, intensive treatment of hypertension, primarily using ACEI and ARB, and treatment of dyslipidemia (fenofibrate, statins). Acetylsalicylic acid used for cardioprotection is not contraindicated in patients with retinopathy and does not pose a risk of retinal hemorrhage.
2. In diabetic macular edema with foveal involvement and vision loss, the recommended first-line treatment are intravitreal injections of anti-VEGF agents aflibercept, ranibizumab, and bevacizumab, optionally in combination with retinal laser therapy. Bevacizumab is used off-label for this purpose and its effectiveness in patients with more severe vision loss is lower.
3. Retinal laser photocoagulation (possible if the optical system of the eye is clear):
   — Early retinal laser photocoagulation reduces progression of diabetic retinopathy;
   — Types of retinal laser photocoagulation:
   • Subthreshold (mostly micropulse) — without tissue coagulation, used in macular edema without its significant thickening and vision loss;
   • Focal — recommended in early extrafoveal diabetic macular edema;
   • Grid-type — in diffuse diabetic macular edema, when the first-line treatment was not effective,
   • Panphotocoagulation — recommended in severe non-proliferative and proliferative retinopathy.
4. Intravitreal or periocular injections of steroids exerting an antiangiogenic and antiedematous effect, e.g. triamcinolone, dexamethasone, or extended-release fluocinolone acetonide, may be considered first-line treatment if contraindications to anti-VEGF agents are present or the monthly visit regimen cannot be maintained.
5. Vitrectomy:
   — Indications:
   • Vitreous hemorrhages unresponsive to other therapies;
   • Vitreomacular tractions running vertically towards the macula;
   • Advanced complicated proliferative retinopathy.
6. In irreversible vision loss, a low vision and blindness specialist should be consulted with view to appropriate rehabilitation.
7. In mild and moderate retinopathy with hard exudates, sulodexide at 250 LSU twice daily may be used.

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21. Prevention, diagnosis, and management of diabetic neuropathy

Most important recommendations

- In patients with diabetes type 1, maintaining optimal blood glucose control since the diagnosis is of key importance for primary and secondary prevention of diabetic neuropathy, both peripheral and autonomic involving the cardiovascular system. [**A**]
- In addition to detailed history, investigation for diabetic neuropathy should include evaluation of thin fiber (pain and/or temperature sensation) and thick fiber (vibration sensation) function. Pressure sensation should be evaluated annually in each patient using a 10 g monofilament to assess for the risk of diabetic foot ulceration. The evaluation should be performed at 5 years since the diagnosis of diabetes type 1 and at the time of the diagnosis of diabetes type 2. [**B**]
- Pregabalin, gabapentin, or duloxetine should be considered as first line medications for neuropathic pain in patients with diabetes. [**A**]

I. Distal symmetric polyneuropathy causes severe complaints, significantly reduces the quality of life, and is an established risk factor for the development of diabetic foot syndrome with ulceration and Charcot neuroarthropathy. Neuropathy increases the risk of amputation, fractures, and falls, increases treatment costs, and is a predictor of mortality. Autonomic cardiovascular neuropathy is an independent risk factor for increased mortality in diabetes. Neuropathy may develop already in prediabetes. For that reason, evaluation for neuropathy should be considered also in prediabetic individuals with symptoms of peripheral neuropathy.

II. Clinical classification of neuropathy:

1. Generalized symmetrical polyneuropathy:
— Chronic sensorimotor peripheral;
— Autonomic;
— Acute sensory.
2. Focal and multifocal neuropathies:
— Involving cranial nerves;
— Involving spinal nerves (thoracic and lumbar);
— Focal limb neuropathies, including compression syndromes;
— Proximal motor neuropathy (amyotrophy).

III. Approach to testing for neuropathy:

1. Testing frequency:
— Evaluation for the evidence of diabetic neuropathy should be performed at least once a year. For the first time:
  - Diabetes type 1 — at 5 years after the diagnosis, unless symptoms suggesting neuropathy develop earlier;
  - Diabetes type 2 — at the time of the diagnosis;
2. Other, non-diabetic etiologies of the peripheral nervous system damage should be considered/ /excluded.

3. In doubtful cases, neurological consultation is indicated.

IV. Diagnostic criteria of diabetic neuropathy

Distal symmetric polyneuropathy

1. Diagnostic methods:

— Tactile sensation using a 10 g monofilament (Semes-Weinstein 5.07);
— Vibration sensation using a biothesiometer or 128 Hz tuning forks;
— Pain sensation using a sterile needle;
— Temperature sensation using a rod with two different (metal and plastic) ends;
— Deep tendon reflexes;
— Muscle strength test;
— Electroneurophysiological testing.

2. Diagnostic principles:

— Symptoms: abnormal sensation, numbness, burning, tingling, spontaneous pain, muscle jerks and cramps, mostly involving feet and calves, persisting for several months (worsened or occurring mostly during the night; exercise does not cause or worsen symptoms);
— Signs: reduced muscle power, reduced or absent tendon reflexes (knee, ankle), reduced or absent vibration, tactile, pain and temperature sensation;
— Peripheral diabetic neuropathy is considered probable based on the presence of 2 out of the following 3 components of the clinical examinations: symptoms, reduced or absent sensation (touch, vibration, pain, and/or temperature) and/or absent tendon reflexes;
— In painful neuropathy, these elements of the physical examination may be normal; in case of typical complaints, neuropathy may be diagnosed even with normal physical examination findings.
— Electroneurophysiological testing may be necessary in selected patients to make a definite diagnosis of neuropathy and possibly for the differential diagnosis; this is particularly recommended with rapid progression of symptoms, asymmetry, predominance of motor neuropathy, or a suspicion of non-diabetic cause;
— In patients with unclear clinical picture, evaluation of corneal nerve fiber density by confocal microscopy or skin biopsy may also be used for the diagnosis of thin fiber neuropathy.

Autonomic neuropathy

Autonomic nervous system function is evaluated indirectly based on the analysis of effector organ function in response to specific stimuli. Due to a non-specific nature of clinical symptoms and signs, the diagnosis should be supported by specific tests. It is necessary to exclude other disease of the effector organ, take into account other organic and functional abnormalities, and exclude an effect of the treatment used.

Autonomic neuropathy mostly manifests with hypoglycemia unawareness, resting tachycardia, orthostatic hypotension, gastroparesis, constipation or diarrhea, erectile dysfunction, neurogenic bladder, or sudomotor dysfunction.

1. Cardiovascular system

Cardiovascular autonomic neuropathy is diagnosed based on the results of tests evaluating heart rhythm variability.

Autonomic neuropathy is considered as 'probable' or 'early' in the case of one abnormal test result, and as 'confirmed' when the results of two of the tests listed below are abnormal. Severe (advanced) cardiovascular autonomic neuropathy is diagnosed in case of abnormal heart rhythm variability testing results and abnormal blood pressure response to the upright posture.

— Tests evaluating the parasympathetic nervous system:
  • Heart rhythm change during deep breathing;
  • Heart rhythm change in response to the upright posture;
  • Heart rhythm change in response to the Valsalva manoeuver;
— Tests evaluating the sympathetic nervous system:
  • Blood pressure change in response to the upright posture.

2. Gastrointestinal system:
— Gastric dysfunction — barium radiography, radioisotope scanning, breathing tests, electrogastrography (EGG), manometry, ultrasonography;
— Small intestine dysfunction — no specific diagnostic tests, exclusion of other causes, manometry, wireless diagnostic capsule – abnormal intestinal motility;
— Large intestine dysfunction — exclusion of other causes (endoscopy), barium follow-through, manometry, wireless diagnostic capsule;
— Gall bladder dysfunction — functional ultrasound.

3. Genitourinary system
— Bladder dysfunction — cystometry (evaluation of bladder volume before and after micturition); bladder sphincter electromyography, uroflowmetry and urethral pressure profile;
— Erectile dysfunction — questionnaires [International Index of Erectile Function (IIEF) and its abbreviated 5-item version (IIEF-5)], vascular studies (Doppler ultrasound), cavernosography, hormonal testing, psychological tests, regional evaluation of vibration sensing threshold, functional testing — nocturnal penile tumescence tests.

4. Dysfunctional sudomotor function — simple perspiration tests, testing using sophisticated equipment (evaluation of sudomotor function using Sudoscan).

5. Pupil dysfunction — pupillometry.

Table 21.1. The algorithm for drug treatment of symptomatic neuropathic pain in somatic diabetic neuropathy. Effective drug doses are given. Gradual dose increase is necessary. If one on first-line drugs is not effective, an alternative drug or combined therapy is indicated. Chronic use opioids is not recommended. At each stage, non-pharmacological methods (physical therapy, acupuncture) may be used

First line treatment — one of the following drugs		Effective doses
Anticonvulsants	Pregabalin	300–600 mg/day
	Gabapentin	900–3,600 mg/day
Selective serotonin and norepinephrine reuptake inhibitors	Duloxetine	60–120 mg/day
	Venlafaxine	75–225 mg/day
Second line treatment		
Tricyclic antidepressants	Amitriptyline	25–100 mg/day
Opioids	Tramadol	200 mg/day
	Tapentadol	Starting at 50 mg twice daily, maximum dose 500 mg/day
Topical medications	Capsaicin, lidocaine	

V. Management

Diabetic neuropathy is asymptomatic in about 50% of cases. The causal treatment is blood glucose control. Optimization of blood glucose control should be promptly initiated in patients with diabetes type 1 and 2 to prevent and/or delay development of neuropathy. In patients with neuropathic pain, treatment of the latter is absolutely necessary as pain impairs the quality of life and patient functioning, and may lead to depression. Various therapeutic options are available for the symptomatic treatment of pain. Treatment of autonomic neuropathy relieves symptoms and improves the quality of life and patient outcomes but is often challenging and its effectiveness is a subject to individual variation.

1. Causal treatment of diabetic neuropathy:
   — Optimal metabolic control of diabetes, with particular attention to avoiding hypoglycemia and large diurnal blood glucose level excursions, is of key importance for the management of diabetic neuropathy;
   — Blood pressure and lipid control, smoking cessation, avoiding alcohol use;
   — Drug therapy: alpha-lipoic acid, benfotiamine, ACEI.
2. Symptomatic treatment of neuropathic pain in somatic diabetic neuropathy (the analgetic effect of the treatment is patient-specific) — Table 21.1.
3. Symptomatic treatment of autonomic diabetic neuropathy:
   — Cardiovascular system:
   • Cardiac arrhythmia — controlled graded exercise, ACEI, beta-blockers (without intrinsic sympathomimetic activity);
   • Orthostatic hypotension — compression clothing to increase venous return, increased salt intake, isometric exercises, mineralocorticoids (fludrocortisone), alpha1-adrenergic receptor agonists (midodrine);
   — Gastrointestinal system:
   • Gastroparesis — diet modification (frequent small meals, semiliquid or liquid diet in severe dysfunction), prokinetic drugs (cisapride, itopride, erythromycin, trimebutine), acid reducers (H2 receptor antagonists, proton pump inhibitors), antiemetics, surgical treatment, gastric electrical stimulation therapy;
   • Intestinal dysfunction — diet modifications (consider gluten- or lactose-free diet), cholestyramine, clonidine, octreotide, antidiarrheals (loperamide), pancreatic enzymes, antibiotics;
   — Genitourinary system:
   • Bladder dysfunction — avoiding urinary retention, regular micturition, anticholinergic drugs (bethanechol), external bladder massage before micturition, bladder catheterization (temporary or permanent);
   • Erectile dysfunction — psychotherapy, phosphodiesterase type 5 inhibitors (sildenafil, vardenafil, tadalafil), vacuum penile pump devices, intracavernosal prostaglandin E1 injections, penile prostheses;
   • Female sexual dysfunction — psychotherapy, mechanical stimulating devices, topic moisturizers, flibanserine;
   — Dysfunctional perspiration:
   • Botulinum toxin, vasodilators, moisturizing creams.

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22. Diagnosis and management of diabetic foot syndrome

Most important recommendations

- Maintaining optimal blood glucose levels, lipid parameters, and blood pressure values reduces the risk of the diabetic foot syndrome. [**A**]
- Effective treatment of the diabetic foot syndrome may only be provided within multidisciplinary clinics. [**B**]
- The gold standard for off-loading of non-infected neuropathic foot is total contact cast that includes the foot and the lower leg. [**A**]
- The key interventions in the treatment of the diabetic foot syndrome are surgical wound debridement, systemic antibiotic therapy for infections, and vascular interventions for foot ischemia. [**A**]

Multidisciplinary (reference) diabetes foot clinics should be created in regional (voivodship, university) diabetologic centers, and basic diabetes foot clinics should be created at diabetology clinics to continue care initiated in a multidisciplinary clinic.

Organizational structure and responsibilities in accordance with the Diabetes Foot Outpatient Treatment Support Program by the Ministry of Health (*www.mz.gov.pl/zdrowie-i-profilaktyka/programy-zdrowotne/wykaz-programow/program-wsparcia-ambulatoryjnego-leczenia-zespolu-stopy-cukrzycowej/*).

I. Definition

Diabetic foot is a foot infection and/or ulceration and/or deep tissue (e.g., bone) destruction caused by a varying degree of damage to peripheral nerves and/or pedal vessels. Implied in the definition is further categorization of this condition into neuropathic, vascular, and mixed diabetic foot.

Investigations in the diabetic foot syndrome include evaluation for peripheral polyneuropathy, leg ischemia, deformations, and other risk factors for foot damage. If a loss of protective pain sensation has been identified, it is recommended that physicians directly inspect patients' feet during each visit.

II. Risk factors for diabetic foot syndrome:

— Peripheral neuropathy and/or vascular ischemic changes within lower limbs;
— Low patient knowledge;
— Long-lasting, poorly controlled diabetes;
— Inappropriate foot hygiene;
— Inappropriate footwear;
— Presence of corns and calluses;
— Foot deformations;
— Increased sole pressure;
— Smoking.

Factors contributing to disease recurrences:

— Previous amputations;
— History of ulcerations;
— Neuropathic arthropathy (Charcot foot).

III. Prevention:

— Systematic foot examination; yearly evaluation for abnormal sensation (physical examination) and ischemia [assessment of dorsalis pedis and posterior tibial artery pulses; consider measurement of the ankle-brachial index (ABI)] in all patients; the frequency of foot examination should depend on the risk of wound development as shown in Table 22.1);
— Regular podiatric care (removal of calluses and hyperkeratosis);
— Systematic patient education regarding prevention of ulcerations, with particular focus on the appropriate footwear choices;
— Education and systematic treatment of other risk factors such as smoking, overweight, hypertension,

Table 22.1. Foot screening frequency according to the risk of ulcer (IWGDF risk stratification system)

Category	Ulcer risk	Characteristics	Frequency
0	Very low	No loss of protective sensation, no ischemia	Once a year
1	Low	Loss of protective sensation or ischemia	Once every 6–12 months
2	Moderate	Loss of protective sensation and ischemia or loss of protective sensation + foot deformity or ischemia + foot deformity	Once every 3–6 months
3	High	Loss of protective sensation or ischemia and one or more of the following: • history of foot ulcer • a lower extremity amputation • end-stage renal disease	Once every 1–3 months

Table 22.2. The PEDIS classification

	Degree of severity			
	1	2	3	4
Perfusion	Normal: palpable pedal pulses or ABI > 0.9	Clinical evidence of impaired perfusion: intermittent claudication, ABI < 0.9, $TcpO_2$ 30–60 mm Hg	Critical ischemia: resting pain, ABI < 0.4, $TcpO_2$ < 30 mm Hg	
Extent	Ulceration size in square centimeters			
Depth	Superficial ulceration within the dermis	Ulceration may involve all soft tissues	Penetration to bone: osteolysis in X-ray or positive probe-to-bone test	
Severity of infection	No clinical evidence of infection	Infection involving the skin and subcutaneous tissue, inflammation within 2 cm from the margin of the ulceration	Locally severe inflammation, beyond 2 cm from the margin of the ulceration, but no evidence of a systemic infection	Evidence of a systemic infection: fever > 38°C, heart rate > 90 bpm, breath rate > 20/min, leukocyte count > 12,000/mm^3 or < 4000/mm^3
Sensory neuropathy	No evidence of sensory neuropathy in basic tests (using a monofilament and tuning forks or Neurotip)	Sensory neuropathy present		

ABI — ankle-brachial index; $TcpO_2$ — transcutaneous oxygen pressure

and dyslipidemia, along with good metabolic control of diabetes;
— Early identification and treatment of limb ischemia;
— Walking training can be recommended in patients with ischemia only in the absence of sole ulcerations.

IV. Clinical classification of diabetic foot syndrome

The PEDIS (Perfusion, Extent, Depth, Infection, Sensation) classification, which takes into account both infections and the ischemic factor (Table 22.2), and the SINBAD (Table 22.3) classification are recommended.

V. Infections in the course of diabetic foot

1. The diagnosis is mostly based on the clinical picture (the presence of at least two typical symptoms and signs of infection) and not only microbiological testing results.
2. Evaluation of the severity of infection (see the PEDIS classification).
3. Microbiological testing (including antibiotic susceptibility) and its interpretation (colonization, contamination, infection):
   — It is recommended to collect tissue samples, aspirate, or scrapings for culture following wound debridement;
   — Testing is necessary if a clinically infected wound is present;
   — When evaluating infection, interpretation of the culture result is difficult, and it is recommended that this evaluation is primarily based on the clinical picture;

Table 22.3. SINBAD Classification

Category	Definition	Score
Site	Forefoot	0
	Midfoot and hindfoot	1
Ischemia	Pedal blood flow intact: at least one palpable pulse	0
	Clinical evidence of ischemia	1
Neuropathy	Protective sensation intact	0
	Protective sensation lost	1
Infection	None	0
	Present	1
Area	$< 1\ cm^2$	0
	$\geq 1\ cm^2$	1
Depth	Ulcer confined to skin and subcutaneous tissue	0
	Ulcer reaching muscle, tendon or deeper	1
Total		6

— Blood culture is recommended only in case of systemic evidence of an infection;
— Culture is not indicated if the wound is clinically not infected; if there is a mild clinical wound infection, and no antibiotics were used previously, it is acceptable not to perform culture and institute empiric antibiotic therapy.

4. Evaluation for osteomyelitis (should be performed in all cases of an infected ulceration, particularly if chronic):
   — Probe-to-bone test;
   — Foot radiography (every 3–6 weeks);
   — Magnetic resonance imaging (indicated);
   — Bone biopsy or bone sample culture and histopathology (indicated); bone biopsy is necessary if the diagnosis of osteomyelitis is questionable or if there is a need to identify the pathogen;
   — Laboratory tests — erythrocyte sedimentation rate > 70 mm at one hour indicates an increased likelihood of osteomyelitis, and lower rates indicate a lower risk. Evaluation of C-reactive protein (CRP) level and leukocyte count may also be useful. A possibility of bone inflammation cannot be definitely excluded based on normal laboratory test results.
5. The nature of the wound (dry or exudative) is the primary criterion for the choice of dressing.

