DYSLIPIDEMIA RECOMMENDATIONS

A. DIAGNOSIS

Recommendation 1 – INITIAL LIPID PROFILING (Level of evidence II)

It is recommended to GPs and other PHC Physicians to assess the lipid profile {total cholesterol (TC), low density cholesterol (LDL-C), triglycerides (TG) and high density cholesterol (HDL-C)} in all men and women (particularly postmenopausal) > 40 years of age, who have not previously had assessed. It is a priority to the adults of any age with suspected or established atheromatic disease, hypertension, diabetes, smoking habit, obesity (BMI> 30 kg/m^2), chronic renal failure, autoimmune disorder (reumatoid arthritis, Systematic erythematosus lupus, psoriasis), and in any age in persons with a family history of premature cardiovascular disease or familial hyperlipidemia, in order to calculate the total cardiovascular risk.

Recommendation 2 – BLOOD SAMPLING (Level of evidence III-2)

It is recommended to GPs and other PHC Physicians to collect the blood sample for the measurement of lipids levels (TC, LDL-C, TG and HDL-C) after a 12-hour fasting period. In case of non-fasting samples, only non-HDL (TC - HDL) levels can be evaluated.

Recommendation 3 – INVESTIGATION OF AETIOLOGY (Level of evidence III-2)

It is recommended, in every person with high levels of TC (>240 mg/dL), LDL-C (>160 mg/dL), TG (>200 mg/dL) or low levels (<40mg/dL for men and <50mg/dL for women) of HDL-C, to investigate the causes of dyslipidemia, by assessing the personal and family history, by performing diligent physical examination as well as by performing supplementary laboratory tests (thyroid hormones, liver enzymes, creatinine, glucose, etc).

Recommendation 4 –OTHER DIAGNOSTIC FACTORS (Level of evidence III-1)

The determination of other atherogenic indicators (e.g. apolipoproteins apoB, apoA1, Lp(a), ratio apoB/apoA1, etc) is not recommended as routine diagnostic tests for the general population.

Recommendation 5 –CARDIOVASCULAR RISK ESTIMATION SYSTEM (Level of evidence II)

It is recommended in any man or woman 40-70 years old, without documented atherosclerotic disease or equivalent: (coronary heart disease, ischemic stroke, peripheral vascular disease, chronic renal disease-CRD, diabetes type 2 or type 1 with microalbuminuria), the application of the Cardiovascular risk estimation system *SCORE* (adapted to Greece), of the European Society of Cardiology for the assessment of the probability (absolute risk) the individual to develop a fatal cardiovascular event in the next 10 years.

Statistical modelling of 10-year fatal cardiovascular disease risk in Greece: the Hellenic SCORE (a calibration of the ESC SCORE project). Panagiotakos DB, Fitzgerald AP, Pitsavos C, Pipilis A, Graham I, Stefanadis C. Hellenic J Cardiol. 2007 Mar-Apr;48(2):55-63.

Recommendation 6 –PRIMARY CARE (Level of evidence IV)

As to low risk individuals (SCORE level <1%), the screening for dyslipidaemia (TC,LDL-C,HDL-C,TG), is recommended to be performed at long time intervals (e.g. every five years) which should however be reduced with increasing age.

Recommendation 7 –COUNSELING AND EDUCATION (Level of evidence IV)

As to low and moderate cardiovascular risk individuals with dyslipidaemia (SCORE level < 5%), it is recommended that they are provided with repeated counseling and education on matters of prevention (ideal body weight, diet, exercise, smoking).

Recommendation 8 –NURSES FOR PREVENTION PROGRAMMES (Level of evidence IV)

It is recommended to nurses and other allied PHC professions in partnership with other GPs and PHC Physicians to provide essential competences concerning the management of prevention programs, in order to provide education and support for the lifestyle change of patients with dyslipidaemia, in collaboration with the primary care physician.

