

Management of metabolic diseases

Diabetes in the practice of the family doctor

Criteria them for testing diabetes or prediabetes 's in asymptomatic adults

1. Overweight or obese patients, adults who have one or more of the following risk factors:
 - first degree relatives with diabetes
 - history of cardiovascular disease
 - hypertension $\geq 140 / 90$ mmHg or antihypertensive treatment
 - HDL-cholesterol <35 mg/dL (0.90 mmol/L) and/or triglycerides > 250 mg/dL
 - women with polycystic ovary syndrome
 - sedentary lifestyle or lack of physical activity
 - other conditions associated with insulin resistance (obesity, acanthosis nigricans)
2. Patients with prediabetes, A1C $\geq 5.7\%$ or 39 mmol / mol, decreased glucose tolerance (IGT) or isolated increase in fasting blood glucose (IFG) should be tested annually.
3. Women who have been diagnosed with gestational diabetes should be tested throughout their lives at least every 3 years
4. For all other patients, testing should begin at age 45.
5. If the results are normal, the test should be repeated at intervals of at least 3 years. The frequency of determinations must be correlated with initial results and risk factors.
6. Patients receiving such medications, such as glucocorticoids, thiazide diuretics, some HIV drugs and antipsychotics, which are known to increase the risk of diabetes
7. Screening periodontal disease is by reference to the dental visits, known as its association with diabetes mellitus

Criteria for testing for diabetes or prediabetes in asymptomatic children and adolescents:

- in young people, after puberty or after 10 years, if they occur earlier, who are overweight (85% percentile) or obese (95 % percentile) and who have one or more risk factors for diabetes:
 - a maternal history of diabetes or gestational diabetes during pregnancy
 - family history of type 2 diabetes in first and second degree relatives
 - signs of insulin resistance or conditions associated with insulin resistance (hypertension, dyslipidemia, polycystic ovary or low birth weight at gestational age)
- If tests are normal, they repeat BP interval of at least three years or more frequently if increasing BMI.

Prevention installation diabetes mellitus type 2

Persons at increased risk of developing type 2 diabetes need to include in programme prevention of diabetes (DPP), programs aimed at lifestyle changes including moderate decrease in weight , the initial loss of 7% body weight A and its maintenance and and regular , moderate physical activity (such as walking) at least 150 minutes / week.

Therapeutic education of the patient

Therapeutic education of the patient is an integral part of diabetes management. The educational process takes place continuously, in different forms and is absolutely necessary for obtaining a good metabolic control and improving the quality of life .

The purpose of this effort is to help people with diabetes to better adapt to the new and the condition of life and prevent complications.

Education can be individual or group and is supported by specially trained people (diabetologist, educating nurses, dietitian, medical staff trained in diabetic foot care , possibly psychologist).

Lifestyle management

Patients with type 2 diabetes are mostly overweight or obese and generally have an unhealthy lifestyle (unhealthy eating habits, sedentary lifestyle) that has contributed, along with other factors, to the onset of the condition. Therefore, it is necessary to identify the ways of intervention on the lifestyle immediately after the diagnosis .

Improving the lifestyle aims to :

- achieving and maintaining ideal body weight,
- decrease in glycemic values,
- normalization of serum lipid and uric acid values (or bringing them as close as possible to normal),
- maintaining optimal blood pressure values, sometimes in association with specific medication.
- smoking is an independent cardiovascular risk factor, so it will push for smoking and alcohol consumption.

Lifestyle management

Standard recommendations:

Eating habits and providing access to a nutritionist

- The diet is individualized according to age, sex, height, weight, degree of physical effort, preferences, local tradition, level of culture
- Carbohydrate monitoring is an essential component of the strategy for achieving optimal glycemic control
- Restrict alcohol consumption to one alcoholic drink per day for women and 2 alcoholic beverages for men
- The intake of saturated fats must represent <7% of the total caloric intake
- Trans fat intake will be kept to a minimum
- Restrict protein intake to 0.8-1 g / kg / day in adults
- Physical exercise is introduced gradually, depending on individual abilities; prolonging the duration and increasing the frequency of physical activity (where necessary) up to 30-45 min / day, 3-5 days / week or 150 min./week is encouraged
- In the absence of contraindications people with type 2 diabetes should be encouraged to practice resistance training three times a week complicated