A. Approach to antibiotic therapy:
— Use only for a confirmed infection (do not use prophylactically);
— Do not delay therapy.
— Initially, use an antibiotic covering the most common causative bacterial flora (staphylocci and streptococci);
— In grade 4 infections by the PEDIS classification, provide coverage also for Gram-negative bacteria and anaerobes;
— Duration of antibiotic therapy — until resolution of the infection and not just healing of the ulceration:
  • Grade 2 infection by the PEDIS classification — usually 1–2 weeks, in some cases longer (in particular in immunocompromised patients and those with limb ischemia);
  • Grade 3–4 infection by the PEDIS classification — 2–4 weeks;
— Route of administration:
  • Intravenous — grade 4 infection by the PEDIS classification, some cases of grade 3 infection (MRSA, *P. aeruginosa*), intolerance of oral antibiotics;
  • Oral — grade 2–3 infection by the PEDIS classification, following improvement of grade 4 infections;
  • Topical — use of collagen sponge with gentamycin (garamycin sponge) may be considered as an adjunct to systemic antibiotic therapy;
  • Intraarterial — not recommended.

B. Choice of antibiotics
— Severe infections:
  • Intravenous therapy — ciprofloxacin + clindamycin, amoxicillin-clavulanate or piperacillin-tazobactam, or carbapenem + vancomycin until a MRSA infection is excluded;
  • Oral continuation — amoxicillin-clavulanate and cotrimoxazole (doubled dose) or ciprofloxacin 750 mg twice daily or moxifloxacin + linezolid;
  • MRSA infection: linezolid, vancomycin;
— Less severe infections:
  • Usually oral therapy, using similar antibiotics as in severe infections, e.g.:
  • Gram-positive bacteria: semisynthetic penicillins/ /first-generation cephalosporins;
  • Recent antibiotic therapy, Gram-positive or Gram negative bacteria: fluorochinolones, beta-lactams or if allergy to beta-lactams: clindamycin, fluorochinolones, cotrimoxazole;
— Management of osteomyelitis (no consensus treatment approach):
  • Surgical removal of the affected bone (small amputation);
  • Antibiotic therapy as in severe infections;
  • Monitoring of the treatment effectiveness: laboratory tests (erythrocyte sedimentation rate, CRP), foot radiographs.

VI. Multidisciplinary management of the diabetic foot syndrome

Effective treatment of the diabetic foot syndrome may only be provided within multidisciplinary clinics. This concept encompasses an organizational structure that allows patient access to the required specialists knowledgeable and experienced in the treatment of diabetic foot syndrome who form a therapeutic team and communicate with each other.

The management of the diabetic foot syndrome includes:

— Metabolic control of diabetes: insulin therapy (intensive insulin therapy is preferred), treatment with oral antidiabetic agents is acceptable in some cases if it allows appropriate metabolic control of diabetes and insulin treatment is not required;

— Foot off-loading: temporary footwear to off-load the forefoot or hindfoot, compensatory footwear for the healthy foot, therapeutic insoles, crutches, wheelchair, total contact cast in case of forefoot or midfoot ulcerations (conventionally a plaster cast but may also be a plastic one, optimally up to the knee level but may also be up to the ankle level if the former is not possible or not accepted by the patient), specialized footwear, limiting mobility also in home conditions. In other locations (e.g., heel) and with limb infection and/or ischemia, removable off-loading devices are the first and second choice treatment. The factors to consider when making the decisions regarding the approach to limb off-loading include the patient status and fitness level, other concomitant conditions, patient preferences, and therapeutic team competences. In many patients (particularly with the loss of preventive pain sensation, ischemia, and existing deformations), it is recommended to use appropriate footwear insoles to prevent ulcerations or their recurrences by correcting excessive pressure acting on the foot sole.

— Antibiotic therapy (oral or intravenous), see above;

— Surgical treatment — removal of necrotic tissues, drainage, incisions;

— Intravascular and vascular surgical procedures, hybrid procedures (diabetic foot with a predominant ischemic etiology — patients with low ABI (< 0.5), $TcPO_2$ < 25 mm Hg and/or a history of intermittent claudication should be referred for further vascular investigations and to a vascular surgeon or angiology specialist). Imaging studies and revascularization should also be considered — even if the results of the above mentioned tests are normal — if there is no progress in wound healing within 4 weeks despite the standard management. Of note, limb ischemia may not manifest with typical pain symptoms in many diabetic patients. The goal of revascularization should be to restore blood supply to at least one artery, preferably the one supplying the anatomical area of the ulcer;

— Podiatric treatment (regular wound care at intervals dependent on the local wound condition);

— Traditional wound dressings and therapy providing a moist wound environment. Consideration should be given to using TLC-NOSF dressings in uninfected wounds with neuropathic-ischemic etiology (but without critical/significant ischemia) that do not heal despite optimal standard care;

— Other — hyperbaric chamber (ischemic wounds not healing despite standard treatment), negative-pressure wound therapy (use in parallel with standard care should be considered, especially for postoperative wounds); medications to improve perfusion (ischemic or predominantly vascular etiology); low-molecular-weight heparins (acute ischemia, critical limb ischemia); acetylsalicylic acid; walking training. Sulodexide treatment may be considered.

— Skin transplantation, growth factors, ozone therapy, and autologous platelet gel are not recommended.

— In selected cases, wound cleaning may be considered using *Lucilia sericata* larvae cultured in sterile conditions in specialized laboratories.

Each patient with the diabetic foot syndrome should receive education regarding ulcer prevention.

Neuropathic osteoarthropathy (Charcot foot)

1. Evaluation:

— The diagnosis is made based on history and clinical presentation (unilateral edema, erythema, increased warmth of the foot, particularly if no ulceration is present, in a patient with features of diabetic polyneuropathy), after other causes have been excluded, particularly deep vein thrombosis and gout.

2. Management:

— Acute condition — off-loading for 24 hours a day (total contact cast, other forms of off-loading), bisphosphonate therapy with vitamin D and calcium administration may be considered but currently studies are lacking that would provide the evidence for long-term effectiveness of drug treatment. Off-loading should be maintained until stabilization of the process – transition to an inactive phase. The return to full limb loading should be very slow;

— Chronic condition — education, foot hygiene, special orthopedic footwear with therapeutic insoles to correct deformations, surgical and orthopedic

procedures to correct deformations (exostectomy, arthrodesis).

Multidisciplinary team management is recommended.

VII. Indications for hospital admission

Acute admissions:

— Grade 4 infection by the PEDIS classification;

— Grade 3 infection by the PEDIS classification if intravenous antibiotic therapy is needed;

— All cases of critical limb ischemia.

Elective admissions:

— No improvement despite 2 months of outpatient treatment;

— Preparation before planned surgery (small amputation, skin transplantation, revascularization procedures).

VIII. Amputation

Before each amputation, it is obligatory to assess the blood supply to the limb.

— **Large amputation (above the ankle) should be considered in case of:**

- A life-threatening condition due to inflammation, extensive necrosis (an absolute indication);
- Debilitating, treatment-resistant pain, particularly due to ischemia (a relative indication);
- Loss of the support function of the foot (a relative indication);

— **Small amputation (below the ankle) should be considered in case of:**

- Liquefactive necrosis;
- Osteomyelitis involving distal phalanges of the foot (avoidance of chronic antibiotic therapy, faster healing);
- In dry necrosis, awaiting until autoamputation is recommended.

The choice of the level of amputation depends on tissue perfusion, and reconstruction and rehabilitation possibilities.

Amputation should always spare as much limb as possible.

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23. Diabetes in children and adolescents

Most important recommendations

- Children with diabetes type 1 should be treated with intensive insulin therapy and use continuous glucose monitoring (CGM) systems from the onset of the disease. [**A**]
- Blood glucose levels should be measured in fasting conditions and before meals, before bedtime, before, during and after exercise, if feeling unwell, 1–2 hours after the meal as needed, and during the night. [**B**]
- Use of CGM with intensive insulin therapy in children and adolescents improves the metabolic control of diabetes (HbA_{1c} level lowering, increased TIR) and decreases the risk of acute and chronic complications of the disease. [**B**]
- Insulin pumps with an automatic insulin-delivery suspension feature are particularly useful in the prevention of hypoglycemia. [**B**]
- Recommended target HbA_{1c} level in children is ≤ 6.5% with stable blood glucose levels, minimized hypoglycemia episodes, and maintenance of good quality of life. [**E**] Guidelines for assessing CGM parameters can be found in Chapter 4.

The following chapter deals with variations from the general recommendations related to specific pediatric issues.

I. Diabetes types in the pediatric population

1. Autoimmune diabetes type 1 is the most common form.
2. In obese subjects, impaired fasting glucose and/or impaired glucose tolerance may develop, followed by diabetes type 2. OGTT is recommended every two years in children above 10 years of age (or earlier, if the puberty has already commenced) with BMI > 95th percentile.
3. Of note, monogenic diabetes is the second most common form of diabetes in the pediatric population in Poland. Indications for investigations for monogenic diabetes are presented in Chapter 1.
4. The number of children with cystic fibrosis and dysglycemia or diabetes is increasing. Diabetes in these patients is usually asymptomatic. Annual OGTT with blood glucose measurements at 30, 60, 90 and 120 minutes should be performed in children > 10 years of age with cystic fibrosis.
5. Primary diagnostic work-up for hyperglycemia or revision of the diagnosis includes testing for antibodies against glutamic acid decarboxylase (anti-GAD) along with 1–2 of the following antibodies: islet cell antibodies (ICA), insulin autoantibodies (IAA), insulinoma-associated autoantigen 2 (IA-2) autoantibodies, and antibodies against zinc transporter family member 8 (ZnT8) in justified cases (testing should always be performed in a reference laboratory). These tests may also be performed in individuals at a high risk of developing diabetes type 1. The presence of a high titer of one type of antibody or elevated titers of two types of antibodies indicates an active autoimmune process involving apoptosis of pancreatic beta cells and is consistent with the diagnosis of preclinical stage 1 diabetes. If IFG and/or IGT develops, preclinical stage 2 diabetes may be diagnosed. Due to a significant risk of developing clinically apparent type 1 diabetes (stage 3), patients require health education regarding periodic blood glucose level measurements to prevent the development of ketoacidosis.
6. The possibility of a mixed diabetes etiology should always be borne in mind.

II. Therapeutic targets

1. Prevention of acute and chronic diabetes complications.
2. Achieving and maintaining normal, harmonious physical development including body height, weight, and composition (as evaluated using percentile growth charts), and the course of puberty that is appropriate for age and gender, and providing an appropriate quality of life of the patient and his/her family.
3. Therapeutic targets for cardiovascular risk reduction:
   — HbA_{1c} ≤ 6.5% with stable blood glucose levels and minimized hypoglycemia episodes, while maintaining a good quality of life, TIR > 70% (each increase of TIR by 5% is associated with cardiovascular risk reduction in adults);
   — Total cholesterol < 170 mg/dL (< 4.4 mmol/L), LDL cholesterol < 100 mg/dL (< 2.6 mmol/L), triglycerides < 100 mg/dL (< 1.1 mmol/L);
   — Blood pressure < 90th percentile for age, gender, and height (> 16 years of age: < 130/85 mm Hg);
   — BMI < 85th percentile for age and gender;
   — Physical activity of at least moderate intensity > 1 hour per day;
   — Sedentary activities < 2 hours per day;
   — Avoidance of smoking.

III. Management of diabetes

1. Drug therapy

Diabetes type 1 — insulin therapy:

— The approach to insulin therapy should be adjusted to individual patient needs and accepted by the patient and his/her caregivers;

— Intensive insulin therapy is the treatment of choice, either as:

• Continuous subcutaneous insulin infusion (CSII) using a personal insulin pump;

• Multiple daily injections using insulin pen needles with the length of ≤ 6 mm;

— Indications for and contraindications to CSII — see respective Chapter;

— Initiation of CSII therapy at the disease onset is recommended, if not contraindicated, and this treatment approach is accepted by the patient and/or his parents;

— Bolus calculator function use from the beginning of the therapy is indicated, as it increases the stability of blood glucose values and reduces the risk of hypo- and hyperglycemia; it is necessary to regularly verify and modify bolus calculator settings;

— The choice of rapid-acting and long-acting insulin analogs should be individualized based on patient's needs, taking into account pharmacological differences between various preparations and their licensed indications;

— In pediatric patients, daily insulin requirement is characterized by a large variability and increases significantly in the pubertal period, but it should not exceed 1.5 U/kg/day;

— During intensive insulin therapy: the magnitude of the basal dose (20–50% of the daily dose) and its profile depend on the age of the child and the type of insulin pump;

— Rapid-acting/short-acting insulin is best administered 15–20 or 30 minutes before a meal, respectively, and the ultra-rapid-acting analog — 2–10 minutes before meals; in the youngest children, in whom planning the timing and size of the meal is not possible, consider dose splitting and administering half of the dose before a meal and the other half during or after a meal, and in exceptional cases administering the whole dose after a meal;

Diabetes type 2 — treatment options for this age group include insulin, metformin and GLP-1 receptor agonists (age limits according to the summary of product characteristics).

In case of:

— Absent symptoms, HbA_{1c} < 9%, and no acidosis, drug treatment may be started with metformin;

— Present symptoms and/or HbA_{1c} ≥ 9% and no acidosis, initial drug treatment includes metformin and basal insulin;

— Ketoacidosis — initial treatment as in diabetes type 1.

Monogenic diabetes and diabetes in genetic syndromes — treatment depends on the type of disease (use of sulfonylureas is off-label).

Diabetes in cystic fibrosis — see Chapter 1.

2. Nutrition in diabetic children and adolescents

The basic principles of healthy nutrition in diabetic children are the same as in their non-diabetic peers. It is recommended to maintain normal energy balance and reduce absorbable carbohydrate intake, maximally to 45–50% of the daily calorie requirement. Reduction of simple sugar intake to 10% of the daily calorie requirement and including portions of vegetables in every meal is recommended.

3. Self-monitoring:

— Blood glucose monitoring may be undertaken by blood glucose self-monitoring using flash glucose monitoring (FGM) and intermittently scanned continuous glucose monitoring (isCGM) systems, and real-time continuous glucose monitoring (rtCGM) generating messages and sound alerts without user input;

— Use of CGM is indicated in all children since the disease onset.

— Frequency of blood glucose measurements should be individualized — not less than 8 times a day in case of functional intensive insulin therapy (FIIT). Blood glucose levels should be measured in fasting conditions and before meals, 1–2 hours after the meal, before bedtime, and before, during and after exercise. The night-time blood glucose profile should also be measured. Blood glucose level should be measured promptly if the patient is unwell.

Use of CGM systems requires structured diabetes education regarding proper interpretation of current readings, treatment modifications based on blood glucose trends, and retrospective analysis of the results as per the guidance for evaluating TIR (Chapter 4). In patients using rtCGM systems, the education should be extended to include the principles of sensor calibration, and the appropriate choice and programming of alarm limits and messages (see Chapter 9).

CGM systems allow more effective adjustment of insulin doses to blood glucose trends, resulting in more stable blood glucose values, a reduced number of hypoglycemia episodes, better metabolic control, improved quality of life of patients and their caregivers, and a reduction of the cardiovascular risk.

In patients with hypoglycemia unawareness or frequent nocturnal hypoglycemia, it is recommended to use rtCGM, and optimally insulin pumps integrated with CGM, with a function of automatic temporary cessation of insulin administration in case of low blood glucose values or imminent hypoglycemia. Only permanent use of CGM is effective therapeutically (minimum 70% of the time).

Blood betahydroxybutyrate testing using a test strip is a more sensitive marker of ketonemia than testing for ketones in urine.

4. Therapeutic education:
   - Education is a key element of diabetes management; it should always be targeted at the patient and his/her caregivers;
   - Patient and his/her parents/caregivers need initial education and regular educational reinforcements at least once in 1–2 years;
   - Educational methods and programs should be varied and adjusted to the patient's age, intellectual capabilities, and educational tasks of the parents;
   - In adolescents and young adults, particular attention should be paid to prevention of chronic diabetes complications, contraception, pregnancy, and addictions.
   - The process of developing self-monitoring skills should be gradual; too early or too late placement of this responsibility on children and adolescents with diabetes is associated with treatment failures;
   - Workshops and camps for children, adolescents and young adults with diabetes are a useful and effective educational tool;
   - Members of the diabetology team who care for patients below 18 years of age participating in camps without parental attendance must provide continuous medical care at these facilities, including night duties. Legal and organizational support is expected from the administrative units involved in care for children with diabetes;
   - Initiating and continuing diabetes education is a responsibility of the whole therapeutic team, with a particular role of a diabetes educator.
5. Psychological care:
   - Continuous psychological care of children, adolescents and young adults with diabetes and their families is required since the disease onset;
   - Common problems include subclinical and clinical depressive syndromes, eating disorders including anorexia nervosa (particularly in adolescent girls), and other non-specific conditions (eating disorders not otherwise specified, ED-NOS);
   - Care should be provided by an experienced psychologist who is well versed with the problems of pediatric and adolescent diabetes.
   - Screening for depressive disorders should be performed in all patients every 1–2 years, and additionally in all patients with poor metabolic control of the disease.
6. Additional remarks:
   - The whole patient family should be involved in the process of treating diabetes in children and adolescents, with joint discussions on therapeutic targets;
   - Patients should be encouraged to be independent and take responsibility for their treatment to a degree that is appropriate for their age, intellectual development, and emotional maturity;
   - Children > 10 years of age should be able to measure blood glucose using a glucose meter and FGM/CGM, inject insulin using a pen, and change infusion sets in personal insulin pumps and FGM/CGM sensors.

IV. Concomitant conditions in patients with diabetes type 1

The most frequent comorbidities include:

- Autoimmune thyroiditis and celiac disease; their course is usually oligo- or asymptomatic (e.g., increased blood glucose excursions, impaired growth and sexual maturation);
- IgA deficiency;
- Some concomitant chronic diseases (e.g. epilepsy, Asperger disease, mental and intellectual disorders) may be associated with additional requirements to be considered when planning diabetes therapy.

V. Acute and chronic diabetes complications (see also respective chapters)

1. Acute complications:
   - In case of blood glucose levels ≤ 70 mg/dL (3.9 mmol/L) or clinical symptoms of hypoglycemia, glucose should be administered at about 0.3 g/kg body weight (dose depending on blood glucose values and active insulin, usually up to 15 g of glucose in a child with the body weight of ≥ 50 kg), and blood glucose measurement should be repeated after 15 minutes;
   - Blood glucose levels < 54 mg/dL (3.0 mmol/L) indicate clinically significant hypoglycemia;
   - If CGM is used, hypoglycemia is diagnosed if blood glucose levels are < 54 mg/dL for > 15 minutes;
   - Severe hypoglycemia in children is diagnosed in case of altered consciousness and/or seizures;
   - Management of severe hypoglycemia is described in Chapter 15;
   - Diagnostic criteria for acute hyperglycemic conditions in children and adolescents are shown in Table 23.1;

Table 23.1. Biochemical criteria for the diagnosis of acute hyperglycemic conditions in children and adolescents with diabetes

	Diabetic ketoacidosis (DKA)			Hyperglycemic--hypermolar state	Hypermolar DKA
Parameter	Mild	Moderate	Severe		
Plasma glucose level (mg/dL)	> 200	> 200	> 200	> 600	> 600
Venous blood pH	< 7.3	< 7.2	< 7.1	> 7.3	< 7.3
Bicarbonate (mmol/L)	< 15	< 10	< 5	> 15	< 15
Ketonemia (beta-hydroxybutyrate) (mmol/L)	> 3	> 3	> 3	—	> 3
Ketonuria	Moderate or high	Moderate or high	Moderate or high	Absent or mild	Moderate or high
Effective plasma osmolality (mOsm/kg)	< 320	< 320	< 320	> 320	> 320

— Management of diabetic ketoacidosis in children is summarized in Figure 23.1. It is emphasized that rehydration can be carried out using either 0.45% or 0.9% NaCl;

— Management of hyperglycemic hyperosmolar state:

- **Fluid therapy:** rapid initial infusion ≥ 20 mL/ /kg body weight of 0.9% saline, with next doses administered until restoration of peripheral tissue perfusion, followed by fluid replacement during 24–48 hours using 0.45% saline. The optimal rate of serum sodium reduction is 0.5 mmol/L per hour, and of blood glucose is 50–70 mg/dL per hour and no more than 90 mg/dL per hour. If blood glucose decreases by > 90 mg/dL per hour, addition of 2.5–5% dextrose should be considered after a few initial hours of hydration therapy;
- **Insulin therapy:** insulin should be added if blood glucose does not decrease by at least 50 mg/dL per hour during appropriate fluid therapy only; initial insulin dose is 0.025–0.05 unit/kg/hour, with further adjustment to achieve blood glucose reduction at the rate of 50–70 mg/dL per hour;
- **Electrolytes:** potassium, phosphorus, and magnesium deficit is higher than in diabetic ketoacidosis; potassium supplementation should be started as soon as renal function and diuresis is stabilized; intravenous administration of potassium phosphate and potassium chloride (1:1) allows adequate phosphate supplementation; phosphate administration may result in hypocalcemia; magnesium supplementation should be considered in hypomagnesemia;

— Each center treating children with diabetes should develop a protocol for the management of patients with diabetic ketoacidosis that specifies the local indications for hospitalization in intensive care units (ICUs) taking into account diabetes-unit staffing level, training of the therapeutic team, and access to ICUs.