C. TREATMENT

Recommendation 9 – DIET IN GENERAL POPULATION (Level of evidence IV)

The Mediterranean diet combined with an ideal body weight, is recommended as the most appropriate general nutritional standard for the decrease of the atherogenic load as well as of the cardiovascular mortality concerning the general population.

Recommendation 10 – DIET COUNSELING AND DYSLIPIDAEMIA (Level of evidence III-1)

As to patients of high cardiovascular risk (Score level >5%) and dyslipidaemia and to patients with isolated high LDL-C (>160 mg/dL) regardless of risk, more specialized dietary interventions such as a low-unsaturated fat diet and the increase of soluble fiber intake, along with medication(if needed), is recommended.

Recommendation 11 – PHYTOSTEROLS (Level of evidence II)

The daily consumption of 2 gr of phytosterols may be an option to some patients with dyslipidaemia.

Recommendation 12 – HIGH TG (Level of evidence III-1)

It is recommended to patients with hypertriglyceridemia in combination to pharmacotherapy the control of hyperglycemia, the reduction of weight, the reduction of the intake of mono- and disaccharides and carbohydrates, the avoidance of alcohol and the increase of daily physical exercise.

Recommendation 13 –DIET (Level of evidence IV)

To patients with dyslipidaemia with low to moderate cardiovascular risk (Score level <5%) the application of an individualized lipid-lowering diet, is recommended, as the only therapeutic intervention for at least 3 months period.

Recommendation 14 -EXERCISE (Level of evidence IV)

Daily aerobic exercise (e.g fast walking or any equivalent exercise) for at least thirty minutes/ 5 days per week, in a manner respective to the physical condition of the individual, is recommended to the patients with dyslipidaemia.

Recommendation 15- SMOKING AND ALCOHOL (Level of evidence IV)

Repeated counseling and pharmacological intervention for smoking cessation and decrease of the excessive alcohol intake (for men: 2-3 drinks or 20-30 gr alcohol per day and for women: 1-2 drinks or 10-20 gr alcohol per day) is recommended to patients with dyslipidaemia. Alcohol intake is prohibited to patients with marked hypertriglyceridaemia (> 500 mg/dl) due to increased risk for pancreatitis.

Recommendation 16 – LDL CHOLESTEROL (Level of evidence I)

The major target in the treatment of dyslipidemia is to reduce LDL cholesterol level according to the stratification of the cardiovascular risk of the individual.

Recommendation 17- non-HDL CHOLESTEROL (Level of evidence II)

It is recommended the use of non-HDL-C [TC–(HDL-C)] as secondary therapeutic goal (30 mg/dL higher than the LDL cholesterol goal) to patients with high triglycerides (>200 mg/dL), such as those with diabetes, hypertriglyceridaemia, mixed dyslipidaemia and metabolic syndrome.

Recommendation 18 –VERY HIGH RISK AND LDL –C GOAL (Level of evidence II)

In patients with dyslipidaemia of very high risk (documented atherosclerotic disease or diabetes type II with an additional risk factor, or type I diabetes with target organ damage or microalbuminuria, or CRD with GFR < 60 mL/min/1.73 m^2, or with Score level >10%) the LDL cholesterol goal is <70 mg/dL or if that's not possible, that there should be a decrease >50% from the initial levels of LDL cholesterol.

Recommendation 19- HIGH RISK AND LDL-C GOAL (Level of evidence II)

It is recommended to high risk patients with dyslipidaemia (with Score level >5% and <10%, or with diabetes without any other risk factor, or with more than 2 risk factors in addition to age, or with a very elevated single risk factor, that the LDL cholesterol goal is <100 mg/dL.

Recommendation 20 –DIABETES AND LDL-C GOAL (Level of evidence III)

It is recommended to type 2 and type 1 patients with diabetes over 40 year old without known cardiovascular disease, that the LDL cholesterol goal is <100 mg/dL. However, if one or more of the other risk factors or documented atherosclerotic disease coexist then, the optimum target is <70 mg/dL.