The benefits of exercise are as follows:

- improves long-term glycemic control;
- increases insulin sensitivity in non-obese patients;
- improves the lipid profile (cholesterol, triglycerides);
- decreases body fat and fat distribution;
- reduces the effect of stress on the body;

- lowers blood pressure ;
- reduces arterial atheromatous plaque

Current therapeutic targets

Targets recommended by the ADA, adult , outside pregnancy are :

- ✓ HbA1c <7% (53mmol / mol)
- ✓ capillary blood pre-prandial blood glucose 80 - 130 mg / dl
- ✓ Postprandial capillary blood glucose <180 mg / dl (10.0 mmol / L)

Regarding glycemic control in women with gestational diabetes, it is recommended to reduce glucose levels in the whole maternal capillary blood:

- pre-prandial ≤ 95 mg / dl
- postprandial 1 hour after a meal ≤ 140 mg / dl, 2 hours after meals ≤ 120 mg / dl

For women with type 1 or 2 diabetes who become pregnant, the ADA recommends the following therapeutic targets provided that they can be achieved without severe hypoglycaemia :

- preprandial, bedtime and overnight blood glucose 60-99 mg / dl,
- maximum postprandial blood glucose value 100 -129 mg / dl,
- HbA1c <6%

Monitor glycemic control using HbA1c performed at least twice a year in patients who meet therapeutic goals and have stable metabolic control.

HbA1c will be determined quarterly in patients whose therapy has been modified or who do not meet the objectives of glycemic control

Less stringent target values of Hb A1c are appropriate for people with :

- history of severe hypoglycaemia,
- limited life expectancy,
- severe complications ,
- comorbidities or significant
- when the objectives are difficult to achieve when intensive education measures, repeated counseling and multiple doses of hypoglycaemic agents have been administered

Therapeutic strategies

Treatment of type 1 diabetes

Standard recommendations:

- Administration of insulin in multiple injectable doses or by continuous subcutaneous infusion of insulin (insulin pump)
- Correlation of prandial insulin dose with carbohydrate intake, preprandial glycemia and anticipated physical activity
- Nutritional therapy
- Self-monitoring of blood glucose (performing at least 4 daily blood glucose determinations: preprandial, before main meals and at bedtime)

Treatment of type 2 diabetes

Standard recommendations

- The patient will be monitored, the effectiveness of the therapeutic scheme will be assessed based on basal and postprandial blood glucose, and in cases selected using HbA1c
- The initiated therapeutic schemes will be maintained only if they have led to the achievement of the therapeutic goals and the insistence on the modification of the lifestyle is insisted on.
- Drug combinations and transition to a higher stage of treatment are required when glycemic targets are not met. At HbA1c $\geq 8.5\%$, a drug other than insulin is unlikely to be effective
- Insulin therapy may be initiated in patients with type 2 diabetes from the time of diagnosis under the following conditions: patients with weight loss or other signs or symptoms of severe hyperglycaemia, pregnancy and lactation, surgery, severe infections, myocardial infarction, stroke, liver and kidney disease in an advanced stage of development

Treatment with oral antidiabetics

Biguanides: Metformin

- Metformin is started in small doses (500 mg x 2 times / day), gradually increasing to maximum doses (1000 mg x 2 times / day). During treatment, discomfort may occur in the abdomen (pain, gas formation, diarrhea). To reduce side effects, it is recommended that they be taken with or without food.
- If you are taking Metformin, your blood sugar should be checked before main meals.

Sulfanylureas: Gliclazide, Glimepiride, Gliquidone

- The selection of the preparation from this group will be made according to certain criteria by the family doctor or diabetologist :
- How well it lowers blood glucose: Glibenclamide > Glimepiride > Gliclazide > Gliquidone;
- How fast it acts: Gliclazide > Glimepiride;
- After duration of action: Glimepiride > Gliclazide > Gliquidone.
- The administration of the preparations from this group is performed 15-30 minutes before the meal, most of them are administered in a single dose, in the morning.

Meglitinides: Repaglinide

- The duration of action is shorter, up to 4-5 hours, which is why they will be administered only 15-30 minutes before main meals (or meals that cause postprandial hyperglycemia).
- The risk of hypoglycaemia in this group persists, but is lower compared to sulfonylureas.