— Indications for treatment in an intensive observation room within the diabetes unit or in ICU:

- Severe diabetic ketoacidosis (pH < 7.1) with long duration of symptoms, circulatory disorders, decreased level of consciousness;
- Increased risk of cerebral edema (age < 5 years, rapidly developing acidosis, low pCO2, high urea nitrogen);
- Hyperosmolal diabetic ketoacidosis.

2. Chronic complications:

— Regular follow-up evaluations are needed to prevent complications (Table 23.1);

— If any chronic complication is diagnosed, screening for other abnormalities (e.g., nephropathy, retinopathy, neuropathy, and macroangiopathy) is necessary;

— With persistent albuminuria, when albumin level is above the upper limit values, ACEI or ARB treatment is indicated to reduce its progression. Treatment effectiveness should be monitored with follow-up testing for albuminuria;

— ACE or ARB treatment is recommended to normalize blood pressure; treatment effectiveness should be constantly monitored, and obtaining nocturnal blood pressure reduction is indicated, as confirmed by ambulatory blood pressure monitoring (ABPM);

— Management of dyslipidemia: LDL cholesterol levels > 100 mg/dL (2.6 mmol/L) require improvement of blood glucose control and lifestyle modifications;

— In children > 8 years of age, if previous attempts at making lifestyle modifications did not result in beneficial changes in serum lipids or other risk factors for atherosclerosis are present, genetic testing for LDL cholesterol receptor gene mutations and statin treatment should be considered if LDL cholesterol level is > 159 mg/dL (4.1 mmol/L).

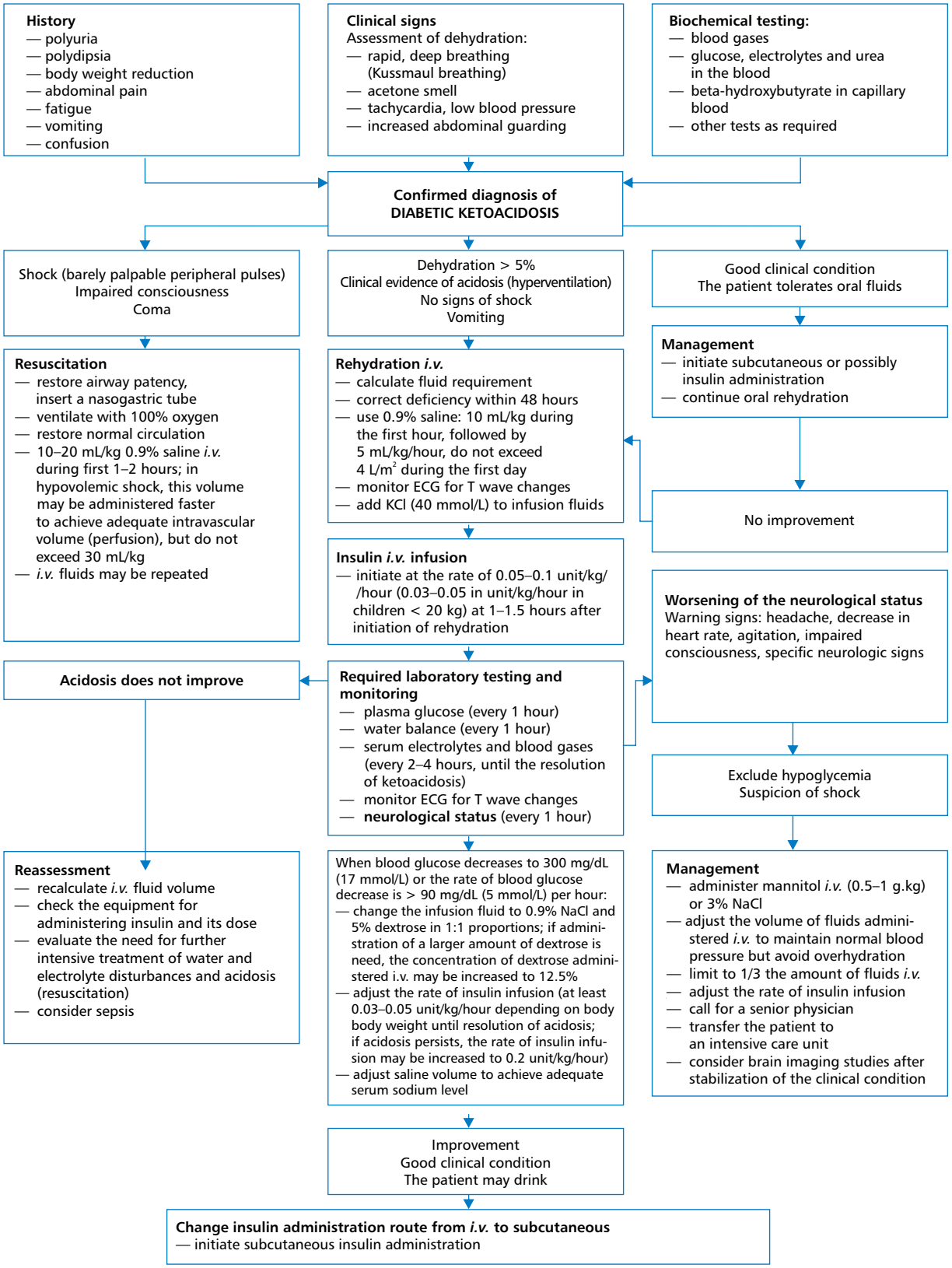

Figure 23.1. Management of diabetic ketoacidosis in children; ECG — electrocardiogram; i.v. — intravenous

Table 23.2. Recommendations regarding diabetes care in children and adolescents

Therapeutic education targeted at the patient and his/her caregivers	At the diagnosis and afterwards as required, at the discretion of the treating physician or education nurse
Nutritional education targeted at the patient and his/her caregivers	At the diagnosis and afterwards as required, at the discretion of the treating physician or education nurse/dietitian
Psychological care of the patient and his/ /her caregivers	At the diagnosis and afterwards as required, at the discretion of the treating physician or education nurse or psychologist
Diagnostics to determine the type of diabetes	At the diagnosis and revision of the diagnosis: clinical picture; family history; assessment of insulin secretion, pancreatic antibodies#, insulin sensitivity*; genetic tests*
HbA_{1c}	3–4 times a years, may be measured less frequently in patients who regularly use CGM//FGM
Serum total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides	After stabilization of glycemia, and then, if in normal range, every 2 years in patients older than 10 years of age
Abdominal ultrasound	At the diagnosis
Body weight and growth monitoring	At each visit using percentile charts for age and gender
Monitoring of pubertal development using the Tanner scale	At the discretion of the physician, at least annually, assessment of menstrual regularity
Blood pressure	During each visit, children < 7 years of age at least twice a year, children > 10 years of age, 24-hour ABPM — every 2 years or in the case of elevated blood pressure values in random measurements
Investigations for celiac disease	According to the respective ESPGNH guidelines, screening every 2 years if no clinical symptoms
Evaluation of thyroid function/ /investigations for thyroid disease	At the onset of the disease: TSH, FT4, anti-TPO and anti-TG (USG in case of positive antibody testing and/or thyroid dysfunction), followed by TSH, anti-TPO and anti-TG every 2 years (at the discretion of the treating physician)
Screening for chronic complications:creatinine, albuminuria, urinalysis ophthalmological consultation	After stabilization of glycemia, and then every 2 years in patients older than 10 years of age or with diabetes duration of more than 5 years. In the case of abnormal results, the frequency of subsequent tests should be individualized according to the patient's needs
Specialist consultations	According to general pediatric indication and at revision of the diagnosis

*When needed

#At the diagnosis, in the first 5 days after initiation of insulin therapy

FGM/CGM — flash glucose monitoring/continuous glucose monitoring; ABPM — ambulatory blood pressure monitoring; ESPGHN — The European Society of Gastroenterology, Hepatology and Nutrition, Children; TSH — thyroid-stimulating hormone; fT4 — free thyroxine

VI. Perioperative management (see respective chapter)

VII. Recommendations regarding diabetes care in children and adolescents (Table 23.2)

1. General recommendations:
   - — Every child with new-onset diabetes should be admitted to a specialist pediatric diabetes unit, and later remain under regular specialist care in a pediatric and adolescent diabetes clinic until transition to adult diabetes care (for transition see Appendix 1);
   - — A 24-hour access to diabetes information for patients and their caregivers should be provided;
   - — Admission to a diabetes unit should be always considered with disease decompensation (persistent hyperglycemia, blood glucose excursions, recurrent hypoglycemia);
   - — In diabetes care, data from the memory of insulin delivery devices and glucose monitoring systems should be retrieved and interpreted at each hospitalization and diabetologist consultation.
2. Therapeutic team:
   - — Inpatient care — per 10 pediatric diabetes beds: physicians (specialist in pediatric diabetes, specialist in pediatric diabetes and endocrinology, if unavailable: pediatrician/endocrinologist with an experience in diabetology confirmed by the voivodship diabetes consultant in diabetology or pediatric endocrinology or diabetology) — two full-time posts; nursing personnel devoted exclusively to diabetes education or diabetes educators — two full-time posts; dietitian (full post), psychologist (full post), and a social worker (1/4 post). In diabetes units

with intensive observation room a nurse dedicated to this care is required;
— Outpatient care — per a therapeutic team caring for 300 patients: specialist in pediatric diabetes (if unavailable: pediatrician), specialist in pediatric diabetes and endocrinology, if unavailable: pediatrician/endocrinologist with an experience in diabetology confirmed by the voivodship diabetes consultant) — one full-time post; nursing personnel with duties limited to diabetes care or diabetes educators — 1–2 full-time posts; dietician — 1/2 post; and psychologist — 1/2 post.

3. Outpatient visits
— Unlimited frequency of diabetes visits, recommended frequency every 6–8 weeks, at least 4 times a year;
— Some outpatient visits may be replaced with video or telemedicine visits, provided that the following data may be remotely retrieved and transferred to the diabetes clinic:
• Data from blood glucose monitoring devices;
• Data from the devices used for administering insulin or electronic self-monitoring diary apps.
— Outpatient visits must be performed at least once in 6 months.
— The recommended mean duration of a visit: 20–30 minutes for a specialist visit and 30–40 minutes for a procedural and diagnostic visit (treatment with a personal insulin pump);
— Educational visits do not always constitute a part of a physician consultation and may also be conveyed using electronic means;
— Additional tasks of the therapeutic team include organization of care for diabetic children in educational facilities, organization of educational camps/workshops, and preparation of educational materials.

4. Outpatient clinic and hospital unit equipment:
— Equipment: automatic syringes, personal insulin pumps, glucose meters, CGM systems, ambulatory blood pressure monitors, ophthalmoscope, monofilaments, food scales, computer equipment to retrieve and print data from therapeutic systems;
— Space and necessary teaching equipment for education;
— Hospital units: ≥ 1 intensive metabolic care bed per 10 regular diabetes beds, equipped with pulse oximetry and ECG monitor, oxygen source, USG machine with vascular flow measurement option.

VIII. A child with diabetes in an educational facility

1. Cooperation between the therapeutic diabetes team, pedagogical personnel, school nurse, and the patient family is needed to ensure child safety at school and prevent diabetic patient stigmatization:
— Following the diagnosis of diabetes, the pedagogical personnel should be provided with written information about the disease and necessary help in life-threatening situations, along with contact telephone numbers of the parents, treating physician, and education nurse;
— Appropriate training of the pedagogical personnel regarding diabetes self-management;
— Training of the school nurse regarding the use of a glucose meter, insulin pen, or insulin pump;
— The educational facility should be adequately provided with glucose and glucagon by the patient's caregivers;
— Diabetes is not an indication for an individualized education plan or exemption from any activities (e.g., sport activities or school trips).

2. Duties of the pedagogical personnel:
— **Providing immediate first responder diabetes treatment/assistance in acute life-threatening conditions;**
— Comprehensive help allowing rapid and safe patient return to the educational facility and full integration with peers;
— Basic knowledge of diabetes self-management;
— Allowing on-site diabetes self-monitoring in the educational facilities by patients of all age groups, with supervision by the school staff in younger children;
— Strict cooperation with the therapeutic diabetes team and the patient's caregivers.

IX. Travel

— Responsibilities of the patient and his/her caregivers include informing the organizer about the disease, its management, nutrition, and help in acute situations, and providing contact telephone numbers of the members of the therapeutic diabetes team;
— An appropriate certificate in English informing about the disease should be prepared before an international travel;
— Insulin, glucagon, glucose, glucose meter with reagent strips, insulin pens, and equipment for insulin pumps and CGM systems should be appropriately stored and placed in the hand-luggage.

X. Physical activity and participating in sport

1. Children and adolescents with diabetes:
— should be encouraged to engage in daily moderate or intensive physical activity;
— may engage in sport similarly to children without diabetes.

2. Recommendations regarding physical activity and participating in sport are given in Chapter 7 and Appendix 7.

XI. Choice of future profession

— Particular attention should be paid to education of diabetic patients, and providing them with as good education as possible;

— A task of the therapeutic diabetes team is to help the patient with the choice of future profession by evaluating his/her health status, presence of complications, and intellectual and mental capabilities.

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24. Diabetes and pregnancy

Most important recommendations

- Pregnancy planning in women with diabetes reduces adverse maternal and fetal/neonatal outcomes and should be a part of standard diabetes care for diabetic women of child-bearing age. [**A**]
- Contraception using barrier methods or oral hormonal contraceptives should be used for pregnancy planning in women with diabetes. [**B**]
- Universal screening for hyperglycemia during pregnancy is recommended in Poland. Categorization and diagnostic criteria of hyperglycemia during pregnancy are in accordance with the WHO guidelines. [**A**]. Screening is recommended at the first visit during pregnancy and at 24–28 weeks of gestation.
- In many women with gestational diabetes, behavioral modifications allow adequate blood glucose control, and drug treatment using insulin should be initiated if therapeutic targets are not met. [**A**]
- General principles of diabetes treatment during pregnancy:
  - Hyperglycemia during pregnancy increases the risk of maternal and fetal/neonatal complications and thus blood glucose control should be optimized both in pre-pregnancy diabetes and hyperglycemia first detected during pregnancy. **[A]**
  - Blood glucose self-monitoring is recommended as the first line approach to metabolic control in all types of diabetes complicating pregnancy. Currently, the following target self-measured blood glucose values are recommended – fasting and before meals: 70–90 mg/dL (3.9–5.0 mmol/L); maximum blood glucose level at one hour after a meal: < 140 mg/dL (< 7.8 mmol/L); between 2 and 4 AM > 70–90 mg/dL (> 3.9–5.0 mmol/L). **[B]**
  - HbA_{1c} level measurements are a tool to evaluate blood glucose control in women with pre-pregnancy diabetes. The recommended values are < 6.5% in the first trimester and < 6.0% in the second and third trimester. **[B]**
  - Insulin is the only antidiabetic drug recommended in pregnancy. Based on the current knowledge, use of other antidiabetic drugs, either oral agents or GLP-1 receptor agonists and SGLT-2 inhibitors, is not recommended. **[A]**
- Patients with a history of gestational diabetes mellitus should be tested for diabetes before the next pregnancy and if diabetes is diagnosed, these patients should be treated to reduce the risk of congenital anomalies in the offspring. [**E**]

Pregnancy planning in all women with diabetes has a major effect on the course of the disease, reducing adverse maternal and fetal/neonatal outcomes.

Diabetes in pregnancy includes:

— Pregestational diabetes mellitus (PGDM) — diabetes preexisting in a woman who becomes pregnant (regardless of the diabetes type).
— Hyperglycemia first detected at any time during pregnancy.

I. Contraception

Patients should be informed that diabetes itself is not a contraindication for hormonal contraception. Patients should be evaluated for conventional contraindications to hormonal contraception and be offered an opportunity to choose an individually preferred, effective contraception method, taking into account the risk associated with unplanned pregnancy. Intrauterine devices or progestogen-only contraceptive pills are recommended if the duration of diabetes is > 20 years or neurovascular complications are present (nephropathy/retinopathy/neuropathy). Patients who plan a pregnancy should be informed that the risk of pregnancy complications increases with the duration of diabetes, presence of target organ damage, and worse metabolic control.

Combined oral contraceptives containing less than 35 μg of ethinylestradiol are recommended due to their minimal effect on carbohydrate and lipid metabolism. Preferred progestins include levonorgestrel and norethisterone.

A progestin-releasing IUD is recommended as a contraceptive method in obese women > 35 years of age, patients with diabetes type 2, and in those with concomitant vascular complications.

II. Model of care for pregnant diabetic women

1. During pregnancy planning, pregnancy, and the postpartum period, all diabetic women should remain under care of an experienced team of diabetologists and obstetricians. Women with diabetes type 2 treated with oral antidiabetic medications require initiation of insulin therapy already when planning pregnancy to achieve adequate blood glucose control. It is only acceptable to use metformin in women with diabetes type 2 in the preconception period if this treatment allows adequate metabolic control. SGLT-2 inhibitors and GLP-1 receptor agonists are currently not approved for use during pregnancy and should not be used during pregnancy planning.

   Each clinician caring for a woman with diabetes type 2 should regularly initiate a discussion about her reproductive plans and inform her about the need for pregnancy planning due to complex risk factors for adverse obstetric outcomes present in this patient population.

