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Coronary Artery Disease Prevention

Preventive Medicine
mgr Anna Tarkowska

Department of Non-Invasive Cardiology,
Chair of Internal Medicine and Cardiology,
Medical University of Lodz

- ▶ As cardiovascular diseases have been constituting the main health problem all around the world for many years 43% of cardiovascular deceases are caused by **ISCHEMIC HEART DISEASE**

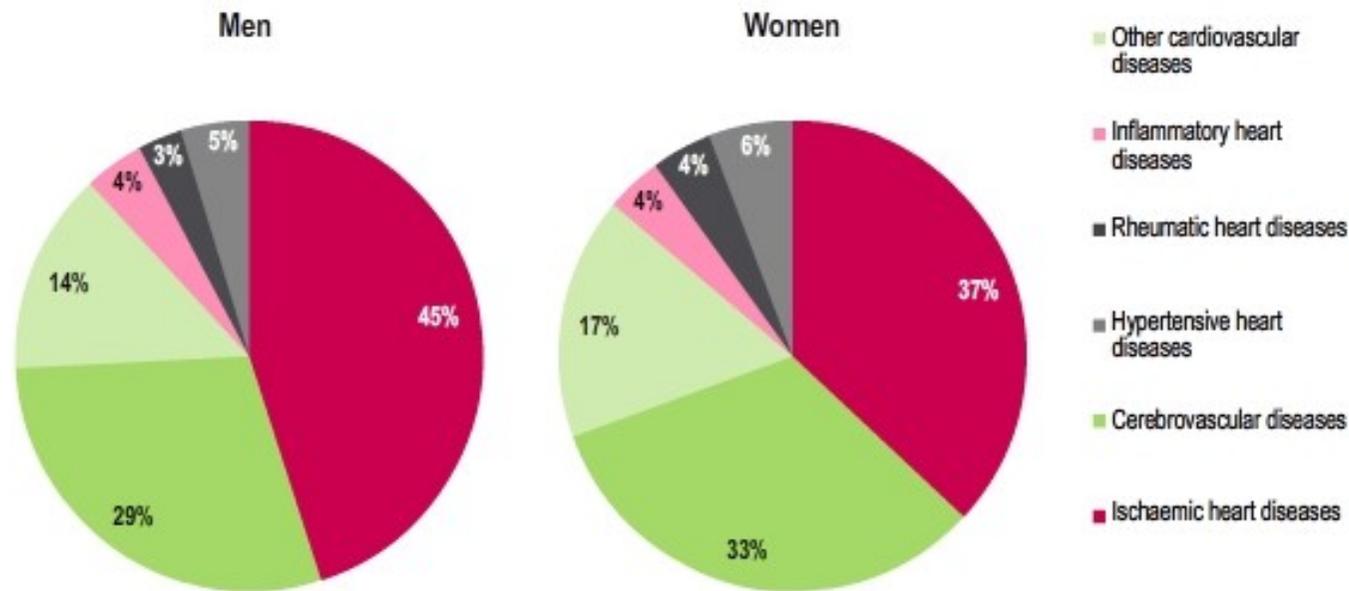


Ischemic heart disease occurs due to insufficient supply of myocardium to nutrients and oxygen.

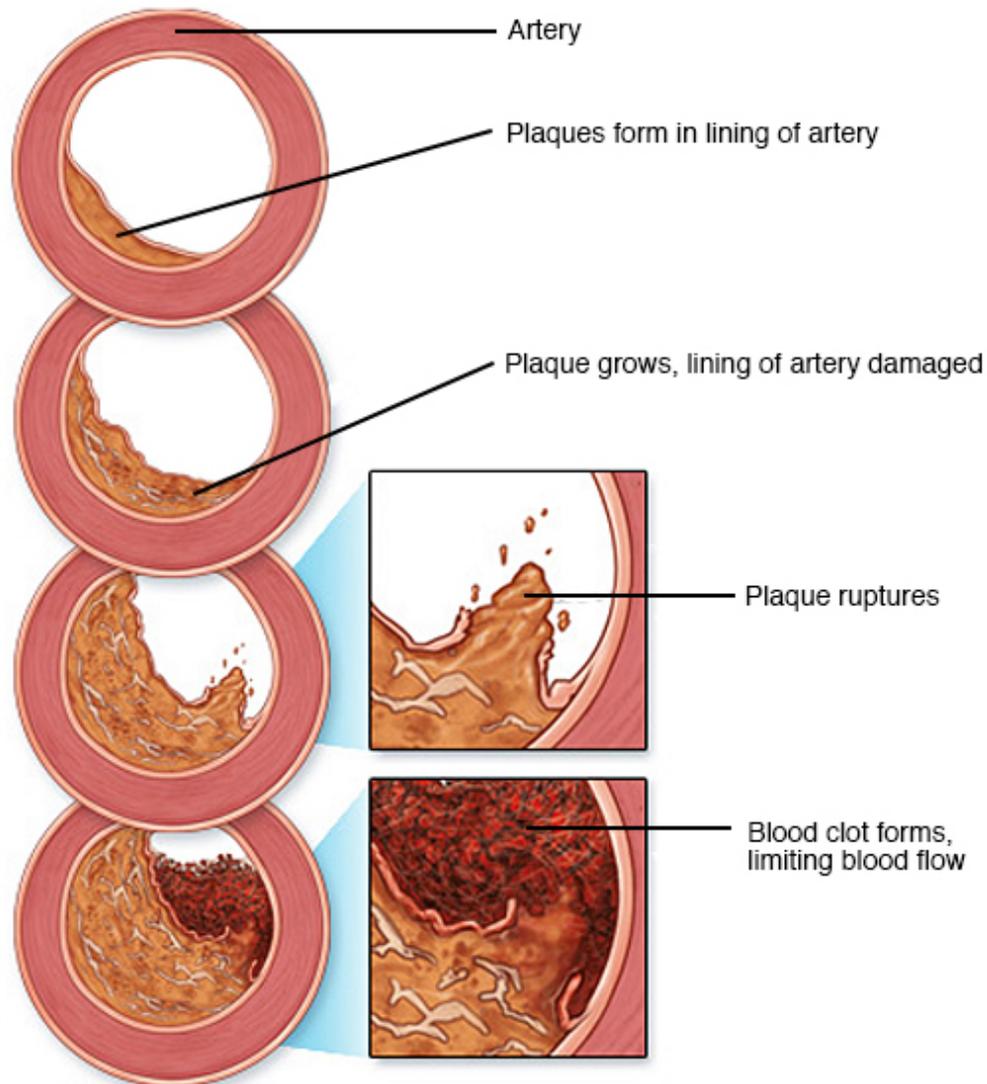
- With the imbalance between the need for myocardial cells in oxygen and the possibility of its delivery, there is a reduction in blood perfusion and in consequence the decrease in coronary.
- The inclusion of treatment is intended to inhibit the disease progression by abolishing the condition of myocardial ischemia and to ensure secondary prevention by eliminating risk factors of coronary heart diseases