DPP4 inhibitors: Sitagliptin, Vildagliptin

- Sitagliptin should be given in a single dose, and Vildagliptin in two doses /day.
- The risk of hypoglycaemia is negligible.

Thiazolidinedione: Pioglitazone

- Pioglitazone is the most potent insulin sensitiser.
- It is contraindicated in case of heart failure, acute coronary episodes, advanced liver and kidney dysfunction.

- Does not cause hypoglycaemia.

GLP1 receptor agonists: Liraglutide. Lixisenatide

- These injections stimulate insulin secretion while blood glucose is increased and inhibit glucagon secretion. It also delays gastric emptying, influences satiety centers (decreases appetite) and reduces body weight.

SGLT2 inhibitors: Dapagliflozin, Canagliflozin

- These drugs act on the kidneys. They inhibit the absorption of glucose by the kidneys. The therapeutic result is the massive elimination, with urine, of glucose from the body.
- Precautions for use in people with kidney disease or genitourinary tract infections.

Treatment of obesity

When indicated, weight loss should be at least 5%.

The diet should ensure a deficit of 500-750 Cal / day.

It does not matter the content in carbohydrates, proteins and lipids, but rather the caloric restriction for 24 hours.

In order to maintain the weight loss obtained in the long term, it is recommended to add to the regular daily activities a physical effort in the form of moderate intensity exercises with a total duration of at least 200-300 minutes per week.

Short-term weight loss can also be achieved by using a very calorie-restricted diet (≤ 800 Cal / day), possibly by replacing a meal with a food supplement specially designed for this purpose.

This approach can be maintained for a maximum of 3 months. It will be followed by a careful long-term weight monitoring and control program.

Screening and management of cardiovascular complications

Objectives. Blood pressure control, with maintenance of BP values $<130/80$ mmHg is one of the therapeutic targets pursued in the patient with diabetes

Treatment.

Patients with a systolic blood pressure of 130 - 139 mmHg or a diastolic blood pressure of 80 - 89 mmHg can benefit from interventions aimed at changing lifestyles (weight loss, hyposodium diet, reducing alcohol consumption, combating sedentary lifestyle) for maximum 3 months and then if the target values are not reached pharmacological agents must be associated.

Patients with blood pressure values $\geq 140/90$ mmHg should receive drug therapy along with lifestyle changes.

Initiation of hypotensive therapy in diabetic patients is recommended with angiotensin converting enzyme inhibitors or an angiotensin receptor blocker.

If one of the classes is not tolerated it will be replaced with the other.

If necessary to reach the target blood pressure values, other hypotensive classes will be added, of which the metabolically neutral ones are preferred (calcium channel blockers, diuretics).

The use of angiotensin converting enzyme inhibitors, angiotensin receptor blockers, diuretics requires close monitoring of renal function and serum potassium levels.

Dyslipidemia / lipid management

Screening. In most adult patients, the lipid profile of fasting will be assessed at least once a year

Objectives:

- primary endpoint - LDL-cholesterol level <100 mg / dl (2.60 mmol/l), and in patients with documented atherosclerotic cardiovascular disease, respectively patients with high cardiovascular risk LDL-cholesterol <75 mg / dl,
- desirable targets - triglyceride levels <150 mg / dl (1.7 mmol / l), and HDL - cholesterol levels > 40 mg / dl (1.0 mmol / l) in men and > 50 mg / dl (1.3 mmol / l) in women

Statin therapy should be associated with lifestyle changes regardless of baseline lipid levels in diabetic patients with overt cardiovascular disease and in those without cardiovascular disease but over 40 years of age who have one or more risk factors for cardiovascular disease. Severe hypertriglyceridemia may require immediate treatment by lifestyle changes and drug therapy to reduce the risk of acute pancreatitis.

Combination therapy with statins and other lipid-lowering agents may be considered to obtain target lipid values.