2. Management aims include:
   — Optimization of diabetes treatment;
   — Evaluation and treatment of diabetic complications;
   — Diabetes education, including nutritional advice;
   — Recommendation to stop smoking;
   — Evaluation of thyroid function (to exclude hypothyroidism): the upper limit of the reference range for thyroid-stimulating hormone (TSH) should be defined as 2.5 μIU/mL in the first trimester and up to 3.0 μIU/mL in the second and third trimester;
   — During pregnancy, visits related to diabetes should occur at least once a month, and in some cases every 2–3 weeks. This is due to, among others, changing insulin requirements and the need to monitor body weight, renal function, eyesight, and blood pressure;
   — If gestational hypertension develops, treatment should be initiated with blood pressure values above 140/90 mm Hg;
   — In diabetic women with chronic hypertension, target systolic blood pressure is < 135 mm Hg and target diastolic blood pressure is < 85 mm Hg (methyldopa is the first-choice drug during pregnancy);
   — In women with pre-pregnancy diabetes, acetylsalicylic acid at the dose of 1 mg/kg (75–150 mg/day) is recommended from 12 to 34 weeks of gestation (prevention of preeclampsia).
3. Pregnancy is discouraged in diabetic women in the following clinical situations:
   — Nephropathy with GFR < 40 mL/min;
   — Treatment-resistant proliferative retinopathy;
   — Cardiac conditions:
     • Advanced, treatment-resistant ischemic heart disease;
     • Hypertrophic cardiomyopathy or severe left ventricular dysfunction (left ventricular ejection fraction < 30%, New York Heart Association class III/IV);
     • History of peripartum cardiomyopathy with any residual left ventricular dysfunction;
   — Autonomic neuropathy involving the cardiac conduction system or the gastrointestinal system.

Ultimately, decisions regarding procreation are to be made by the patient herself, but the patient must be informed about the health risks of pregnancy in such cases.

Pregnancy does not seem to be associated with a risk of post-partum worsening of chronic diabetes complications. Unless the above listed complications are present, women with diabetes are free to plan any number of children they wish.

III. Diagnostic criteria and classification of hyperglycemia first detected during pregnancy

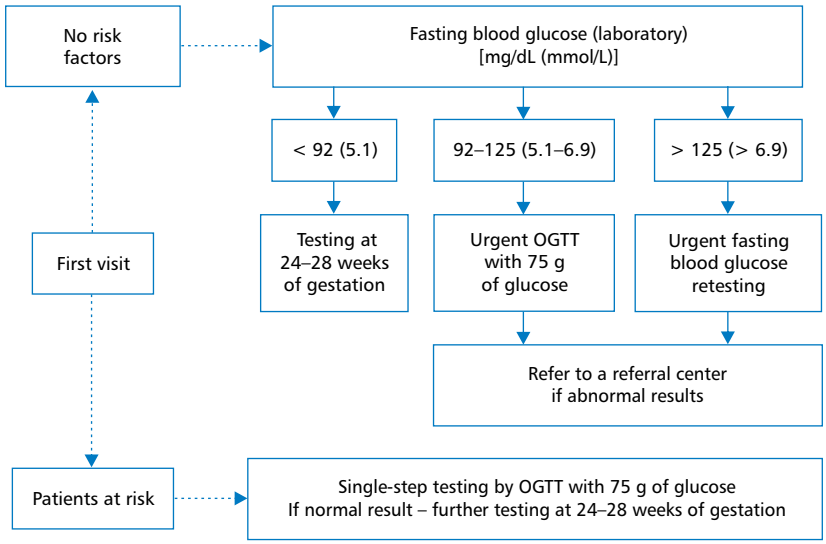

Figure 24.1. Evaluation of dysglycemia during pregnancy. Note: Fasting blood glucose > 92 mg/dL but < 125 mg/dL on one occasion during the first trimester cannot serve as a basis for the diagnosis

Table 24.1. Risk factors for hyperglycemia during pregnancy

— pregnancy beyond 35 years of age
— history of macrosomia (birth weight > 4000 g)
— previous delivery of a neonate with a congenital anomaly
— history of intrauterine fetal demise
— hypertension
— overweight or obesity
— family history of diabetes type 2
— gestational diabetes during previous pregnancies
— multiparity
— polycystic ovary syndrome

All pregnant women should be evaluated for dysglycemia as soon as pregnancy is diagnosed. In pregnant women at risk, an OGTT with 75 g of glucose (described in Chapter 1) should be performed at the first visit during pregnancy, and the other patients should have their fasting blood glucose measured. If blood glucose is normal (see Figure 24.1), the diagnostic test should be repeated between 24 and 28 weeks of gestation or if symptoms suggesting diabetes develop. In patients without risk factors and with normal blood glucose at the first test during pregnancy, single-step diagnostic investigation by OGTT with 75 g of glucose should be performed between 24 and 28 weeks of gestation.

Hyperglycemia first detected at any time during pregnancy should be diagnosed and categorized using the 2013 WHO classification:

Table 24.2. Diagnostic criteria for gestational diabetes based on an oral glucose tolerance test with 75 g of glucose according to IADPSG (2010) and WHO (2013)

Measurement	Plasma glucose	
	[mg/dL]	[mmol/L]
Fasting	92–125	5.1–6.9
60 minutes	≥ 180	≥ 10.0
120 minutes	153–199	8.5–11.0

— Diabetes mellitus in pregnancy — if general conditions for the diagnosis of diabetes are met, i.e.:
  - Fasting blood glucose ≥ 7.0 mmol/L (126 mg/dL); or
  - Blood glucose at 2 hours of OGTT with 75 g of glucose ≥ 11.1 mmol/L (200 mg/dL); or
  - Random blood glucose ≥ 11.1 mmol/L (200 mg/dL) accompanied by clinical symptoms of hyperglycemia;

— Gestational diabetes mellitus (GDM) — if at least one of the criteria in Table 24.2 is met.

In the postpartum period, blood glucose normalizes in most women but all women should be evaluated for dysglycemia, as diabetes in pregnancy is a risk factor for overt diabetes during later life. An OGTT with 75 g of glucose is recommended at 6–12 weeks postpartum, followed by fasting blood glucose measurements every year. An OGTT with 75 g of glucose should be performed before the next planned pregnancy. Women with a history of GDM should

be consider at high risk of diabetes and cardiovascular disease; annual investigations for dysglycemia are required in this group above 40 years of age.

IV. Multidisciplinary, integrated approach to the management of pregestational diabetes mellitus and hyperglycemia during pregnancy

Hyperglycemia during pregnancy increases the risk of complications in the pregnant woman and the developing fetus, and also affects further child development. Thus, blood glucose values seen in healthy pregnant women should be aimed for regardless of the type of pregnancy (PGDM or hyperglycemia during pregnancy). Currently, the following target self-measured blood glucose values are recommended:

- Fasting and before meals: 70–90 mg/dL (3.9––5.0 mmol/L);
- Maximum blood glucose level at one hour after a meal: < 140 mg/dL (< 7.8 mmol/L), and < 120 ml/ /dL (< 6.7 mmol/L) at 2 hours after a meal;
- Between 2 and 4 AM: 70–90 mg/dL (3.9––5.0 mmol/L).

Pregnant women should perform SMBG after an appropriate training by a nurse experienced in caring for diabetic patients. The number and timing of SMBG should depend on the severity of dysglycemia and the treatment used. Continuous glucose monitoring (CGM) is recommended in women treated with continuous subcutaneous insulin infusion (CSII). It is recommended that in patients using CGM, time spent in blood glucose values of > 140 mg/dL (7.8 mmol/L) be less than 25% daily, in the range of 63–140 mg/dL (3.5–7.8) mmol/L) — more than 70% daily, values < 63 mg/dL (3.5 mmol/L) — less than 4%, and < 54 mg/dL (3.0 mmol/L) — less than 1% daily.

HbA_{1c} level in women with PGDM should be measured every 6 weeks, aiming for values < 6.5% in the first trimester, and < 6.0% in the second and third trimester. No evidence supports the usefulness of HbA_{1c} measurements as a tool to monitor metabolic control in GDM.

1. Nutritional therapy:
   - Carbohydrates — 40–50% of the daily calorie intake (< 180 g carbohydrates/day); low glycemic index carbohydrates are preferred;
   - Protein — 30% of the daily calorie intake (1.3 g/kg body weight) per day;
   - Fats — 20–30% of the daily calorie intake (saturated fat < 10%);
   - Daily calorie intake depending on body weight, height, physical activity and age — the mean daily calorie requirement is about 30 kcal/kg body weight or 1500–2400 kcal;
   - Calorie intake of 25–30 kcal/kg body weight is recommended in overweight patients;
   - Body weight increase during pregnancy should be monitored, as excessive body weight increase in pregnant diabetic women is associated with an increased risk of having a large for gestational age infant (Table 24.1);
   - Use of artificial sweeteners is allowed, except for saccharin which crosses the placenta and its effect on the developing fetus is not entirely clear (see Appendix 5);
   - When planning pregnancy, folic acid supplementation (at least 0.4 mg/day) should be initiated at least 6 weeks before conception and continued until 12 weeks of gestation.
2. Physical exercise: aerobic activity of moderate intensity is recommended unless contraindicated.
3. Insulin therapy in PGDM:
   - Human insulins have been long used for the treatment of diabetes during pregnancy and their safety has been established. Safety of insulin analogs lispro and glargine has been shown in a number of observational studies, and that of aspart and determir also in randomized studies;
   - Intensive insulin therapy with multiple insulin injections (see Chapter 12, section III);
   - Insulin therapy with CSII — rapid-acting insulin analogs are recommended. Patient selection for personal insulin pump therapy and managing PGDM patients using this approach should be undertaken in diabetes units experienced in CSII therapy. Treatment should be preferably initiated while planning pregnancy or during early pregnancy (before 12 weeks of gestations), and only exceptionally later in those patients in whom adequate metabolic

Table 24.3. Recommendations regarding body weight increase during pregnancy

Pre-pregnancy body mass index [kg/m^2]	Recommended body weight increase [kg]	Recommended body weight increase in the second and third trimester [kg/week]
< 18.5	12.5–18.0	0.51 (0.4–0.58)
18.5–24.8	11.5–16.0	0.42 (0.35–0.50)
25.0–29.9	7.0–11.5	0.28 (0.23–0.33)
≥ 30	5–9	0.22 (0.17–0.27)

Assuming that body weight increase in the first trimester is 0.5–2.0 kg

control cannot be achieved during treatment with multiple insulin injections.

4. Insulin therapy in hyperglycemia first detected during pregnancy:
   — The recommended approach is intensive insulin therapy with multiple insulin injections or using a personal insulin pump;
   — Insulin requirement is sharply reduced postpartum and insulin therapy may be withdrawn in most patients with GDM.
5. Oral antidiabetic agents are currently not recommended for the treatment of diabetes during pregnancy due to the fact that they pass through the placenta. Randomized studies are available indicating their negative long-term effect on the development of the offspring. In women treated with oral antidiabetic agents, initiation of insulin therapy while planning pregnancy or as early as possible after the diagnosis of pregnancy is recommended.
6. Educational system:
   — Clinical issues — instruction provided by a physician, nurse, or dietitian knowledgeable in personal insulin pump therapy;
   — Technical issues regarding the use of a personal insulin pump — instruction provided by a nurse or physician certified as a technical instructor or an employee of the company producing personal insulin pumps;
   — Education program is undertaken according to the training card which serves to document the course of treatment;
   — Education program may be undertaken in outpatient and/or inpatient settings;
   — Treatment initiation is possible when the patient absorbs basic clinical and technical knowledge regarding CSII (understanding the therapeutic principles and technical details of using main insulin pump functions).
7. Breastfeeding should be widely promoted and recommended in women with PGDM and DGM unless contraindicated for other reasons.
8. Oral medications and lactation

Available literature and clinical data indicate that metformin is secreted to the breast milk at a very low level, not exceeding 1% of the maternal level, expressed as the maternal drug dose/kg of her body weight. Thus, it seems that metformin may be safely used during lactation by patients with diabetes type 2.

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25. Diabetes in individuals above 65 years of age

Most important recommendations

- When initiating diabetes treatment in subjects above 65 years of age, therapeutic targets should be set individually depending on the health status of the patient, his or her cognitive function, and socioeconomic status. [**C**]
- When treating diabetes in subjects above 65 years of age, one of the main goals is to prevent hypoglycemia by individualization of therapeutic goals and avoiding drugs associated with a high risk of hypoglycemia. [**B**]
- In subjects above 65 years of age without significant complications, therapeutic targets may be similar to those in younger adults. [**C**]
- When intensifying treatment, the target values of blood glucose, blood pressure and lipid levels should be adjusted according to the specificity of the age group and comorbidities. [**B**]

I. The prevalence of diabetes in the population > 65 years of age may be as much as 25–30%.

II. Symptoms of hyperglycemia in patients > 65 years of age may be less evident than in younger subjects, leading to a delayed diagnosis.

III. The expected survival time is much reduced in diabetic patients at an advanced age, and thus when planning the therapy, it should be remembered that preventing complications that develop after several years of the disease becomes less important than in younger subjects.

IV. Management goals in diabetic patients > 65 years of age:

— The major management goal in the elderly diabetic patients is to improve or at least preserve their previous quality of life. Avoiding hypoglycemia while reducing the symptoms of hyperglycemia is of key importance;

— If a diabetic patient > 65 years of age does not have significant complications or comorbidities, diabetes control should be gradually instituted with the target HbA_{1c} level of ≤ 7%;

— In patients at an advanced age with long-standing diabetes and significant macroangiopathic complications (previous myocardial infarction or stroke), the target HbA_{1c} level is ≤ 8.0%;

— Investigating for diabetic complications, preventing their progression, and recommending appropriate therapy;

— Management of concomitant conditions to reduce functional impairment and improve the quality of life.

V. Physical exercise — following initial determination of the individual risk and patient's exercise tolerance, outdoor exercise characterized by gradual onset and termination should be recommended, with avoidance of straining and breath-holding exercises and due attention to the risk of trauma, in particular the risk of developing diabetes foot syndrome.

VI. Nutritional recommendations — general recommendations apply; no age-specific recommendations; diet modifications are of little effectiveness due to long-lasting dietary habits.

VII. Oral antihyperglycemic agents:

— Metformin — see Chapter 11, section II (stage 1 treatment of diabetes type 2); consider concomitant conditions that are associated with an increased risk of metabolic acidosis; particular attention is required in patients with estimated GFR < 60 mL/min/1.73 m^2;

— Sulfonylureas — treatment should be initiated with low doses due to a risk of hypoglycemia;

— DPP-4 inhibitors, GLP-1 receptor agonists, alpha-glucosidase inhibitor, PPAR-γ agonist, SGLT-2 inhibitors — no specific contraindications exist regarding use of these agents in patients > 65 years of age; these agents may be particularly useful in this age group due to a minimal risk of hypoglycemia. Do not use the PPAR-γ agonist in patients with heart failure or a high fracture risk.

VIII. Insulin therapy:

— No specific indications and contraindications exist regarding insulin therapy in the elderly;

— If indicated, insulin therapy should not be delayed;

— Insulin preparations characterized by the lowest risk of hypoglycemia should be selected when initiating or modifying insulin therapy;

— Age > 65 years is not a contraindication to intensive insulin therapy;

— In some very elderly patients (> 80 years of age), it may be effective to use low doses of a short-acting insulin or a rapid-acting insulin analog before main meals without basal long-acting insulin;
— If meal size is unpredictable (e.g. patients with poor appetite or advanced dementia), rapid-acting insulin analogs administered directly after the meal in a dose adjusted to the meal size may be indicated.

IX. Diabetes education — should be targeted to both patients and their caregivers.

X. Antihypertensive therapy:
— Age is not a criterion when selecting antihypertensive drug classes;
— Benefits of antihypertensive therapy in patients > 65 years of age are similar compared to those in younger subjects.

XI. Lipid-lowering therapy:
— Although direct evidence are lacking, it may be concluded that benefits of lipid-lowering therapy seen in both primary and secondary prevention in younger subjects may also be extended to patients > 65 years of age.

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26. Preparing a patient with diabetes for a surgical procedure

Developed in cooperation with Prof. Wojciech Szczeklik

Most important recommendations

- Elective surgery in diabetic patients should be delayed if HbA_{1c} level is > 8.5%. [**C**]
- In patients treated with insulin before surgery, insulin therapy must not be interrupted preoperatively, and temporary insulin treatment should be initiated in most patients with diabetes type 2 who have been treated with oral antidiabetic drugs. [**B**]
- In critically ill diabetic patients receiving parenteral feeding, intravenous insulin should be administered at doses guided by blood glucose levels. [**C**]
- Blood glucose monitoring in the perioperative period in diabetic patients reduces the risk of complications and mortality. [**B**]
- Target blood glucose levels in the perioperative period are 100–180 mg/dL. [**C**]

I. Investigations necessary before the planned surgical procedure:
— 24-hour blood glucose profile (7 measurements during 24 hours, with an additional measurement at 3 AM in insulin-treated patients);
— HbA_{1c} level;
— Complete blood count;
— Serum creatinine, electrolytes (Na^+, K^+), aminotransferases (AST, ALT);
— International normalized ratio (INR), bleeding time, activated partial thromboplastin time (APTT);
— Acid-base balance (blood gases), if disorders are suspected;
— Urinalysis;
— Fundoscopy (current examination result);
— Resting ECG (see Remark 1);
— Chest radiograph.

Remark 1: Complete non-invasive diagnostic work-up (exercise testing, echocardiography, ECG Holter monitoring) should be performed in patients at high or very high cardiovascular risk, and those scheduled for an extensive procedure (e.g. abdominal or iliac vascular surgery, cardiac surgery).

Remark 2: One-day surgery may be performed in diabetic patients with good metabolic control treated with intensive insulin therapy, and in patients with type 2 diabe-

Table 26.1. Dosing of 10% and 5% dextrose and insulin infusion in relation to blood glucose levels

Blood glucose	10% dextrose [mL\hour]	5% dextrose* [mL\hour]	Insulin [units\hour]
< 90 mg/dL (< 5.0 mmol/L)	50	100	Stop infusion for 15–30 minutes
90–120 mg/dL (5.0–6.7 mmol/L)	50	100	0.5–2
120–180 mg/dL (6.7–10 mmol/L)	50	100	2–3

*5% dextrose is preferred with greater volume deficit and/or higher plasma osmolality

tes who do not require temporary insulin treatment in the postoperative period, Withholding the antihyperglycemic drug on the day of surgery will not result in an increase in blood glucose of > 180 mg/dL (10 mmol/L).

II. Preoperative management

1. Diabetic patients requiring intermittent insulin therapy should be admitted 2 days before the planned surgery.
2. Elective surgery should be delayed in patients with inadequate metabolic control [persisting blood glucose values > 250 mg/dL (13.9 mmol/L), HbA_{1c} > 8.5% and/ /or the presence of glucosuria with acetonuria].
3. If a patient with type 2 diabetes treated with two or three antihyperglycemic drugs will not eat their meals on the day of the procedure, or will undergo major surgery with an increased risk of hemodynamic instability, it is recommended to temporarily suspend current therapy and use insulin instead.
4. For temporary insulin therapy, a multiple injection model (basal-bolus) is recommended.
5. Daily insulin dose — 0.3–0.7 unit/kg body weight:
   — 50–60% of the daily dose — a short-acting insulin or rapid-acting insulin analog administered 15–30 minutes before main meals according to the following regimen: 50–20–30% of the daily dose of short-acting insulin/rapid-acting insulin analog;
   — 40–50% of the daily dose — a long-acting insulin (NPH) administered in two doses — at 7–8 AM (40%) and 10–11 PM (60%), or a long-acting analog given once daily, most commonly in the evening.
   — **A well-trained diabetic patient with good metabolic control is able to self-adjust insulin doses to his/her current needs and thus this practice should be allowed to be continued in the hospital instead of initiating treatment with fixed, unmodifiable insulin doses.**

   Individuals using personal insulin pump should maintain the current treatment by the day of the surgery.
6. If preparation for the surgery requires a nil-by-mouth regimen during the day(s) before the surgery, intravenous infusion of 500 mL dextrose 10% with 12 units of short-acting (rapid-acting) insulin and 10 mmol of KCl is recommended instead of meal.
7. Blood glucose control: in the perioperative period, blood glucose levels should be kept within the safe range of 100–180 mg/dL (5.6–10.0 mmol/L).
8. The surgical and anesthetic team should be informed about complications that increase the operative risk (cardiac and renal disease, neuropathy, proliferative retinopathy).