Recommendation 21 – ELDERLY AND TREATMENT TARGET (Level of evidence III)

It is recommended to GPs and other PHC Physicians to set the same therapeutic goals and take the same preventive measures for the elderly (>75 years old) as for the younger subjects (taking into account comorbidities, general condition and life expectancy), taking care to use such doses of statins in order to avoid side effects.

Recommendation 22–MODERATE RISK AND LDL-C GOAL (Level of evidence III)

It is recommended to moderate risk individuals with dyslipidaemia (Score level >1% και <5%) without an aggravating risk factor that the LDL-C goal is <130 mg/dL.

Recommendation 23 – LOW RISK AND LDL-C GOAL (Level of evidence III)

It is recommended to low risk individuals (Score level <1%) that the LDL cholesterol goal is <160 mg/dL, primarily interfering with lifestyle interventions or with statins if LDL-C level remains above 190 mg/dL.

Recommendation 24–FAMILIAL HYPERCHOLESTEROLEMIA (Level of evidence IV)

It is recommended, to individuals with (heterozygous) familial hypercholesterolemia without known cardiovascular disease, the administration of statins in higher tolerable doses possible or/and in combination with ezetimibe, and/or colesevelam in order to reduce LDL-C level <100 mg/dL.

Recommendation 25- EZETIMIBE (Level of evidence II)

It is recommended the administration of ezetimibe as monotherapy in case of statin intorerance or in combination with the highest tolerant dose of statin when the therapeutic goal of LDL-C is not achieved.

Recommendation 26 – FIBRATES (Level of evidence IV)

Monotherapy with fenofibrate is recommended to patients with dyslipidaemia for the treatment of severe hypertriglyceridemia (>500 mg/dL) and additionally to statin in individuals with atherogenic dyslipidemia {triglycerides> 200 mg/dL and HDL-C <35 mg/dL).

Recommendation 27 – N-3 FATTY ACIDS (Level of evidence II)

Daily administration of 2-4 g of n-3 fatty acids [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)] is recommended to patients with high triglycerides (>200 mg/dL) additionally to statin therapy or even fenofibrate when fasting triglycerides remain > 500 mg/dL.

Recommendation 28 - COLESEVELAM (Level of evidence IV)

The administration of colesevelam combined with a statin is recommended to patients with dyslipidaemia for an additional reduction in LDL cholesterol levels.

Recommendation 29 – MONITORING INITIAL CONTROL (Level of evidence IV)

It is recommended to the patients with dyslipidaemia that the initial blood tests to monitor the safety and efficacy of the lipid-lowering treatment, includes the assessment of lipids (TC, TG, LDL-C, HDL-C), fasting glucose, liver enzymes (ALT, AST) and creatine kinase (CK) and it should be conducted 8-12 weeks after initiating lipid lowering medications.

Recommendation 30- MONITORING FOLLOW UP (Level of evidence IV)

To patients with dyslipidaemia of high and very high risk (with documented atherosclerotic disease or equivalent or Score level >5%) it is recommended that the monitoring of the lipid-lowering treatment is conducted annually. The progress of atheromatic disease, weight gain and drug administration that may affect the safety and effectiveness of the treatment, can shorten the interval of lipid control.

Recommendation 31 – CONTRAINDICATIONS (Level of evidence IV)

It is recommended to the patients with dyslipidaemia to avoid the coadministration of statins with drugs metabolized by the same cytochrome in the liver. When coadministration of these drugs is necessary and/or in case of severe renal or hepatic dysfunction, for a greater safety, statins should be selected according to the main route of drug metabolism (hepatic or renal).

Recommendation 32- MUSCLE SYMPTOMS (Level of evidence IV)

Immediate check of CK levels in patients with myalgia and muscle weakness receiving hypolipidemic drugs is recommended. If the level of CK is 5 times the upper normal limit, the temporary cessation of the statin is suggested.