Antiplatelet agents

- Acetylsalicylic acid therapy will be used as a primary prevention strategy in people with high cardiovascular risk (men > 50 years of age or women > 60 years of age who have at least one additional major risk factor - family history of cardiovascular disease, hypertension, smoking, dyslipidemia or albuminuria)
- Acetylsalicylic acid therapy will be used as a secondary prevention strategy in diabetics with a history of cardiovascular disease
- Other antiplatelet agents may be a reasonable alternative for patients at high risk for aspirin allergy

Screening and treatment of retinopathy

Screening

Adults and adolescents with type 1 diabetes should have a thorough initial eye exam with pharmacologically induced mydriasis in the first 5 years after the onset of diabetes.

Patients with type 2 diabetes should have a thorough initial eye exam with pharmacologically induced mydriasis shortly after diagnosis.

Subsequently, patients with type 1 and type 2 diabetes will be re-examined annually. Examinations should be more frequent if retinopathy progresses.

Women with pre - existing diabetes who are planning to become pregnant or who are already pregnant should have a thorough eye examination and advice on the risk of developing and / or progressing to diabetic retinopathy. Ophthalmological examination should be performed in the first trimester of pregnancy, with careful follow-up throughout the pregnancy and another 1 year postpartum

Treatment.

Laser photocoagulation therapy is indicated to reduce the risk of blindness in patients with clinically significant macular edema, severe nonproliferative diabetic retinopathy or proliferative diabetic retinopathy.

The presence of retinopathy is not a contraindication for acetylsalicylic acid therapy, as this therapy does not increase the risk of retinal bleeding.

Screening and treatment of neuropathy

Diabetic neuropathies are heterogeneous, with various clinical manifestations. The most common are: symmetrical peripheral diabetic polyneuropathy, sensory-motor and autonomic neuropathy.

The major clinical consequences of polyneuropathy refer to a typical symptomatology in which hyperalgesic forms can sometimes be disabling for the patient, on the one hand, and the loss of protective sensitivity of the legs increases the risk for ulcers and amputations. Approximately 60-70% of patients with diabetes have moderate to severe forms of neuropathy.

Early recognition and management of neuropathy in diabetic patients are important because:

- non-diabetic neuropathies may be present in patients with diabetes and may be treatable;
- there are a number of therapeutic options for symptomatic diabetic neuropathy;
- up to 50% of diabetic polyneuropathy may be asymptomatic and patients have an increased risk of not being aware of the lesions in the legs;
- autonomic neuropathy can affect all the body's apparatus and systems;
- autonomic cardiovascular neuropathy causes substantial morbidity and mortality

There is currently no specific treatment for underlying nerve damage other than improved glycemic control, which may slow progression but do not reverse the neuronal destruction already present.

All diabetic patients should be investigated for symmetrical distal polyneuropathy at the time of diagnosis and thereafter at least annually thereafter using simple clinical trials.

Screening for signs and symptoms of autonomic neuropathy should be instituted at the time of diagnosis in patients with type 2 diabetes and 5 years after the diagnosis of type 1 diabetes .

Major clinical manifestations of autonomic diabetic neuropathy include: resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile dysfunction, sweat dysfunction, neurovascular dysfunction, unstable diabetes, and autonomic hypoglycemic insufficiency.

Pharmacological therapy is recommended to relieve specific symptoms because they improve patients' quality of life.

Screening and treatment of nephropathy

The initial development of diabetic nephropathy is asymptomatic and can be highlighted strictly by laboratory screening.

General recommendations: to reduce the risk or progression of diabetic nephropathy, it is recommended to optimize glycemic control and blood pressure

Screening.

- Urinary albumin excretion will be assessed annually in patients with developing type 1 diabetes ≥ 5 years and in all patients with type 2 diabetes from the time of diagnosis.
- Serum creatinine will be re-administered annually in all adults with diabetes, regardless of the degree of urinary albumin excretion. Serum creatinine should be used to estimate the rate of glomerular filtration and to stage the degree of kidney disease.

Treatment

- Angiotensin converting enzyme inhibitors or an angiotensin receptor blocker should be used in the treatment of patients with micro- or macro-albuminuria (excluding pregnant women).
- The use of angiotensin converting enzyme inhibitors, angiotensin receptor blockers, diuretics requires close monitoring of renal function and serum potassium levels.
- Reduction of protein intake to 0.8 - 1.0 gr / kg body weight / day in patients with diabetes and chronic kidney disease in early stages and to 0.8 gr / kg body weight / day in patients with diabetes and chronic kidney disease in advanced stages is recommended .
- Continuous monitoring of urinary albumin excretion is recommended to assess both response to therapy and disease progression.