Remark 3: Temporary insulin therapy is not required in patients undergoing minor procedures (tooth extraction, abscess incision, small amputation performed in the outpatient settings, cataract surgery) but only if preparation for the surgery does not require any change in nutrition. If 1 or 2 meals need to be omitted due to the surgery, intravenous glucose, insulin, and potassium infusion is recommended (500 ml of 10% dextrose with 12 units of a short-acting (rapid-acting) insulin and 10 mmol KCl), administered at the rate of 100–150 ml/hour. Insulin and potassium doses may need to be modified according to blood glucose and serum potassium levels.

III. Management on the day of the surgery

1. Use intravenous glucose, insulin, and potassium infusion with blood glucose monitoring:
   — Algorithm 1: In patients with absolute insulin deficiency, separate continuous intravenous infusions of insulin (1 unit of short-acting human insulin in 1 mL 0.9% saline) and dextrose (5–10%) using infusion pumps are recommended. For each 1 g of exogenous dextrose, 0.2–0.3 unit of insulin is needed (Table 26.1). If blood glucose during the procedure increases by 30–50 mg/dL over 180 mg/dL, the rate of insulin infusion should be increased by 1–2 units/hour. If blood glucose increases above 250 mg/dL (13.9 mmol/L), dextrose infusion should be stopped and resumed only after blood glucose decreases below 180 mg/dL (10 mmol/L). At the same time, it is also recommended to increase the rate of insulin infusion. This treatment should be continued until resumption of oral feeding. During intravenous insulin infusion, blood glucose should be monitored every 1 hour, followed by every 2 hours after blood glucose is stabilized in three subsequent readings;

Table 26.2. Perioperative management in children. An algorithm for intravenous insulin dosing in relation to blood glucose levels

Infusion of a 1 unit of insulin/1 mL solution (add 50 units of insulin to 50 mL 0.9% saline) using a syringe pump		
Blood glucose [mg/dL]/[mmol/L]	**Insulin infusion rate**	**Hydration**
< 90/5.0	Stop infusion for 10–15 minutes	Type of fluid:
90–109/5–6.1	0.02 mL/kg/hour	• Blood glucose > 250 mg/dL: 0.9% saline
110–126/6.1–7.0	0.025 mL/kg/hour (basal infusion rate)	• Blood glucose < 250 mg/dL: 10% dextrose
127–143/7.0–8.0	0.035 mL/kg/hour	Rate:
144–216/8.0–12.1	0.05 mL/kg/hour	• 4 mL/kg/hour (for body weight up to 10 kg)
217–271/12.1–15.1	0.075 mL/kg/hour	• Add 2 mL/hour per each kg of body weight between 11–20 kg
> 271/> 15.1	0.1 mL/kg/hour	• Add 1 mL/hour per each kg of body weight > 20 kg Maximum rate 2000–2500 mL/day

Table 26.3. Subcutaneous insulin therapy in case of non-major procedures under general anesthesia or conscious sedation

Basal–bolus therapy	Basal insulin: NPH insulin — 50% of the morning dose, long-acting insulin analog — 100% of the morning dose Initiate intravenous fluids; in patients with normal blood glucose levels, non-glucose-containing fluids may be used initially, followed by 5% or 10% dextrose in amounts appropriate to prevent hypoglycemia. Morning procedure: • Bolus — only as a correction dose • Initiate intravenous fluids Afternoon procedure: • Bolus — if the child is allowed to have a breakfast — the usual dose of a rapid-acting insulin analog or 50% of the usual dose of a short-acting insulin; a correction dose may be added • Initiate intravenous fluids 2 hours before the procedure or no later than at noon
Therapy using personal insulin pump	It may be continued only if the anesthesiologist accepts this form of therapy and is able to manage it Continue insulin therapy using a previously programmed basal dose for a given period during the day (modification of the basal dose is usually not required) Hypoglycemia: withhold basal dose administration (for up to 30 minutes) Hyperglycemia: a correction bolus Initiate intravenous fluids 2 hours before the procedure

— Algorithm 2: In patients with diabetes type 2 and preserved insulin secretion, an optional approach is to administer glucose, insulin, and potassium (500 mL 10% dextrose with 8–16 units of short-acting insulin and 10–20 mmol of KCl).
  • A larger insulin dose (≥ 16 units) should be considered in obese patients, with severe infection, during cardiac or lung surgery, in patients operated under hypothermia, and if baseline blood glucose is > 180 mg/dL (10.0 mmol/L);
  • A smaller insulin dose (< 12 units) should be considered in lean patients and in those receiving small insulin doses or oral antidiabetic agents before the surgery.

2. Intravenous glucose, insulin, and potassium infusion should be initiated at 8 AM and continued at the rate of 80 mL/hour until resumption of normal oral feeding.
3. During intravenous glucose, insulin, and potassium infusion, blood glucose should be kept at 100–180 mg/dL (5.6–10.0 mmol/L):
— If plasma glucose level decreases or is close to the lower limit of the recommended range, insulin dose should be reduced by 2–4 units;
— It is recommended to increase the insulin dose by 2 units per each 30 mg/dL (1.6 mmol/L) rise of plasma glucose level over > 180 mg/dL (> 10 mmol/L).
4. If continued surveillance over the operated patient is possible, the algorithm 1 should be preferred.

IV. Postoperative management

1. Insulin treatment with multiple subcutaneous insulin injections or using a personal insulin pump should be initiated upon resumption of oral nutrition and continued (in case of temporary insulin therapy) until surgical wound healing. Depending on blood glucose levels, insulin should be administered subcutaneously 1–3 hours before termination of the intravenous infusion.
For patients with type 2 diabetes who have been on non-insulin medications and had good glycemic control prior to surgery, previous therapy can be resumed

when starting normal nutrition, provided there are no clinical contraindications.

Remark 4: In diabetic patients previously treated with insulin, operated due to an acute or chronic inflammatory condition, a possibility of a reduction of daily insulin requirement should be taken into consideration.

V. Perioperative management in children

Insulin dosing algorithm in case of major procedures and those requiring intravenous insulin therapy (Table 26.2).

In case of non-major procedures (< 2 hours) under general anesthesia or conscious sedation, patients with good metabolic control may be admitted in the morning on the day of the procedure or in the afternoon on the preceding day. Subcutaneous insulin therapy may be continued, or the algorithm for major procedures may be used (Table 26.3).

VI. Urgent surgery

Diabetic patients may sometimes require an urgent surgery.

In these cases, it is necessary to exclude ketoacidosis associated with poor metabolic control of diabetes as the cause of peritonism. Thus, if an acute abdomen is thought to be present in a patient with diabetic acidosis (aceturia and metabolic acidosis as indicated by blood gases), correction of acid-base abnormalities should be attempted immediately.

Ketoacidosis (base excess < –12; pH < 7.3) and hyperglycemic hyperosmolar state should be corrected according to the general management principles. If surgery cannot be postponed, treatment of metabolic disorders should be carried out simultaneously with surgical procedures.

If acute diabetes complications are nor present and the patient took his/her morning insulin dose, intravenous insulin infusion should be administered during the procedure, as described above.

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27. Vaccinations in patients with diabetes

Most important recommendations

- Every child with diabetes should undergo all currently recommended vaccinations. [**C**]
- Annual influenza vaccination is recommended in children > 6 months of age and adults. [**C**]
- Vaccination against hepatitis B virus is recommended in all individuals with diabetes. [**C**]

Every child with diabetes should undergo all currently recommended vaccinations. According to the immunization schedule for Poland, all children born after Jan 01, 2017 should be routinely vaccinated against *Streptococcus pneumoniae*. The vaccination status should be verified and missing doses should be given. Diabetic children born before Feb 01, 2017 should receive compulsory vaccination against *Streptococcus pneumoniae*. Due to their at-risk status, the vaccination should be performed before 5 years of age using 10- or 13-valent pneumococcal vaccine, while older individuals should be vaccinated using the 13-valent pneumococcal vaccine only. Annual influenza vaccination is recommended in children > 6 years of age and adults. Both quadrivalent vaccines available in Poland may be used for that purpose, administered intramuscularly (inactivated virus) or intranasally (live attenuated influenza vaccine). Non-immune patients should be vaccinated against chickenpox (varicella) (2 doses 6 weeks apart) rubella, mumps and measles as these diseases may result in serious decompensation of diabetes.

Since 1996, all infants are vaccinated against hepatitis B virus, and since 2000 this vaccination is also offered to 14-year-olds. Vaccination is recommended in all patients. Unvaccinated subjects at any age should be ac-

tively identified and offered vaccination according to the 0, 1, 6 months regimen. If the anti-HBs antibody titer in previously vaccinated subjects is < 10 IU/L, revaccination using 1–3 doses is recommended. If a protective antibody titer (> 10 U/mL) is not achieved after 3 doses of the vaccine (4–12 weeks after the last vaccination), further vaccination is not attempted. Mandatory and recommended vaccinations should be done before traveling to endemic areas in accordance with the recommendations of the Polish Ministry of Health issued on Sep 16, 2010 (Journal of Laws 2010, No. 180, item 1215), the Centers for Disease Control, and the World Health Organization. Each vaccination should be preceded by a physician examination.

Due to the ongoing COVID-19 pandemic, vaccination using available vaccines as licensed is recommended in all diabetic individuals.

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28. Recommendations regarding professional activity of patients with diabetes

Developed in cooperation with Dr Andrzej Marcinkiewicz and Prof. Jolanta Walusiak-Skorupa from the Institute of Occupational Medicine in Łódź

1. The sole fact of suffering from diabetes should never be a basis for discrimination or unequal treatment. Any professional limitations should be imposed after a careful analysis of the individual patient status and health condition.
2. In addition to providing effective therapy, the role of diabetologist in maintaining professional activity of diabetic patients includes:
   — Health education targeted at the development of health awareness and understanding of limitations arising from potential diabetes complications;
   — Help with producing an objective opinion regarding patient's health predispositions to professional activity by presenting information to the physician authorized for medical review and opining.
3. The patient's attitude should be the key factor taken into account when evaluating the health status for the purpose of professional activities. Each diabetic individual, regardless of the diabetes type and the management approach, must actively participate in the treatment.
4. Patient's health predispositions to professional activities or driving are evaluated and opined by a physician authorized to perform preventive health examinations or medically certify drivers. Due to an incidental nature of contacts with patients (often during a single consultation) leading to opining on the individual health status, it is advisable that a diabetic patient produce an opinion of the treating physician.
5. During the consultation for the purpose of medical review and opining, a diabetes specialist should:
   — Evaluate patient knowledge regarding the disease, its treatment, and possible complications, rating it as extensive, satisfactory, or not satisfactory;
   — Evaluate blood glucose self-management ability, rating it as high, acceptable, or low;
   — Evaluate hypoglycemia awareness and the patient's ability to prevent and counteract hypoglycemia, rating it as good or not satisfactory;
   — Confirm the presence or absence of hypoglycemia prodromes;
   — Categorize the risk of hypoglycemia as low, acceptable, or high;
   — determine the presence of chronic diabetes complications involving the eye, nervous system, and cardiovascular system;
   — Provide additional comments regarding chronic diabetes complications and the health condition of the patient which are important for the assessment of the risk for public safety.
6. Justification of professional activity limitations in diabetic patients is twofold and results from:
   — A risk of a hypoglycemic episode and associated impaired consciousness;
   — A risk of late diabetes complications which reduce the ability to engage in specific professional activities.

Contraindications to driving for holders of various categories of driving license and contraindications to work at specific workplaces are given in Appendix 2.

7. Patients with advanced chronic diabetes complications should not engage in professional activities in which organ damage resulting from diabetes might affect work safety. However, this should not refrain them from undertaking other activities for which a given diabetes complication is not an issue. At the same time, the nature of professional activities and related nuisances should not hinder metabolic control of diabetes, and thus patient protection from the development and acceleration of chronic diabetes complications.
8. A diabetes consultation for the purpose of examining drivers and workers should conclude with issuing a clear opinion on a standardized diabetes consultation card, using a template provided in the Appendix 2.
9. Health requirements for diabetic patients should be divided into two categories depending on patient's professional activities or workplace.
10. The first (higher) category includes professional activities and workplaces requiring unaffected psychomotor skills and related to exposure to adverse psychosocial factors, when performing professional duties might have an effect on the safety of the worker and his/her environment (collaborators and other persons who are not directly involved in these professional activities but are present in the immediate vicinity or are potentially affected by these activities, e.g. road traffic participants, big-box store clients, etc.). More restrictive health requirements should be viewed in the context of the risk of impaired consciousness, which may be an effect of severe hypoglycemia in diabetic patients.
11. Professions requiring a higher category health requirements, and thus particularly requiring consideration of the fact that a worker suffers from diabetes, are those related to public safety, including:
    — Professional driving (passenger transport drivers, truck drivers, train and underground drivers, taxi drivers);
    — Uniformed and emergency services: armed forces (army, navy, airforce), police, fire services, municipal police, paramedic services, shipping, penitentiary service, security guards;
    — Civil aviation: pilots and aviation engineers, flight deck personnel, air traffic controllers;
    — Other professions associated with particular dangers (working at a height, operating moving equipment, work at furnaces, in high ambient temperatures, incineration plants, ironworks, mining, places with high traffic and other places with high risk of accidents).
12. The second (lower) category of health requirements involves professional activities and workplaces with noxious factors and nuisances which may have a negative effect on the course of diabetes. In case of this lower category of health requirements, some professions and workplaces should be viewed as not recommended rather than absolutely contraindicated. Thus, additional attention should be paid to, and individual evaluation of health predispositions of a diabetic patient is required when making a decision regarding initiation or continuation of work at the following workplaces:
    — requiring increased physical effort, particularly of a static nature (e.g. miner, ironworker);
    — involving shift or night work;
    — involving exposure to carbon disulfide and pesticides — 2-chlorophenoxyacetic acid derivatives (e.g. dichlorprop, mecoprop).
13. Diabetologist should serve as an advisor to young patients, in whom particular attention should be paid to the choice of profession. In these cases, the natural history of diabetes should be taken into consideration in addition to the current health status, as future health limitations may prevent not only vocational training but also, in the longer term, work itself.
14. Appendix 3 includes the Charter of Employer and Employee Rights and Duties, serving to increase patient responsibility and their position as employees on one hand, and on the other hand to counteract exclusion of the diabetic patients from the labor market.

29. Diabetes care in penitentiary institutions

Subjects detained in penitentiary institutions (prisons, remand centers, juvenile detention centers) should be offered access to the same level of medical care, including diabetes care, as in the general population.

The penitentiary institution personnel should be informed about the diagnosis of diabetes in a detained subject, and should be trained how to recognize hyper- and hypoglycemia and intervene in such situations as well as in other emergencies.

30. Metabolic surgery

Most important recommendations

- Metabolic surgery should be recommended in patients with diabetes type 2 and BMI > 35 kg/m^2, especially if concomitant conditions are present and lifestyle modifications combined with antidiabetic medications do not allow adequate blood glucose control. [**A**]
- Each patient after surgical treatment of diabetes should remain under the care of a diabetologist and a general surgeon and receive continued vitamin and mineral supplementation to prevent their deficiencies. [**C**]

Metabolic surgery is an effective approach to manage obesity and concomitant conditions, in particular diabetes type 2. Multidisciplinary approach allows proper patient selection for metabolic surgery and choice of an appropriate surgical technique.

I. Patient selection for metabolic surgery

1. Metabolic surgery should be considered in all patients with diabetes type 2 and BMI > 35 kg/m^2, especially if concomitant conditions are present, such as hypertension and lipid disorders. In particular, metabolic surgery should be considered if drug treatment and lifestyle modifications do not allow adequate control of diabetes type 2 and obesity.
2. Referral for metabolic surgery is recommended in all patients with BMI > 40 kg/m^2 and diabetes type 2.
3. Metabolic surgery is indicated in patients with diabetes type 2 between 18 and 65 years of age. The upper age limit may be in some cases extended to 70 years if the individually assessed operative risk is lower than the potential benefits of surgery.
4. Patient selection for bariatric surgery should be performed by a physician team that at least comprises a diabetologist and a surgeon with a large experience in metabolic surgery. It is also recommended that the multidisciplinary team involved in patient selection include a cardiologist, respiratory medicine specialist, psychologist or psychiatrist, anesthesiologist, and dietician.

II. Types of surgical procedures

1. It is recommended that patients be referred for minimally invasive (laparoscopic) surgery.
2. Based on the available study results, patients with diabetes type 2 should be primarily referred for laparoscopic Roux-en-Y gastric bypass, laparoscopic mini gastric by-pass, laparoscopic sleeve gastrectomy, laparoscopic biliopancreatic diversion or single anastomosis duodeno-ileal by-pass (SADI).
3. The decision regarding the type of surgery should be made after a surgical consultation and individual consideration of the advantages and disadvantages of all surgical techniques listed above.
4. Before making the decision regarding metabolic surgery, patients are recommended to become acquainted with the informed consent forms prepared by the Metabolic and Bariatric Surgery Section of the Polish Society of Surgeons.

III. Complications of surgical treatment of diabetes type 2

Thirty-day mortality after metabolic surgery has been estimated at 0.1–0.3%, which is identical with the mortality risk associated with laparoscopic cholecystectomy and may be categorized as low risk. The most common complications of metabolic surgery include suture line dehiscence (3.1%), surgical suite infection (2.3%), pulmonary complications (2.3%), and gastrointestinal bleeding (1.7%).

IV. Evaluating outcomes of surgical treatment of diabetes type 2

Diabetes type 2 resolves in 40–95% of patients, depending on its duration, severity of obesity, and the type of surgical procedure.

The following approach to evaluating outcomes of surgical treatment of diabetes type 2 is recommended:

1. Resolution of diabetes and concomitant conditions

The disease may be considered resolved if after cessation of drug therapy:

— HbA_{1c} level is < 6.5%;
— No hypoglycemia episodes occur in the patient;
— total cholesterol is < 155 mg/dL (< 4 mmol/L), and LDL cholesterol is < 77 mg/dL (< 2 mmol/L);
— Triglyceride level is < 195 mg/dL (2.2 mmol/L);
— Blood pressure is < 140/90 mm Hg;
— Body weight decreased by > 15% compared to baseline, i.e. preoperative body weight.

2. Clinical improvement

The disease may be considered improved following metabolic surgery if after reduction of drug treatment used before the surgery:

— HbA_{1c} level decreased by > 20%;
— LDL cholesterol is < 100 mg/dL (< 2.6 mmol/L);
— Blood pressure is < 140/90 mm Hg.

V. Recommendations following surgical treatment of diabetes type 2

1. Each patient after surgical treatment of diabetes should remain under the care of a diabetologist and a general surgeon.
2. Continued vitamin and mineral supplementation is needed to prevent their deficiencies.