Recommendation 33 – STOP TREATMENT (Level of evidence II)

It is recommended to GPs and other PHC Physicians to temporarily stop the lipid -lowering treatment when liver enzymes (ALT, AST) are raised 3 times above normal values.

Recommendation 34 – COMPLIANCE STRATEGIES (Level of evidence III)

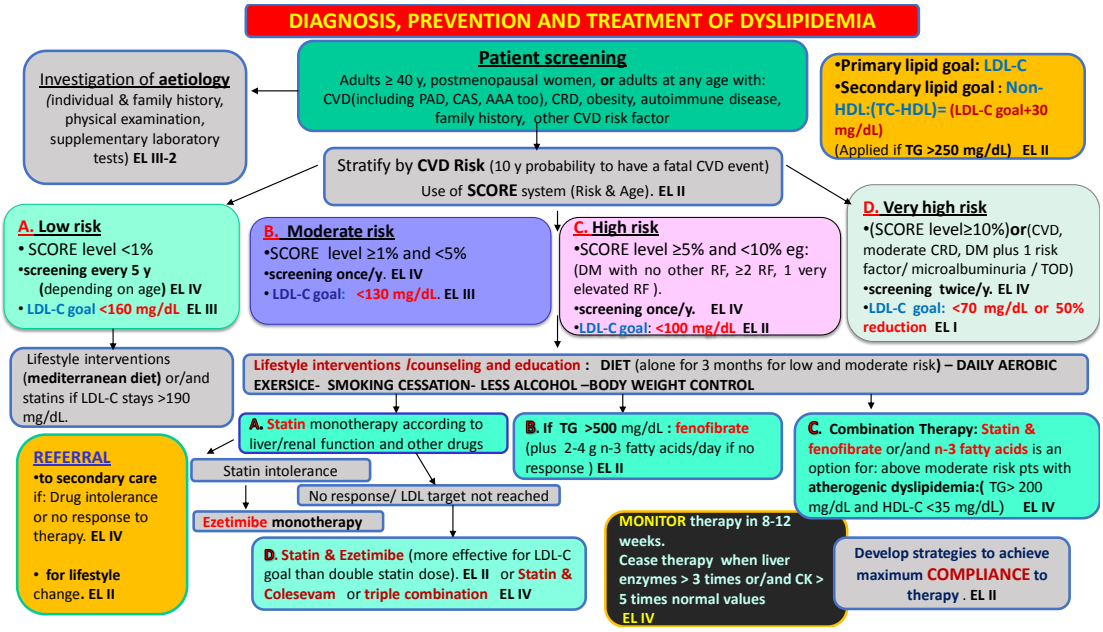
GPs and other Primary care physicians, in partnership with other health professionals, are recommended to use various methods including communication via phone, internet and contact with family members in order to remind to the patients with dyslipidaemia of the

therapy and the follow up of schedule, in order to achieve the maximum compliance of the patients.

D. REFERRAL

Recommendation 35 – REFERRAL TO SECONDARY CARE (Level of evidence IV)

A referral to the hospital services is recommended for all the patients with dyslipidaemia who present severe adverse effects from the treatment (urgent referral), those where genetic dyslipidaemia is suspicious (genetic counseling) and those where therapeutic targets have not been achieved.



Abbreviations:

EL: Level of Evidence, **CVD:** Cardiovascular disease, **H:** Hyperlipidemia, **TC:** total cholesterol, **LDL-C:** LDL cholesterol, **TG:** Triglycerides, **HDL-C:** HDL cholesterol, **CAS:** carotid artery stenosis, **PAD:** peripheral arterial disease, **AAA:** abdominal aortic aneurysm, **DM:** diabetes mellitus, **CRD:** chronic renal disease, **TOD**: target organ damage, CK : creatine kinase, **y:** year, **pts**: patients.