Diabetic foot care

Early and correct prevention and treatment of ulcers can reduce the number of amputations by 50-80%.

This can only be done with the help of a multidisciplinary team that includes: family doctor, diabetologist, surgeon, neurologist, orthopedist, specialist nurses and, of course, the patient. Minor traumas (due to incorrect nail cutting, inappropriate footwear, ulcerated calluses), late recognition of lesions (by the patient or doctor), vision and gait disorders, impaired peripheral sensitivity, social isolation and lack of compliance patients, are important risk factors for ulceration and amputation

The following conditions are associated with an increased risk of amputation:

- peripheral neuropathy with loss of painful sensitivity
- altered biomechanics (in the presence of neuropathy)
- signs of high blood pressure (erythema, hemorrhage underlying a callus)
- weak or absent foot pulse
- history of ulcers or amputations
- severe nail pathology

Standard recommendations:

- All people with diabetes will undergo a thorough examination of the foot annually to identify predictors of ulcers or amputations .
- All diabetic patients will receive general instructions for diabetic foot care.
- Patients who smoke, those with low sensitivity and structural abnormalities or a history of complications in the lower extremities will be referred to a specialist in diabetic foot care for permanent prophylactic care and continuous supervision.

Screening - the initial PAD that had to include the history of lameness. The ankle - arm index will be considered , as most patients with peripheral arterial disease are asymptomatic.

Patients with a significant history of intermittent claudication or an ankle - positive arm index will be investigated for vascular function and will consider physical activity, medication, and surgical treatment options.

For the primary and secondary prevention of diabetes complications (retinopathy, nephropathy, peripheral arteriopathy, diabetic foot, cardiovascular complications) is recommended therapy with sulodexide, glycosaminoglycan with main antithrombotic effect and antiplatelet but also with multiple vascular pleiotropic effects due to action vascular endothelium

Vaccination recommendations

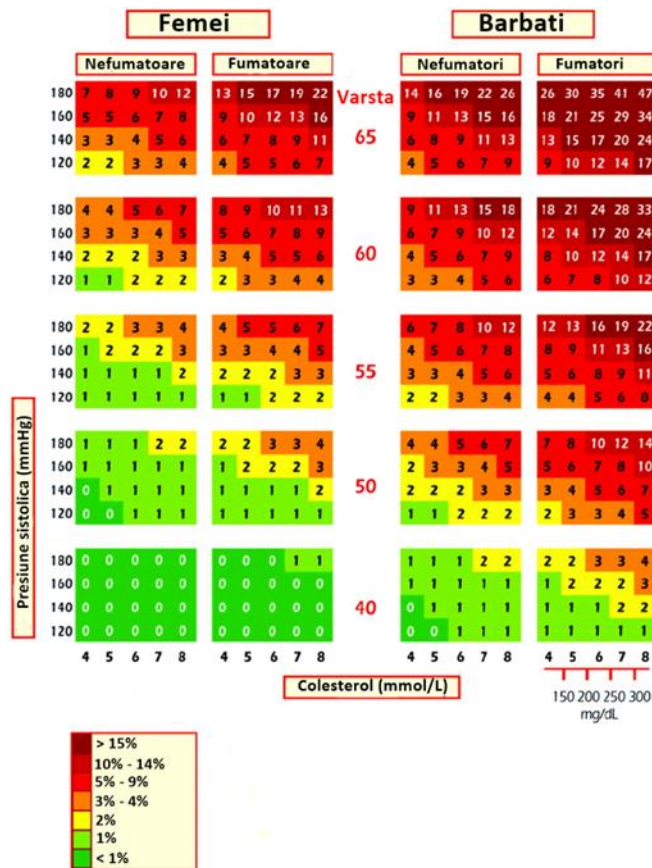
- Influenza vaccination is recommended, repeated annually, from the age of 6 months.
- 13-valent pneumococcal vaccine (PCV13) is recommended in children up to 2 years of age, single administration.
- 23-valent pneumococcal vaccine (PCV23) is recommended once 2 years of age (including adults), single administration.
- After reaching the age of 65, it is recommended to take a dose of 23-valent pneumococcal vaccine (PCV23), regardless of whether it has been administered before or during the lifetime (booster).