VI. Pregnancy and metabolic surgery

1. Pregnancy is allowed (i.e., becomes not contraindicated) 24 months after metabolic surgery.
2. Continued contact with the treating diabetologist is recommended before conception and throughout the pregnancy.

VII. Contraindications to metabolic surgery in patients with diabetes type 2

Absolute contraindications:

1. No patient acceptance for surgical treatment of diabetes type 2.
2. Alcohol or drug dependence (qualification for surgical treatment of obesity may be considered in patients who fulfil the requirement of documented abstinence for preceding 12 months or longer).
3. Mental conditions that cannot be controlled despite non-pharmacological and pharmacological therapy.
4. High cardiovascular risk associated with the procedure.
5. Endocrine diseases underlying obesity (e.g. Cushing's syndrome).
6. Lack of possibility to participate in permanent long-term control after surgical treatment.
7. The period of 12 months preceding the planned pregnancy, pregnancy and breastfeeding.

Relative contraindications:

1. Increase in body weight in the period immediately preceding the surgery, indicating poor compliance;
2. Active peptic ulcer — it requires treatment before surgery; in patients with asymptomatic H. pylori infection eradication before surgery is recommended, but not strictly necessary.
3. Patients who have been treated for a malignancy require an oncology consultation confirming that the malignancy has been cured.

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31. Selected special situations and diseases in patients with diabetes

Developed in cooperation with Prof. Renata Górska

I. Shift work

Shift work may be associated with both an increased risk of diabetes and its worse control. Hours of administration of oral hypoglycemic drugs or insulin may need to be modified.

1. Intensive self-monitoring is required in diabetic individuals working in shifts, particularly during working hours.
2. Antidiabetic drugs associated with low risk of hypoglycemia and allowing greater dosing flexibility (both oral and injected, including insulin) are preferred in diabetic individuals working in shifts.
3. Individuals treated with insulin, particularly those with diabetes type 1, should be able to modify insulin doses during intensive insulin therapy.

II. Time zone change

Travel is not contraindicated in diabetes. Diabetic individuals, particularly those with diabetes type 1 or 2 treated with insulin, should prepare for the travel, taking into account such factors as travel duration, means of transportation, time zone change (the direction of travel should also be considered, i.e., eastbound or westbound) and the climate of the destination country. Particular problems may be posed by a rapid change of the time zone (airplane travel).

1. Diabetic individuals treated with insulin, particularly those with diabetes type 1, should be particularly alert during the period of adaptation to the new time zone (its duration in days equals the time difference in hours). Frequent blood glucose monitoring is necessary during this period.

2. Individuals treated with basal-bolus insulin therapy flying westbound (i.e., with prolongation of the day) should administer a previously used long-acting insulin dose in the evening (new time). Possible hyperglycemia resulting from, e.g., meals consumed onboard, may be corrected with additional doses of a short-acting insulin/rapid-acting insulin analog. When travelling eastbound (i.e., with shortening of the day), it may be necessary to reduce the evening dose of long-acting insulin.
3. Individuals treated with personal insulin pump do not need to adjust the pump clock or modify insulin doses when the time zone change does not exceed 2 hours. With a greater change of the time zone and a longer planned duration of stay in the new time zone, it is recommended to gradually shift basal insulin infusion by 2 hours per day.

III. Glucocorticosteroid therapy

Multiple drugs have a diabetogenic effect. One particularly important class of diabetogenic drugs are glucocorticosteroids, both due to the magnitude of their diabetogenic effect and the frequency of their use. Glucocorticosteroids mostly increase postprandial glycemia.

1. Substitution doses of glucocorticosteroids (hydrocortisone up to 20 mg/day) and inhaled glucocorticosteroids have no significant effect on carbohydrate metabolism.
2. An increased risk of steroid-induced diabetes is affected by the following factors: older age, obesity, impaired glucose tolerance, use of a high glucocorticosteroid dose, and simultaneous use of other diabetogenic medications.
3. The preferred approach to the treatment of glucocorticosteroid-induced diabetes is intensive insulin therapy (or only administration of short-/rapid-acting insulin preparations before meals, if fasting and preprandial glycemia is acceptable). No superiority of any insulin or insulin analog preparation over the others has been shown in steroid-induced diabetes.
4. In patients with diabetes type 2 treated with oral hypoglycemic drugs who require temporary glucocorticosteroid use, particularly in high doses, intensive insulin therapy is recommended.
5. In patients with diabetes type 2 receiving combined therapy with basal insulin (NPH insulin or a long- -acting insulin analog), it is usually necessary to add short-acting insulin before meals.
6. In diabetic patients treated with insulin, glucocorticosteroid use is associated with an increased insulin requirement, particularly during the day.

IV. Periodontal disease

Periodontal disease and other oral diseases are more common in individuals with diabetes. Periodontal disease negatively affects the metabolic control of diabetes and increases the risk of its complications. Treatment of periodontal disease improves the metabolic control of diabetes.

1. Individuals with diabetes should be interviewed and undergo dental physical examination for oral diseases.
2. Every individual with diabetes should have a dental examination once a year.

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Appendix 1
Recommendations regarding the transition of patients with diabetes type 1 from pediatric to adult diabetes care

Transition from pediatric to adult diabetes care is a special period in the life of a young patient with diabetes type 1. The basic principle of this transition should be to provide continuity of care without any significant gap between termination of pediatric care and initiation of adult care. To make the transition smooth, the following recommendations should be adhered to:

1. The moment of transition from pediatric to adult diabetes care should be set individually so as not to interfere with the therapeutic process. Depending on the emotional development, family and educational situation, and other factors, the optimal age for transition of care is 16–21 years.
2. The patient should be prepared for the transition by his/her pediatrician over the period of at least one year. It is recommended that during this time, examinations for chronic disease complications and comorbidities are performed.
3. At the last visit in the pediatric diabetes clinic, which should take place at least 6 months before the transition, the patient should be referred to an adult diabetes clinic in a coordinated effort, which should include in particular:
   — setting the date of first visit in the adult clinic by contacting in advance the clinic, its coordinator, or optimally the future treating physician;
   — providing the patient with the pediatric care discharge summary (see an attached template on pages 79–80) which includes all relevant information regarding previous pediatric diabetic care.
4. Adult care should begin within 6 months after termination of the pediatric care.
5. It is recommended to create regional networks of cooperating pediatric and adult clinics that would develop the policy of continuous contact and patient transfer.
6. If the transition of care involves a large number of patients, it is recommended to appoint, both in pediatric and adult clinics, transition care coordinators who would manage the process of patient referral and care transition by scheduling visits, providing efficient flow of information, etc.
7. Devoting separate days for new arrivals of transitioned pediatric patients to adult clinics is not necessary but may be helpful in terms of organizing care, as these visits are much more time-consuming, particularly in patients treated with personal insulin pumps.

Developed by:

Leszek Czupryniak, Andrzej Gawrecki, Przemysława Jarosz-Chobot, Tomasz Klupa, Małgorzata Myśliwiec, Agnieszka Szadkowska, Bogna Wierusz-Wysocka, and Bogumił Wolnik

PEDIATRIC DIABETES CARE DISCHARGE SUMMARY

PATIENT DATA

Name and surname: PESEL:

Diagnosis: Type 1 diabetes Date of diagnosis (MM/YYYY):

CURRENT THERAPY:

Multiple insulin injections ☐ Type(s) of insulin: ..... Daily dose: ..... Basal dose: ..... Meal boluses: ..... Correction dose:	Continuous glucose monitoring ☐ Type of insulin: ..... Pump report attached ☐ * or: Daily dose: ..... Basal dose: ..... Carb-to-insulin ratios: ..... Correction dose: .....
Other antihyperglycemic drugs:	

Glycemic control: ☐ Glucometer ☐ CGM ☐ FGM

HbA_{1c} range during therapy:

Recent value: (date-value):

The number of visits to diabetes clinic during the previous 12 months

PREVIOUS HOSPITALIZATIONS FOR ACUTE COMPLICATIONS

Cause	Number
Diabetic ketoacidosis	
Severe hypoglycemia	

Episodes of severe hypoglycemia during the previous 12 months (dates):

Chronic complications of diabetes:		GRADE/COMMENTS
Retnopathy	YES/NO	
Diabetc kidney disease	YES/NO	
Somatic neuropathy	YES/NO	
Autonomic neuropathy	YES/NO	

Concomitant conditions:

Diagnosis		Date of diagnosis	Current treatment
Autoimmune thyroid disease	YES/NO		
Celiac disease	YES/NO		

Hypertension	YES/NO		
Hyperlipidemia	YES/NO		

Diabetes education: ☐ needs correction: ☐ satisfactory ☐ very good

Documents attached

Hospital Discharge Summary Report: ☐ YES / ☐ NO

Results of examinations performed dring the last 12 months: ☐ YES / ☐ NO

Date _____ **Physician's signature** _____

PATIENT'S STATEMENT:

I, the undersigned, hereby declare that I have received a Pediatric Diabetes Care Discharge Summary:

Date: _____

Patient's signature: _____

Parent's signature: _____

ADDITIONAL INFORMATION FOR A DIABETES SPECIALIST IN THE ADULT DIABETES CLINIC PROVIDED VOLUNTARY BY THE PATIENT:

I would like to improve the treatment of diabetes in the following areas:

☐ Frequency of blood glucose measurements

☐ Regular administration of insulin before meals and to correct hyperglycemia

☐ Healthier nutriton, e.g. limitng sweets

☐ Carbohydrate counting

☐ Knowing the glycemic index and glycemic load

☐ Knowing the impact of protein and fat on glycemia

☐ Knowing my energy demand

☐ Regular physical actvity

Patients using insulin pumps

☐ Regular replacement of infusion sets

☐ Using the bolus calculator

☐ More frequent use of the temporary basal rate

Patients using contnuous glucose monitoring systems

☐ Checking more frequently glycemic levels and trends

☐ Taking into account glycemic trends when modifying insulin doses and glucose intake

☐ System calibration

☐ Alarm programming

Appendix 2
Medical review and opining in drivers and workers with dysglycemia or diabetes

Developed in cooperation with dr hab. Andrzej Marcinkiewicz and Prof. Jolanta Walusiak-Skorupa (Institute of Occupational Medicine in Łódź)

I. Medical review and opining in drivers

1. Medical review and opining in drivers with dysglycemia or diabetes is regulated by the Appendix No. 6 to the ordinance of the Minister of Health of August 29, 2019 on medical examinations of driving license applicants and drivers (Journal of Laws 2019, item 1659), entitled "Detailed conditions of the medical examinations related to diabetes".
2. Based on the results of a medical examination, laboratory tests, and specialist consultations, a physician authorized to medically certify drivers evaluates the risk for traffic safety and includes it in the medical opinion.
3. According to the section 3a and 4 of the above mentioned Appendix to the ordinance of the Minister of Health, **an opinion of a diabetes specialist or another physician engaged in treating diabetes**, including a statement of no other medical contraindications to driving related to diabetes, **is obligatory in subjects:**
   — Applying for or holding a category C1, C1+E, C, C+E, D1, D1+E, D, D+E driving license, or a tram driving permit;
   — Working as road carriage drivers, within the meaning of the Road Transport Act;
   — Working as drivers of emergency vehicles or armored transportation service vehicles;
   — Driving license instructors and examiners;
   — Applying for or holding a category AM, A1, A2, A, B1, B, B + E or T driving license — in patients with recurrent severe hypoglycemia.
4. In case of diagnostic or medical opining uncertainties, a physician authorized to examine drivers may also order a diabetes consultation.
5. To be considered by a physician authorized to medically certify drivers, a **diabetes consultation for the purpose of medical review and opining in drivers must conclude with issuing a diabetes consultation card** using a template provided in the Appendix No. 6 to the above cited ordinance of the Minister of Health of August 29, 2019 (see page 96).
6. The consulting diabetes specialist, or other physician engaged in treating diabetes, should also assess the patient's ability to drive and enter the relevant information in the consultation card, which may have the following effect of the final medical opinion:
   — No medical contraindications to driving:
     - **Without time constraints** resulting from the investigations for dysglycemia,
     - **With time constraints** resulting from the identified dysglycemia (consistent with a low or increased risk for traffic safety);
   — Medical contraindications to driving resulting from the identified dysglycemia:
     - **Relative**, with indication of a period after which the patient may undergo a repeated medical assessment (consistent with a high risk for traffic safety, and an option of reassessment),
     - **Absolute** medical contraindications to driving (consistent with a high risk for traffic safety and no indication of the timing of a repeated medical assessment).
7. In patients applying for or holding a category AM, A1, A2, B1, B, B+E, or T driving license:
   — An absolute contraindication to driving vehicles is insufficient hypoglycemia awareness, meaning that the patient, when awake, does not feel pathologically low blood glucose levels or does not respond to them, despite alerts generated by an external continuous glucose monitoring (CGM) device, which may lead to severe hypoglycemia and impaired consciousness.
   — A relative contraindication is recurrent severe hypoglycemia (at least two episodes of severe hypoglycemia during the last 12 months),
8. In patients using CGM, a statement of no contraindications to driving vehicles of category AM, A1, A2, B1, B, B+E, or T may be issued by a physician authorized to medically certify drivers upon obtaining the opinion of a diabetologist indicating that:
   — The patient constantly uses a CGM system for self-monitoring;
   — The patient has at least sufficient knowledge about self-monitoring in diabetes, including CGM;
   — The patient adequately responds to alerts generated by a CGM device;
   — Regular diabetes care (minimum 3 visits a year in diabetic clinic, at regular intervals of 3–4-months).
9. In patients with a history of recurrent severe hypoglycemia who are applying for or holding a category AM, A1, A2, A, B1, B, B + E or T driving license, a statement of no medical contraindications to driving can

be issued by a physician authorized to medically certify drivers upon obtaining the opinion of a diabetologist indicating that:
- — At least 3 months have passed since the last episode of severe hypoglycemia during the waking hours;
- — The level of diabetes control ensures traffic safety;
- — The patient constantly uses a CGM system for self-monitoring, including mandatory use of CGM while driving;
- — The patient has at least sufficient knowledge about self-monitoring in diabetes, including CGM;
- — The patient adequately responds to alerts generated by a CGM device;
- — The patient has regular medical check-ups — at least 3 times a year, at regular intervals of 3–4-months (subject to point 13).

10. In patients applying for or holding a category C1, C1+E, C, C+E, D1, D1+E, D, D+E driving license, or tram driving permit, road transport drivers, emergency vehicle or armored transportation service drivers, and driving license instructors and examiners, the absolute contraindications to driving vehicles are:
    - Any history of severe hypoglycemia during the waking hours;
    - Hypoglycemia unawareness during the waking hours, defined in Appendix No. 6 to the above-mentioned ordinance of the Minister of Health of August 29, 2019 as not being aware of pathologically low (< 70 mg/dL or < 3.9 mmol/L) blood glucose levels, occurring as an important complication of the frequent occurrence of hypoglycemic episodes;
    - Other diabetes-related complications that preclude driving.
    - — A positive opinion on the ability to drive can be issued if the following conditions are met:
        - Regular monitoring of blood glucose, i.e. at least four times a day in patients taking more than one insulin injection daily, and once a day and at times relevant to driving vehicles in patients using other treatment models, with glucose readings recorded in a way that allows assessment of the course of diabetes;
        - Documentation of diabetes control by treating physician;
        - Full awareness of the risk of hypoglycemia during the waking hours.
11. The consultation card is handed by the diabetes specialist, or other physician engaged in treating diabetes, to the patient who presents it to the physician authorized to medically certify drivers. In case of a negative opinion regarding the ability to drive, it is recommended that the opining physician who referred a patient for a diabetes consultation is informed directly by the consulting specialist.
12. During the consultation, the driver must be informed that in the event of an episode of severe hypoglycemia during the waking hours, also unrelated to driving, he or she is strictly obliged to have his/her ability to drive reassessed.
13. Diabetes consultation should be performed by a physician certified in diabetology or a physician with other board certification who manages diabetes in the consulted patient.
14. In the following cases, information about the need of repeated medical assessment in order to verify the patient's fitness to drive should be sent to the territorially competent transport department or local government unit using a form referring to Article 75, paragraph 1, item 5 of the Act of January 5, 2011 on drivers of vehicles (Journal of Laws of 2020, item 1268 as amended) (see page 98).
    - — When there are reasonable indications that the patient is driving the vehicle less than 3 months after the last episode of severe hypoglycemia;
    - — When the patient does not attend the scheduled medical examinations (especially if he or she has severe hypoglycemic episodes during the waking hours) and when all available forms of effective notification to the patient about the need for follow-up examinations have been ineffective;
    - — Obligatorily after each episode of severe hypoglycemia.
15. Any insulin-treated patient who has been considered as having no diabetic contraindications to driving vehicles should be advised to monitor blood glucose (glucose meter/scanning system/CGM) each time before driving. The patient should not start driving with blood glucose below 100 mg/dL (5.6 mmol/L), unless the diabetologist individually sets a different blood glucose threshold for driving.
16. While driving, blood glucose should be measured at least every 2 hours, and in the case of a decrease in blood glucose below 100 mg/dL, the patient should stop driving and eat an appropriate amount of carbohydrate.

II. Medical review and opining in workers

1. Medical review and opining in workers and persons taking up work is regulated by the ordinance of the Minister of Health of May 30, 1996 on medical examinations of workers, the extent of preventive care for workers, and issuing medical opinions for the purposes provided for in the Labor Code (Journal of Laws 2016, item 2067).
2. A physician performing a preventive examination may extend it with a diabetes consultation and additional tests if these are considered necessary for proper evaluation of the health status of a worker or a person taking up work.

3. To serve as a useful opinion allowing an objective decision to be made based on individual patient assessment, **diabetes consultation for the purpose of preventive examination should include key information for the evaluation of health predispositions to work in specific conditions and in accordance with specific requirements.** For this purpose, it is recommended to use a diabetes consultation card based on the template provided (see page 97).
4. Based on the results of a medical examination, laboratory tests, and specialist consultations, a physician authorized to perform preventive examinations and medically certify workers issues a medical opinion regarding the absence or presence of medical contraindications to perform or take up work at a specific workplace.
5. **Absolute contraindications to perform work at workplaces associated with higher health requirements include:**
   — Recurrent severe hypoglycemia or even a single previous episode of medically unexplained severe hypoglycemia during the waking hours (a fall in blood glucose level leading to impaired consciousness and the need for medical intervention);
   — Hypoglycemia unawareness during the waking hours without prospects for an improvement, resulting from a chronic diabetes complication of vegetative neuropathy which impairs patient's ability to detect an increasing severity of hypoglycemia, and thus is not associated with an appropriate patient response to decreased blood glucose levels;
   — Advanced eye complications, mostly diabetic retinopathy or cataract with vision impairment;
   — Other advanced chronic diabetes complications;
   — An opinion of a diabetologist or a treating primary care physician which states a high risk of hypoglycemia and/or unawareness of hypoglycemia prodromes during the waking hours.
6. **Relative contraindications to perform work at workplaces associated with higher health requirements exist in conditions with a potential to improve, including:**
   — Lack of metabolic control of the disease ($HbA_{1c} \geq 8\%$);
   — Lacking or low blood glucose self-management ability;
   — Inadequate patient knowledge regarding diabetes, hypoglycemia, and the approaches to prevent hypoglycemia;
   — Non-compliance to physician recommendations.
   In such cases, reassessment should be scheduled within 1–3 months.

Stamp of the healthcare provider or physician's practice

Diabetes consultation card for examining driving license applicants and drivers (Appendix No. 6 to the ordinance of the Minister of Health of August 29, 2019 on medical examinations of driving license applicants and drivers — Journal of Laws 2019, item 1659) with amendments

Patients data

Name and surname

PESEL | | | | | | | | | | |

Personal identity card details and number in non-PESEL holders

Address: City/town Postal code

Street House/apartment number

Driving licence applicant: **Driving licence holder:**

Diabetes: Date of diagnosis Type: Treating physician:

Healthcare provider

Diabetes clinic

Patient knowledge regarding the disease, its treatment, and complications: Extensive Satisfactory **Not satisfactory**

Blood glucose self-management ability: High Acceptable **Low**

Hypoglycemia awareness, ability to prevent and counteract hypoglycemia: Good **Not satisfactory**

Occurrence of hypoglycemia prodromes Yes **No**

Risk of hypoglycemia: Low Acceptable **High**

Presence of chronic diabetes complications y No chronic diabetes complications

Eye Nervous system Cardiovascular system

Comments regarding chronic diabetes complications:

Assessment of the ability to drive:

In patients using continuous glucose monitoring, the following three questions should be answered:

1. Constant use of CGM: ☐ Yes ☐ No 2. Good knowledge of and adequate response to CGM: ☐ Yes ☐ No

3. Regular visits in diabetes clinic (minimum every 3–4 months) with data retrieval from pump and CGM memory: ☐ Yes ☐ No

Other remarks:

.....

(*Date*)

.....

(*Signature and stamp of the diabetes specialist or another physician engaged in treating diabetes*)

Stamp of the healthcare provider or physician's practice

Diabetes consultation card for preventive examinations
— documentation of diabetes control by the treating physician for the purpose of evaluation of patient's health predispositions to professional activity
(developed by A.Marcinkiewicz and D. Szosland)

Patient data

Name and surname

PESEL | | | | | | | | | | |

Personal identity card details and number in non-PESEL holders

☐ **Diabetes** Date of diagnosis: Type: Treating physician: ☐ Primary care ☐ Diabetes clinic

Patient knowledge regarding the disease, its treatment, and complications: ☐ Extensive ☐ Satisfactory ☐ **Not satisfactory**

Blood glucose self-management ability: ☐ High ☐ Acceptable ☐ **Low**

Hypoglycemia awareness, ability to prevent and counteract hypoglycemia: ☐ Good ☐ **Not satisfactory**

Occurrence of hypoglycemia prodromes ☐ Yes ☐ **No**

Risk of hypoglycemia: ☐ Low ☐ Acceptable ☐ **High**

☐ **Presence of chronic diabetes complications** ☐ No chronic diabetes complications

☐ Eye ☐ Nervous system ☐ Cardiovascular system

Comments regarding chronic diabetes complications:

Other remarks:

In patients using continuous glucose monitoring, the following three questions should be answered:
1. Constant use of CGM: ☐ Yes ☐ No 2. Good knowledge of and adequate response to CGM: ☐ Yes ☐ No
3. Regular visits in diabetes clinic (minimum every 3–4 months) with data retrieval from pump and CGM memory: ☐ Yes ☐ No
Other remarks:

..... (Date)

..... (*Signature and stamp of the diabetes specialist or another physician engaged in treating diabetes*)

....., (Date)

.....

(City/town)

Name and address of the referring unit:
.....
.....
.....
.....

Name, surname, address,
identification data of the person
whom the notification concerns:
.....
.....
.....
.....

The name of the territorially competent transport department or local government unit*:
.....
.....
.....
.....

Notification

Pursuant to Article 75, paragraph 1 item 5 of the Act of 5 January 2011 on drivers of vehicles (Journal of Laws of 2020, item 1268 as amended), we inform thatthere are reasonable and serious concerns regarding the health status of:

Mr./Ms.....,

which, if he or she has a driving license or a tram driving permit, require a necessary and urgent assessment of the ability to drive the above-mentioned vehicles and verification of the medical certificate.

……

Signature of the person making the notification

Note:
*territorial competence concerns the person being reported

pracuj z cukrzycą

Appendix 3
Charter of Employer and Employee Rights and Duties

Diabetes is a chronic metabolic disease that affects an increasing number of patients. It has been estimated that the number of subjects with diabetes in Poland is about 2.6 million people, and the disease has been identified and treated in 60% of them. The current scope of this problem and an increasing incidence of both diabetes type 1 and type 2 have very significant medical and socioeconomic consequences, and issues related to the prevention and effective treatment of diabetes and its complications are beyond the responsibility of the medical community and patients themselves.

According to the World Bank estimates, the economic burden of diabetes is second only to that of ischemic heart disease. This economic toll results not only from the costs of diagnosing and treating diabetes but also from the costs of premature termination of professional activity, including inability to work and related social benefits, as well as unemployment which is a particular problem in diabetic subjects.

Due to the fact that:

- unemployment rates among diabetic subjects are more than twice increased compared to the healthy population, and the resulting worse economic status may hinder appropriate diabetes control;
- the place of work is an important link in the process of preventing civilization disorders;

and also due to our belief that:

- drugs currently used in the treatment of diabetes, along with increasing patient awareness regarding self-management, lead to a longer and more effective preservation of a good health condition and the ability to remain professionally active;
- the sole fact of having diabetes does not automatically make the employee inferior

Building on numerous European initiatives targeted at the prevention, early detection, and appropriate treatment of diabetes, and improvement of the quality of life of diabetic patients, including the European Parliament resolution of March 13, 2012 on addressing the diabetes epidemic in the European Union and the Copenhagen roadmap developed during the European Diabetes Leadership Forum on April 25–26, 2012.

On the eve of the 2012 World Diabetes Day, the signatories of the present document, representing the medical community, diabetes patient community, and the employers' community, postulate to write down the rights and duties of diabetic patients and their potential employers to increase patient responsibility and their position as employees on one hand, and on the other hand to counteract exclusion of the diabetic patients from the labor market.

Rights and duties of an employee suffering from diabetes

1. Each diabetic patient should be aware of the fact that effective diabetes control must take place both at home and at work.
2. At work, an employee suffering from diabetes should conform to the same principles of diabetes control as at home, i.e. periodic blood glucose monitoring, taking medications as prescribed by a physician, and adhering to the recommended meal timing and diet.
3. An employee suffering from diabetes should inform the employer about the disease and if possible, individually adjust the nature and timing of the work to allow disease control.
4. Diabetic patients should be aware of the contraindications to engage in some professions (e.g., pi-

lot, public transport driver, working at height, work requiring extremely strenuous exercise) and should inform their employers if their professional responsibilities entail such activities.

5. An employee suffering from diabetes should inform his/her closest collaborators about the disease so as they are able to provide appropriate help in case of an episode of hyper- or hypoglycemia, and maintain continuity of work.

Rights and duties of an employer

1. Each employer should be aware that diabetes does not disqualify subjects with this disease from undertaking professional activities, and any employee discrimination due to incident or prevalent diabetes is unacceptable. Acquirement of the basic knowledge about the disease by the employer is the key to understand the situation of a diabetic patient.
2. Carrying out employer's duties, including the obligation to create safe and hygienic work environment, requires that the employer has the right to and should know which of his/her employees suffer from diabetes.
3. The employer should allow the employee suffering from diabetes to conform to the principles of controlling the disease at work and motivate him/her to a responsible behavior that guarantees the safety of the patient him-/herself and his/her collaborators.
4. If possible, the employer should provide the employee suffering from diabetes with a workplace that allows optimal disease control (e.g., option to discontinue shift work, short breaks for additional meals).
5. If possible, the employer should allow transfer of an employee with newly diagnosed diabetes to another/equivalent workplace if continuing work at the previous workplace might be associated with work safety hazards or would make controlling the disease difficult for the employee.
6. If possible, the employer should promote the healthy lifestyle at work by encouraging employees to engage in physical activity, adhere to a balanced nutrition, and undergo preventive examinations.

On behalf of the signatories
Prof. Leszek Czupryniak
President of Diabetes Poland
Warsaw, November 13, 2012

Appendix 4
Recommendations of the Polish Endocrine Society and Diabetes Poland on screening for thyroid dysfunction in diabetes type 1 and 2

Diabetes type 1

1. During each patient visit to a diabetes specialist, it is necessary to perform clinical examination targeted at thyroid disease. If thyroid dysfunction is suspected, thyroid-stimulating hormone (TSH) level should be measured.
2. It is recommended to determine TSH level and thyroid peroxidase autoantibody (TPOAb) titer in all patients with newly diagnosed diabetes type 1 and in patients with established diabetes type 1 in whom thyroid function was not evaluated previously.
3. In patients with anti-TPO antibody titer above the reference range and TSH level ≥ 2 mIU/L, free thyroxine (fT4) should be measured and TSH level measurement should be repeated annually.
4. In patients with anti-TPO antibody titer within the reference range and TSH level ≥ 2 mIU/L, TSH level should be measured every 2 years.
5. In patients with TPOAb titer within the reference range and TSH level < 2.0 mIU/L, TSH level should be determined every 5 years.
6. In patients with a positive family history of hypothyroidism due to chronic autoimmune thyroiditis, TSH level should be determined annually.
7. TSH level should be determined in diabetic patients with uncontrolled lipid parameters.
8. TSH level and TPOAb titer should be determined in any patient planning pregnancy (particularly with an adverse obstetric history).
9. TSH level and TPOAb titer should be determined in all patients at 4–8 weeks of gestation (initial obstetric visit).
10. In all patients with a history of Graves disease, TSH level and thyrotropin receptor antibody (TRAb) titer should be determined at 4–8 weeks of gestation (initial obstetric visit). In addition, TRAb titer should reevaluated at the end of the second trimester (before 22 weeks of gestation).

Diabetes type 2

1. During each patient visit to a diabetes specialist, it is necessary to perform clinical examination targeted at thyroid disease. If thyroid examination is abnormal, TSH level should be measured.
2. It is recommended to determine TSH level in all patients with newly diagnosed diabetes type 2 and in patients with established diabetes type 2 in whom thyroid function was not evaluated previously.
3. TPOAb titer should be determined in patients with TSH level ≥ 2.0 mIU/L.
4. If TPOAb titer is above the reference range, the diabetes type should be verified, primarily by measuring anti-glutamic acid decarboxylase (anti-GAD) autoantibodies.
5. In patients with TPOAb titer above the reference range and TSH level ≥ 2.0 mIU/L, fT_4 level should be measured, and TSH level should be determined annually.
6. In patients with TPOAb titer within the reference range and TSH level ≥ 2.0 mIU/L, and TSH level should be determined every 2 years.
7. In patients with TPOAb titer within the reference range and TSH level < 2.0 mIU/L, TSH level should be determined every 5 years.
8. TSH level should be determined in diabetic patients with uncontrolled lipid parameters.
9. TSH level should be determined in any patient planning pregnancy.
10. TSH level and TPOAb titer should be determined in all patients at 4–8 weeks of gestation (initial obstetric visit).
11. In all patients with a history of Graves disease, TSH level and thyrotropin receptor antibody (TRAb) titer should be determined at 4–8 weeks of gestation (initial obstetric visit). In addition, TRAb titer should reevaluated at the end of the second trimester (before 22 weeks of gestation).

Source: Sowiński J, Czupryniak L, Milewicz A, Hubalewska-Dydejczyk A, Szelachowska M, Ruchała M, Lewiński A, Górska M, Siewko K, Wender-Ożegowska E, Zozulińska-Ziółkiewicz D, Junik R, Sawicka N, Gutaj P. Recommendations of the Polish Endocrine Society and Diabetes Poland for the diagnosis and management of thyroid dysfunction in diabetes type 1 and 2

Appendix 5
Position of the Polish Society of Obesity Research and Diabetes Poland on the use of low-calorie sweeteners

An increasing prevalence of overweight and obesity along with their complications, primarily diabetes type 2 and cardiovascular disease, is one of the major challenges of modern medicine. Obesity has been considered a 21st century epidemic by the World Health Organization. The epidemic of obesity is caused by lifestyle changes such as lack of physical activity and excessive consumption of highly processed high-energy-dense foods, leading to a positive energy balance.

Effective prevention and treatment of overweight and obesity together with their complications requires permanent lifestyle changes which are difficult due to numerous intrinsic and extrinsic factors that tend to decrease the motivation of a person forced to stop consuming favorite foods. **A reduction of the energy density of the available foods by changing their production technology and composition is an important component of prevention efforts at the societal level.** However, introduction of such changes requires consumer acceptance regarding the choice of low-calorie products, which in turn requires preservation of an attractive taste by the food industry. In humans, sweet taste preferences develop already in childhood, as human milk contains lactose and has a mildly sweet taste. To satisfy consumer preference for sweet taste and at the same time reduce the calorie content of foods and beverages, low-calorie sweeteners are used by the food industry.

Low-calorie sweeteners are substances with a sweet taste and the energy content of zero to few calories. As their sweet taste is very intensive, they may be added to foods in very low quantities. Currently, sweeteners are used in the production of non-alcoholic beverages, sweets, frozen desserts, yoghurts and puddings, as well as many medications.

A natural low-calorie sweetener, stevia, may be used for baking and cooking, as it is resistant to temperatures up to 200°C.

Based on safety studies and positive opinions of the European Food Safety Authority and the Panel on Food Additives and Nutrient Sources Added to Food, eleven low-calorie sweeteners are approved for use in the European Union: acesulfame K (E950), aspartame (E951), aspartame-acesulfame salt (E962), cyclamate (E952), neohesperidine dihydrochalcone (DC) (E959), saccharin (E954), sucralose (E955), thaumatin (E957), neotame (E961), erythritol (E968), and steviol glycosides (E960). According to the Regulation (EC) No. 1333/2008 on food additives, food products containing these substances should be labeled accordingly. In addition, the Regulation (EC) No. 1333/2008 specifies the maximum content of specific low-calorie sweeteners for different food product categories.

During the process of approving low-calorie sweeteners, the acceptable daily intake (ADI) in mg/kg body weight per day is also determined, defined as the amount of the substance which may be safely taken daily on a long-term basis (throughout life) without any harmful effects on the health. ADI values for specific low-calorie sweeteners are shown in Table 1.

The remaining approved substances are very rarely used by the food industry and therefore respective ADI values have not been determined.

European studies indicate that the intake of all low-calorie sweeteners is lower than their ADI.

Regarding reports of a purportedly increased risk of some neoplasms in experimental animals given saccharine, aspartame, and cyclamate, it should be emphasized that the results of recent human studies did not confirm these suggestions.

Based on these data, the **Polish Society of Obesity Research and Diabetes Poland confirm the safety of**

Table 1. Acceptable daily intake (ADI) of specific low-calorie sweeteners

Substance	Code	ADI [mg/kg body weight/day]
Acesulfame K	E950	0–15
Aspartame	E951	0–40
Cyclamate	E952	0–7
Saccharin	E954	0–5
Sucralose	E955	0–15
Neotame	E961	0–2
Steviol glycosides	E960	0–4

low-calorie sweetener use in food products and recommend substituting these substances for saccharose by overweight and obese subjects, particularly if dysglycemia (impaired fasting glucose, impaired glucose tolerance, or diabetes type 2) is also present.

Of note, a beneficial effect of low-calorie sweeteners on body weight in children and adolescents has been recently confirmed in randomized studies published in the *New England Journal of Medicine*.

A separate issue is the use of low-calorie sweeteners during pregnancy. While saccharine crosses the placenta and should not be used during pregnancy due to its unclear effects on the fetus, other low-calorie sweeteners are allowed during pregnancy.

The Polish Society of Obesity Research and the Diabetes Poland would like to draw attention of patients and physicians to the need to evaluate the energy value of the products in which low-calorie sweeteners have been substituted for sugar and which are marketed as safe for diabetic patients due to the fact that they have no significant effect on postprandial glucose and insulin levels. Despite this modification, some of these products may still be characterized by a high energy value due to their fat content and may contribute to an increase in body weight, thus worsening blood glucose control. The best way to make sure that a product in which low-calorie sweeteners were substituted for sugar is actually a low-calorie product is to compare its energy value with the energy value of a similar sugar-containing product, and to note its fat content.

The Polish Society of Obesity Research and Diabetes Poland emphasize that consumption of food products with a reduced energy value due to their low-calorie sweetener content may not be the sole lifestyle change introduced. This is only an approach to satisfy the need for sweet taste without consuming mono- and disaccharides, which may facilitate adherence to the nutritional recommendations and blood glucose control. However, another factor that plays an important role in the development of overweight and obesity along with their complications is fat intake which also needs to be reduced. It should also be emphasized that decreasing food energy value alone leads to a reduction of not only adipose tissue mass but also muscle mass. Thus, regular physical activity is required to prevent muscle mass loss (30 minutes of aerobic exercises at least 5 times a week, e.g. walking, cycling, swimming).

Magdalena Olszanecka-Glinianowicz
President of the Polish Society of Obesity Research

Leszek Czupryniak
President of the Diabetes Poland

Appendix 6
Recommendations on the management of diabetes using a personal insulin pump

I. Requirements for centers initiating and/or providing treatment with a personal insulin pump. Place of service provision: diabetes clinic or hospital ward, unit equipped with computers allowing the retrieval and analysis of data from insulin pumps and continuous glucose monitoring (CGM) systems. **Unit personnel experienced in treating diabetes with personal insulin pumps:** physicians with board certification in pediatric endocrinology and diabetology, physicians with board certification in diabetology skilled in the treatment with personal insulin pumps (Polish Society of Diabetes certification); nurses/educators trained in the treatment with personal insulin pumps. During visits, it is necessary to regularly retrieve and analyze data from personal insulin pumps, glucose meters, and CGM systems.

II. Therapy initiation includes patient selection for personal insulin pump treatment, patient education regarding continuous subcutaneous insulin infusion, setting up the insulin pump, and a verification visit to evaluate the patient skills and the achieved metabolic control of diabetes. Patients opting for personal insulin pump treatment should be aware of the functions and technical parameters of specific pump models. This includes the type of bolus calculator, integration with a CGM system, and the type of infusion set — using a drain or a drain-free pump ("patch").

III. Indications and contraindications for insulin pump therapy reimbursed by the National Health Fund.

A. Indications for personal insulin pump reimbursement in patients with diabetes type 1 below 26 years of age:

1. Early morning hyperglycemia following the end of a remission period*.
2. Frequent hypoglycemia episodes following the end of a remission period*:
   — Severe hypoglycemia episodes more frequently than once a year;
   — Hypoglycemia < 70 mg/dL not requiring help of another person ≥ 4 times a week;
   — Inability to achieve target hemoglobin A_{1c} (HbA_{1c}) level without frequent hypoglycemia episodes, i.e. ≥ 4 times a week;
   — Impaired awareness of typical hypoglycemia symptoms.
3. Persistently elevated HbA_{1c} level > 6.5% but < 9.0% despite treatment intensification in a patient who is well educated regarding the principles of intensive insulin therapy, cooperates with the diabetes treatment team, and adheres to blood glucose self-monitoring recommendations (≥ 7 blood glucose measurements per day).
4. Subjects engaged in shift work, with irregular professional activity, or traveling frequently to other time zones, with HbA_{1c} level < 9.0%.
5. Subjects engaged in competitive sport or undertaking regular intensive physical activity, with HbA_{1c} level < 8.5%.
6. Children and/or their parents accepting this form of insulin therapy.
7. Continuation of previous treatment with personal insulin pump if no contraindications exist**.