Dyslipidemia in the practice of the family doctor

Dyslipidemia and cardiovascular risk

Estimating the total risk using SCORE charts is recommended

- adults with asymptomatic cardiovascular disease for risk factors screening, including a profile of the lipids in men over 40 and women over 50 years or postmenopausal
- Documented cardiovascular disease
- Type 1 or 2 diabetes
- High levels of personal risk factors
- Chronic kidney disease



Factors that change the SCORE risk

- Socially disadvantaged people - the origin of many causes of cardiovascular disease
- Obesity and central obesity measured by BMI and waist circumference, respectively
- Sedentarism
- Psychosocial stress which includes vital exhaustion
- Autoimmune diseases and other inflammatory diseases
- Psychiatric illness
- Treatment for HIV infection
- Atrial fibrillation
- Left ventricular hypertrophy
- Chronic kidney disease
- Sleep apnea syndrome
- Heredo-collateral history of early CVD (male <55 years; female <60 years)

Therapeutic targets

The approach in lipid management is mainly aimed at reducing LDL-C.

LDL-C therapeutic target

- ✓ In patients at very high CV risk, LDL-C below 1.8 mmol / L (70mg / dL) or a reduction in baseline of at least 50% if it is between 1.8 mmol / L and 3.5 mmol / L L (70 mg / dL and 135 mg / dL) .
 - ✓ Treatment with statins is initiated.
 - ✓ The therapeutic target is a constant level below 1.8 mmol / L (70 mg / dL)

- ✓ In patients at high CV risk, LDL-C below 2.6 mmol / L (100 mg / dL) or a 50% reduction in baseline if between 2.6 mmol / L and 5.2 mmol / L (100 mg / dL and 200 mg / dL) .
 - ✓ Treatment with statins is initiated.
 - ✓ The therapeutic goal is a constant level below 2.6 mmol / L (100mg / dL)
- ✓ In patients with low or moderate risk, LDL-C below 3 mmol / L (below 115 mg / dL)

Lifestyle modifications in order to improve the profile lipid levels

There is clear evidence of the influence of nutrients on atherogenesis, either directly or through their effects on traditional risk factors such as plasma lipids, blood pressure or blood glucose levels.

We recommend DASH diet (Dietary Approaches to Stop Hypertension) and Mediterranean diet which offers dietary fat from vegetable oil non-tropical, instead of those from animal sources .

Lifestyle changes that reduce CT and LDL-C levels :

- ✓ Reduction of unsaturated fats e
- ✓ Reduction of saturated fats e
- ✓ Increasing fiber in the diet
- ✓ Consumption of functional foods enriched with phytosterols
- ✓ Consumption of supplements with red rice yeast
- ✓ Reducing excessive body weight
- ✓ Reduction of cholesterol in the diet
- ✓ Intensification of regular physical activity
- ✓ Use of soy protein products

Lifestyle changes that reduce the level of lipoproteins rich in TG

- ✓ Reducing excessive body weight
- ✓ Reducing alcohol consumption
- ✓ Intensification of the usual physical activity
- ✓ Reducing the total amount of carbohydrates in the diet
- ✓ Use of supplements with n-3 polyunsaturated fats
- ✓ Reducing the intake of mono and disaccharides
- ✓ Replacement of saturated fats with mono or polyunsaturated

Lifestyle changes that increase HDL-C levels

- ✓ Reduction of unsaturated fats in the diet
- ✓ Intensification of regular physical activity
- ✓ Reducing excessive body weight
- ✓ Reducing carbohydrates in the diet and replacing them with unsaturated fats
- ✓ Moderate alcohol consumption
- ✓ Quitting smoking
- ✓ Among the foods rich in carbohydrates, it is recommended to consume those with low glycemic index and high fiber content
- ✓ Reducing the intake of mono and disaccharides

Dietary recommendations for lowering LDL-C and improving the lipoprotein profile :

- ✓ Whole grains
- ✓ Raw and cooked vegetables
- ✓ Pulses: it targets, bean, fava beans, peas, chickpeas, soybeans
- ✓ Fresh or frozen fruits
- ✓ Non-caloric sweeteners
- ✓ Lean or fatty fish, skinless poultry
- ✓ Skim milk and yogurt

Supplements food and food functional for treating dyslipidemia

Fitosterols

Fitosteroli is found naturally in vegetable oils and in smaller quantities in vegetables, fresh fruits, nuts, cereals and pulses. Consumption of plants rich in phytosterols varies from 250 to 500 mg per day in Mediterranean countries.

Fitosterols compete in the intestinal absorption of cholesterol. Fitosterols were added and the spreadable fats and oils (margarine functional cooking oils and butter) as well as yoghurts and other foods . Daily consumption of 2 grams of fitosterols, may decrease the efficient CT and LDL-C by 7-10% in humans (with some degree of heterogeneity among individuals), while has little effect, if any, of over HDL -C and TG.

It is recommended for people at risk of intermediate or elevated CV, with high cholesterol, who do not qualify for pharmacotherapy; as an adjunct to pharmacological therapy in high and very high risk patients who fail to achieve LDL-C targets with statins, or are intolerant to statins; in adults or children over 6 years of age with familial hypercholesterolemia .

Red rice yeast

Red rice yeast is a source of fermented pigment that has been used in China as a food coloring and flavor enhancer for centuries.

Its hypocholesterolemic effects are similar to the mechanism of statins.

Nutritional supplements containing purified yeast may be considered in patients with elevated plasma cholesterol who do not qualify for statin treatment in terms of overall CV risk.

Dietary fiber

Existing consistent evidence demonstrates a decreasing effect of TC and LDL-C on water- soluble fibers in oats and barley. The food enriched with these fibers are well tolerated, efficiency and t 's and recommended for lowering LDL-C at a dose of at least 3 g / day.

Soy protein

This is indicated because it may introduce a modest decrease in LDL-C when replacing animal proteins .

Unsaturated fatty acids n-3

Observational evidence recommends consuming, at least twice a week, fish and low-dose n-3 fatty acid supplements , which can lead to reduce the risk of CV death and stroke in primary prevention, but it does not have a major effect on plasma lipoprotein metabolism. Pharmacological doses of n-3 fatty acids (2-3 grams / day) reduce the level of TG by up to 30%, but a higher dose increases the level of LDL-C. Alpha-linoleic acid (an n-3

fatty acid present in hazelnuts, some vegetables and some seed oils) is less effective on TG levels . PUFA n-3 also reduces the postprandial lipemic response .

Medication used in the treatment of dyslipidaemia

Statins

Statins are the first line of treatment used to lower LDL-c levels. There are statins with different potencies, rosuvastatin and atorvastatin having the highest potency and long action , and simvastatin, lovastatin, pravastatin and fluvastatin having lower potencies. Statins also reduce TG by 30-50%, but can increase HDL-C by 5-10%.

Side effects of statins

Muscle symptoms are the most commonly described side effects of statin treatment . Rhabdomyolysis is the most severe form of statin-induced myopathy, characterized by severe muscle pain , muscle necrosis, and myoglobulinemia that can lead to acute and fatal kidney failure .

The mean increase in ALT occurs in 0.5-2% of patients on statin therapy , most commonly with potent or high-dose statins . The common definition of clinically relevant ALT elevation is an increase of 3 times the upper limit of normal at 2 assessments.

Patients taking statins may present a risk increased by hyper glycemia and the development of diabetes mellitus type 2.

A high frequency of proteinuria and was reported for all statins .

Statin-induced proteinuria is of tubular origin and is thought to be due to reduced tubular reabsorption and not glomerular dysfunction. In clinical trials, the frequency of proteinuria is generally low and in most cases not higher than placebo.

Fibrates

Fibrates lower triglycerides and to a lesser extent LDL-c. Fibrates can be used alone or in combination with statins, although there are warnings about the safety and effectiveness of the combination with most statins. Although fibrates generally increase HDL-c levels, in some patients the use of fenofibrate has led to a reduction in HDL-c. Therefore, it is recommended to monitor the level of HDL-c after initiation of fibrates therapy and discontinuation of treatment if severe HDL-c decreases are observed.

Gastrointestinal side effects (most often, flatulence, constipation, dyspepsia and nausea) are often present with these drugs, even at low doses.

which limits their practical use. These side effects can be alleviated by starting treatment with low doses and high fluid intake. Therefore, the dosage should be increased gradually. Reduced absorption of fat-soluble vitamins has been reported. Furthermore , these drugs may increase the level of circulatory TG in some patients.