In selected cases, the decision on insulin pump purchase reimbursement may be made by the voivodship diabetes consultant or the voivodship pediatric endocrinology and diabetes consultant after reviewing the patient's medical records and obtaining an opinion of the treating diabetes specialist (including such issues as concomitant conditions and corticosteroid treatment).

B. Contraindications for National Health Fund reimbursement of personal insulin pump in patients with diabetes type 1 below 26 years of age.

1. HbA_{1c} level ≥ 9.0% — an average value during the last year.
2. Mental disorders — psychosis and severe depression, also those affecting the parents of children below 16 years of age.
3. Intellectual disorders, also those affecting the parents of children below 16 years of age, which prevent understanding the principles of intensive insulin therapy and personal insulin pump handling.
4. Eating disorders.
5. Addiction to alcohol and psychoactive substances also those affecting the parents of children below 16 years of age.
6. Unexplained missing visits to a diabetes clinic (attendance at only one visit or no visits during a year).
7. Non-adherence to or non-comprehension of the principles of intensive insulin therapy (no adequate blood glucose self-monitoring, failure to test for ketone bodies in cases of prolonged hyperglycemia, imprecise estimation of prandial insulin doses).
8. More than one episode of ketoacidosis during a year.
9. Severe, rapidly progressing proliferative retinopathy before or during laser therapy.

10. No disease acceptance despite full diabetes care and psychologic support (a written opinion of psychologist experienced in diabetes care).
11. Poor personal hygiene.
12. Regular exposure to strong magnetic fields.

C. Contraindications to continuation of treatment with a personal insulin pump and equipment reimbursement* in patients with diabetes type 1.**

1. No improvement or worse metabolic control of diabetes after one year of treatment using a personal insulin pump.
2. More than one episode of diabetic ketoacidosis during a year.
3. More episodes of severe hypoglycemia compared to during treatment with insulin pen devices.
4. Non-adherence to the principles of intensive insulin therapy.
5. Severe skin reactions at the site of infusion set implantation despite an attempt to change the type of the infusion set.
6. Irregular exchanges of infusion sets (less frequently than every 3 days).
7. Unexplained missing visits to a diabetes clinic (attendance at only one visit or no visits during a year).
8. Persisting HbA_{1c} level ≥ 9.0% (two subsequent readings).

IV. Patient selection for the initiation or continuation of personal insulin pump treatment

The patient presenting to a center offering the reimbursed service submits:

- A filled application form documenting the initial patient selection performed by a physician working in a diabetes clinic/ward;
- A glucose meter or CGM report covering the last 4 weeks — at least 7 measurements per day are required (glucose meter or CGM device may be read in the clinic); or a report from rtCGM or isCGM/FGM.
- In some patients with inadequate metabolic control, providing additional information regarding the amount of consumed carbohydrate equivalents and insulin doses is indicated before considering personal insulin pump therapy. This information may be provided using a self-control diary or appropriate application (electronic data).

In children with newly diagnosed diabetes, the initial patient selection is performed by a diabetologist or pediatric endocrinologist and diabetologist working in a pediatric diabetes ward;

V. Patient education regarding the principles of personal insulin pump treatment

Patient and/or patient family education to the extent enabling self-management regarding the use of insulin pump and other required equipment (confirmed by a physician certification or hospital discharge summary) (the extent of education is described in Chapter 9, section III.6).

Particular attention should be paid to the **management in case of an insulin pump failure**.

Organizational requirements: minimum duration of training 9 hours, split into minimum 3 sessions. In case of an insulin pump integrated with CGM, the duration of training should be extended by 2 hours. Training should be performed in groups not larger than 6–8 persons. Parents or legal guardians should participate in training of children and adolescents. Patients should be offered an opportunity to practice with infusion sets using phantoms. It is also recommended to practice subcutaneous insertion of an infusion set in the period before initiating treatment with continuous subcutaneous insulin infusion.

Training should continue until the patient/caregiver is well versed with practical aspects of personal insulin pump use. The responsibility for appropriate training is borne by the center initiating the treatment or the center referring the patient for personal insulin pump treatment. The patient's knowledge should be verified by the education team. It is recommended to develop a test based on own educational materials.

It is recommended to teach the patient how to use the software for data retrieval from the personal insulin pump, glucose meter, and CGM system, which will allow clinically effective telemedicine visits.

VI. Providing the patients with a personal insulin pump adjusted to the patient preferences and his/her perception capabilities which should be taken into account during the education and treatment individualization process.

Requirements for insulin pumps to be used in centers providing treatment with a personal insulin pump are listed in a table in the Appendix 6. It is recommended that different types of insulin pumps should be available at the diabetes centers, enabling patients to choose the pump that best suits their needs.

VII. Setting and initiating insulin pump treatment in the patient

The initial settings of the insulin pump are set in the unit initiating the treatment, including activation of the bolus calculator function. The infusion set is attached to the patient.

In case of insulin pumps with CGM option, alarm presetting is recommended, taking into account the current level of metabolic control, additional pump functions, and patient capabilities.

*Remission criteria according to Schölin A et al. Diabet Med. 2011; 28: 156: normoglycemia in blood glucose profile with insulin requirement < 0.3 unit/kg body weight per day and peptide C level > 0.5 ng/mL.
**Patients previously treated with a personal insulin pump which failed undergo the same selection process as new patients. Previous treatment with a personal insulin pump does not automatically lead to reimbursement of a new device.
***An order for personal insulin pump supplies may be issued only by a physician working in a diabetes clinic or a hospital unit.

Specification of personal insulin pumps — 2021 Diabetes Poland recommendations. Recommended necessary requirements

Issue/subject		Children < 6 years of age	Children > 6 years of age and adults
Pump stopped		Pump stop warning alarm	Pump stop warning alarm
Pump blockade		Electronic input key blockade	Electronic input key blockade
Bolus programming	Simple/standard bolus	Precision not less than 0.1 unit/bolus	Precision not less than 0.1 unit/bolus
	Extended/square wave bolus	Precision not less than 0.1 unit/bolus	Precision not less than 0.1 unit/bolus
		Maximum duration of a bolus — not less than 7 hours	Maximum duration of a bolus — not less than 7 hours
	Complex/double/multiwave bolus	Precision not less than 0.1 unit/bolus	Precision not less than 0.1 unit/bolus
Temporary change of a basal rate	Settings:	Possible percent or absolute (in units) increase or decrease of a basal rate, every 30 minutes with an automatic return to previous settings after the programmed time	Possible percent or absolute (in units) increase or decrease of a basal rate, every 30 minutes with an automatic return to previous settings after the programmed time
	Information about the current basal rate	Available on the main screen or retrieved using a single key	Available on the main screen or retrieved using a single key
	Time	Up to 24 hours	Up to 24 hours
Basal rate programming	Entering hourly doses (units/hour)	Precision not less than 0.05 unit/hour At least two additional profiles of the basal rate, with a possibility of an advance programming, recalling from the device memory, and activation	Precision not less than 0.1 unit/hour At least two additional profiles of the basal rate, with a possibility of an advance programming, recalling from the device memory, and activation
Pump memory	History of boluses, alarms, basal rate, temporary changes of a basal rate, infusion set primings; software for pump data retrieval should also be able to retrieve data from a glucose meter with reagent strips eligible for reimbursement at the date of the tender, and integrate data from both sources	Minimum 30 days using a computer software and a reading device Company provides the diabetes treatment unit with free software (installed locally or cloud-based) and equipment for data retrieval into a computer — software requirements specified in Appendix 1 **Information available directly on the pump:** Current basal rate, minimum last 20 boluses (dose and type), mean daily doses over the last 30 days	Minimum 30 days using a computer software and a reading device Company provides the diabetes treatment unit with free software (installed locally or cloud-based) and equipment for data retrieval into a computer — software requirements specified in Appendix 1 **Information available directly on the pump:** Current basal rate, minimum last 20 boluses (dose and type), mean daily doses over the last 30 days
Bolus calculator which is an integral element of the insulin infusion system (function available in the insulin pump or by wireless communication with the pump		Required functions: Possibility of setting the settings in several time periods Entering carbohydrate intake in grams or carbohydrate exchanges by the user Calculation of active insulin with duration of insulin action set by the user; the function which reduces only the correction insulin bolus Possibility of manually entering a blood glucose reading to the bolus calculator or communication with a glucose meter with reagent strips eligible for reimbursement at the date of the tender	Required functions: Possibility of setting the settings in several time periods Entering carbohydrate intake in grams or carbohydrate exchanges by the user Calculation of active insulin with duration of insulin action set by the user; the function which reduces only the correction insulin bolus Possibility of manually entering a blood glucose reading to the bolus calculator or communication with a glucose meter with reagent strips eligible for reimbursement at the date of the tender

Automatic infusion set primings	Yes — unlimited number of infusion set primings during the day, activated directly using a pump function	Yes — unlimited number of infusion set primings during the day, activated directly using a pump function
Infusion sets	Needles — metal (stiff) and plastic (elastic), all types covered by reimbursement Tubing length — at least 2 lengths available	Needles — metal (stiff) and plastic (elastic), all types covered by reimbursement Tubing length — at least 2 lengths available
Servicing	24-hour telephone contact with an authorized helpline (knowledgeable on pump functioning, including all possible alarms and error messages) subjected to customer assessment Webpage with information specified in Appendix 2 Pump replacement within 24 hours (on workdays) Pump shipping costs borne by the company	24-hour telephone contact with an authorized helpline (knowledgeable on pump functioning, including all possible alarms and error messages) subjected to customer assessment Webpage with information specified in Appendix 2 Pump replacement within 24 hours (on workdays) Pump shipping costs borne by the company
Batteries — pump power supply	Size AA, AAA batteries widely available at retail outlets, gas stations, home appliance stores, etc. Sound alarm and a warning displayed on the device screen if battery power level is below 30%	Size AA, AAA batteries widely available at retail outlets, gas stations, home appliance stores, etc. Sound alarm and a warning displayed on the device screen if battery power level is below 30%
Additional accessories necessary to use personal insulin pump	Additional accessories for personal insulin pump which must be regularly replaced as per the pump manual are provided free by the manufacturer for the duration of the period of pump use (does not apply to infusion sets, insulin containers, batteries, insulin pump case)	Additional accessories for personal insulin pump which must be regularly replaced as per the pump manual are provided free by the manufacturer for the duration of the period of pump use (does not apply to infusion sets, insulin containers, batteries, insulin pump case)
Warranty period	At least 4 years for the pump; in case of malfunction Replacement with a new pump with the warranty period not shorter than originally specified	At least 4 years for the pump; in case of malfunction Replacement with a new pump with the warranty period not shorter than originally specified
Menu	Full menu in Polish or icons	Full menu in Polish or icons
User manual	Full user manual in Polish, must describe all messages displayed by the pump	Full user manual in Polish, must describe all messages displayed by the pump
Continuous glucose monitoring (CGM) system which is an integral part of the insulin pump system (applies to insulin pumps with CGM option)	(applies to insulin pumps with a continuous glucose monitoring function) **In patients with frequent hypoglycemia episodes and/or hypoglycemia unawareness** Option of automatic interruption of basal insulin infusion by the CGM system	**In patients with frequent hypoglycemia episodes and/or hypoglycemia unawareness** Option of automatic interruption of basal insulin infusion by the CGM system

Specification of personal insulin pumps — 2020 Diabetes Poland recommendations. Recommended additional requirements

Issue/subject	Children < 6 years of age	Children > 6 years of age and adults
Reminder about the need to replace infusion set	Alarm informing about the need to replace infusion set	Alarm informing about the need to replace infusion set
History of infusion set primings	To be checked directly in the device memory	To be checked directly in the device memory
IPX 8 standard	IPX 8	IPX 8
Additional device to read pump memory at home and transmit data to the physician	Reader and software	Reader and software
Additional basal rate profiles	More than 3	More than 3
Bolus calculator	User settings: mg/dL or mmol/L (blood glucose readings) Possibility of manually entering a blood glucose reading to the bolus calculator	User settings: mg/dL or mmol/L (blood glucose readings) Possibility of manually entering a blood glucose reading to the bolus calculator
Continuous glucose monitoring (CGM) system	CGM system integrated with the insulin pump or an additional supporting CGM device	CGM system integrated with the insulin pump or an additional supporting CGM device

For selected groups of patients it is acceptable to modify the personal specifications of insulin pumps taking into account the patient's ability to learn and personalization/individualization of treatment.

Appendix 1

Requirements for the computer software for pump memory data retrieval:

— Current basal rates (all available at single data retrieval, with data on graphs or in tables, exact doses and time with accuracy of insulin administration at a given basal rate);
— Used correction factors with time periods set in bolus calculators;
— History of boluses (precise information on bolus type, dose, and timing of administration, including extended boluses);
— History of infusion set primings;
— Daily graphs showing:
  • Basal rate on a given day;
  • Temporary changes of the basal rate;
  • Timing of pump switching on and off;
  • Blood glucose readings transmitted from a compatible glucose meter and/or a CGM system;
— History of alarms;
— Free provision of the software to the patients;
— Data retrieval software should also be able to retrieve data from a glucose meter with reagent strips eligible for reimbursement at the date of the tender, and integrate both types of information.

Appendix 2

Required information available on the webpage:

— Telephone number of a 24-hour helpline providing information to insulin pump users in case of technical problems associated with pump use;
— Telephone numbers of local representatives with their working hours;
— Data on pump supplies (types of needles, syringes, batteries along with their pricing etc.).

RECOMMENDED ADDITIONAL OPTIONS

1. Integration with a glucose meter: wireless communication with at least one type of a glucose meter, possibility to activate and deactivate the option of data transmission from the glucose meter to the pump, possibility of recording blood glucose values with the bolus calculator function switched on or off.
2. Insulin pumps that have a dedicated glucose meter should be distributed together with that glucose meter.
3. Alarms to remind about boluses or blood glucose measurements at times set by the user.
4. Price of infusion sets not exceeding the monthly reimbursement limit in persons < 26 years of age and 30% of that limit in persons > 26 years of age.

ADDITIONAL NOTES

The ordering party may determine additional parameters in accordance with the needs of specific patient groups. In addition, the offer should include accessories necessary for therapy initiation and educations: serters, various types of infusion sets, insulin containers, batteries for the pump, protective cases.

When evaluating a pump during a tender, the pump price should count for 60%, and additional functions for 40% of the overall assessment.

Appendix 7
Recommendations of the Diabetes Poland and the Polish Society of Sports Medicine on obtaining a consent for participation in sports by patients with diabetes type 1

Developed by the experts of the Diabetes Poland: Leszek Czupryniak, Andrzej Gawrecki, Przemysława Jarosz-Chobot, Tomasz Klupa, Bartłomiej Matejko, Krzysztof Pawlaczyk, Agnieszka Szadkowska, Agnieszka Szypowska, Bogumił Wolnik, Dorota Zozulińska-Ziółkiewicz and the Polish Society of Sports Medicine: Grzegorz Biegański, Andrzej Bugajski, Anna Jegier, Jarosław Krzywański, Marek Pietruszewski, Katarzyna Szmigielska, Wiesław Tomaszewski, Andrzej Ziemba

Patients with diabetes type 1 may be cleared by a sports medicine specialist for participation in any sport after obtaining a positive diabetologist opinion.

One prerequisite for such clearance for participation in sports is intensive insulin therapy with good understanding of its principles. This may be undertaken with either a pen or a personal insulin pump. The latter approach is preferred in athletes as it allows more physiological administration of insulin. A responsibility of an athlete with diabetes is to perform systematic blood glucose monitoring using a glucose meter, at least 6 times a day, with additional measurements during training and competitions. It is also recommended to use continuous glucose measurement (CGM) or flash glucose monitoring (FGM) systems to guide insulin therapy and increase its safety in athletes.

Diabetes type 1 should not be a contraindication to participation in sports classes at each level of education and in school sports competitions.

Optimal blood glucose levels at the onset and during sport activities are in the range of 126–180 mg/dL (7–10 mmol/L) for aerobic activities and 90–180 mg/dL (5–10 mmol/L) for anaerobic activities.

I. Contraindications to participation in sports by children and adults with diabetes type 1 who require clearance by a sports medicine specialist:

1. HbA_{1c} — mean level over the last 12 months > 8.5% or current value ≥ 9%.
2. More than one episode of ketoacidosis during the last 12 months.
3. More than one episode of severe hypoglycemia during the last 12 months.
4. Blood glucose self-monitoring: < 6 measurements per day using a glucose meters in athletes not using CGM or FGM.
5. Diabetology clinic visits: < 4/year in children, < 2/year in adults.
6. Hypoglycemia unawareness when awake — a relative contraindication, may be overturned depending on sports discipline or when using CGM or FGM.
7. Chronic complications of diabetes — depending on their severity and sports discipline:
   - — Proliferative retinopathy until the end of laser therapy — absolute contraindication to all sport activities;
   - — Overt autonomic neuropathy — contraindication to high-intensity physical exercise;
   - — Macrovascular complications — clearance following cardiac investigations including echocardiography, exercise test, and 24-hour Holter monitoring;
   - — Proteinuria > 0.3–0.5 g/day (A3) — relative contraindication, follow-up necessary — reassessment of proteinuria every 3–6 months, regular evaluation of blood pressure and renal function*;
   - — Proteinuria > 0.5 g/day — temporary disqualification from sport activities;
   - — eGFR 45–60 mL/min/1.73 m^2 (G3a) — reassessment of serum creatinine and eGFR at least every 3 months;
   - — eGFR 30–45 mL/min/1.73 m^2 (G3b) — relative contraindication to competitive sports, temporary disqualification, reassessment of serum creatinine and eGFR every 4–6 weeks;
   - — eGFR < 30 mL/min/1.73 m^2 (G4) — absolute contraindication to sport activities.

II. Investigations required for the assessment of an athlete with diabetes type 1

Initial (preparticipation) assessment: current test results according to the Diabetes Poland guidelines.

HbA_{1c} levels over the last 3 months, reports from a glucose meter and/or CGM/FGM and from an insulin pump.

III. High-risk sport disciplines: motor, aquatic, air sports, climbing

Sport disciplines in which hypoglycemia poses particularly high risk for the safety of the patient and others

*eGFR calculated using the Schwartz formula in subjects ≤ 15 years of age, using the CKD-EPI formula in subjects ≥ 16 years of age.

nearby are not recommended for patients with diabetes type 1.

Participation is acceptable if the following conditions are met:

— The patient is very well educated in regard to diabetes treatment and meets the treatment goals;

— Blood glucose measurement within 15 minutes before the onset of an activity yields a value of ≥ 120 mg/dL (6.7 mmol/L), with further blood glucose monitoring by a glucose meter every 60 minutes or less frequently is CGM or FGM is used.

CGM is recommended when participating in high-risk sport disciplines.

IV. Contraindications to participation in sport training and competitions

1. Severe hypoglycemia within the last 24 hours.
2. Hyperglycemia > 250 mg/dL (13.9 mmol/L) with concomitant ketonemia/ketonuria due to insulin deficit and not carbohydrate excess.
3. Ketonemia ≥ 1.5 mmol/L is an absolute contraindication to initiation and continuation of physical exercise.
4. Hyperglycemia > 300 mg/dL (16.7 mmol/L) persisting for more than 2 hours.
5. Any acute event requiring physician's assistance, e.g. vision disturbances, chest pain, syncope/presyncope, acute infection etc.