Bile acid sequestrants have a major interaction with several commonly prescribed medications, and should be given 4 hours in advance, or with a hours after other medications.

Lipid profile testing

At least two doses should be made 1-12 weeks before the start of treatment, except for diseases for which concomitant treatment is indicated , such as acute coronary syndrome or very high risk patients.

- 8 (\pm 4) weeks after initiation.
- 8 (\pm 4) weeks after dose adjustment until target values are reached
- In patients keep to who achieved target values Annual (unless there are problems with compliance or other reasons that would require more frequent checks).

Monitoring of liver and muscle enzymes

Before treatment :

- First time 8-12 weeks after initiation or dose adjustment.
- Subsequently, routine TGP control is not recommended.

With lipid-lowering therapy

If GPT $<3x$:

- Continue treatment.
- Reassessment of liver enzymes after 4-6 weeks.

If the value $\geq 3x$:

- Stop treatment or reduce the dose with re-evaluation of liver enzymes after 4-6 weeks.
- Precautionary reintroduction of treatment may be considered if GPT has returned to normal.
- If GPT remains elevated, investigate other causes.

E , and evaluate bad CK in patients under lipid-lowering therapy

- Before treatment.
- If the initial value of CK is $4x$, treatment is not started; reevaluation.

monitoring:

- Routine CK monitoring is not required.
- Check CK if the patient develops myalgias.

Lipid-lowering treatment in special situations

- Elderly patients with documented cardiovascular disease
- In all patients with type 1 diabetes, with the presence of microalbuminuria and / or kidney disease, a decrease in LDL-C (at least 50%) with first-line statins is recommended regardless of the initial LDL-C concentration.
- In patients with type 2 diabetes mellitus and CVD or CKD and those without chronic kidney disease , but who are > 40 years old and have one or more CV risk factors or signs of target organ damage, the main recommended target is LDL-C < 1.8 mmol / L (< 70 mg / dL) and the secondary is non-HDL-C < 2.6 mmol / L (< 100 mg / dL) and apoB < 80 mg / dL.
- In all patients with type 2 diabetes and without additional risk factors and / or evidence of target organ damage , LDL-C < 2.6 mmol / L (< 100 mg / dL) is the primary endpoint. Non-HDL-C < 3.4 mmol / L (< 130 mg / dL) and apoB < 100 mg / dL are secondary targets.
- It is recommended to initiate or continue therapy with high dose statins early after hospitalization of all patients with no signs of acute coronary syndrome or history of intolerance, regardless of initial LDL-C values .
- Lipid-lowering treatment is not recommended (but is not harmful) in patients with heart failure in the absence of other indications that recommend their use .
- Lipid-lowering treatment is not recommended in patients with aortic valve stenosis without coronary heart disease

- Patients with chronic kidney disease stage 3-5 should be considered as patients with high or very high cardiovascular risk and have an indication for lipid-lowering treatment
- The use of statins or the statin / ezetimib combination is indicated in patients who are not on dialysis
- Peripheral arterial disease is a very high risk pathology and lipid-lowering treatment (mostly with statins) is recommended in these patients.
- For the primary prevention of stroke , it is recommended the treatment with statins with the achievement of therapeutic targets in patients with high and very high cardiovascular risk .
- For the secondary prevention of stroke , treatment with high dose statins is recommended in patients with a history of stroke

Monitoring active a patient with dyslipidemia in family doctor practice

- periodic review of therapeutic control;
- evaluation of the evolution of the disease - screening for complications / damage to the target organs;
- treatment / adjustment of medication, as appropriate.

Active monitoring consultations include:

- clinical examination in the family doctor's office;
- referral note - case management, for specific paraclinical investigations : complete blood count, blood glucose, complete lipid profile, serum ionogram, serum uric acid, serum creatinine, microalbuminuria, urinary protein dosage, depending on the level of risk
- EKG
- referral note - case management, depending on the level of risk for specialized consultation in cardiology, internal medicine, diabetes, nutrition and metabolic diseases, ophthalmology, nephrology;
- hygienic-dietary advice and self-care education.