Epidemiology

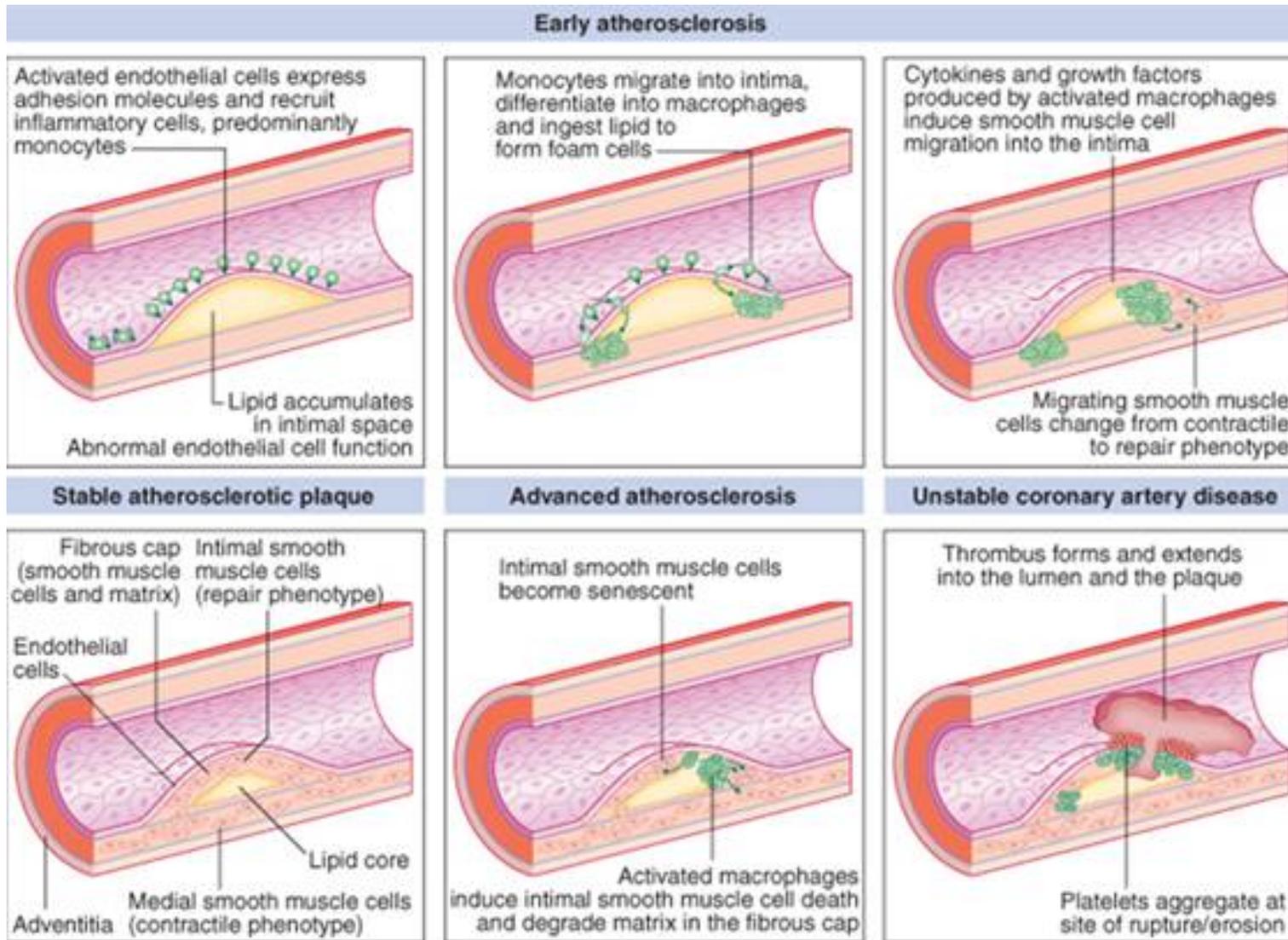
- ▶ Atherosclerotic CVD - **leading cause** of premature death worldwide
43% due to CVD in women and 36% in men.
- ▶ Prevention works:
 - 50% of the reduction seen in CHD mortality relate to changes in risk factors
 - 40% to improved treatments



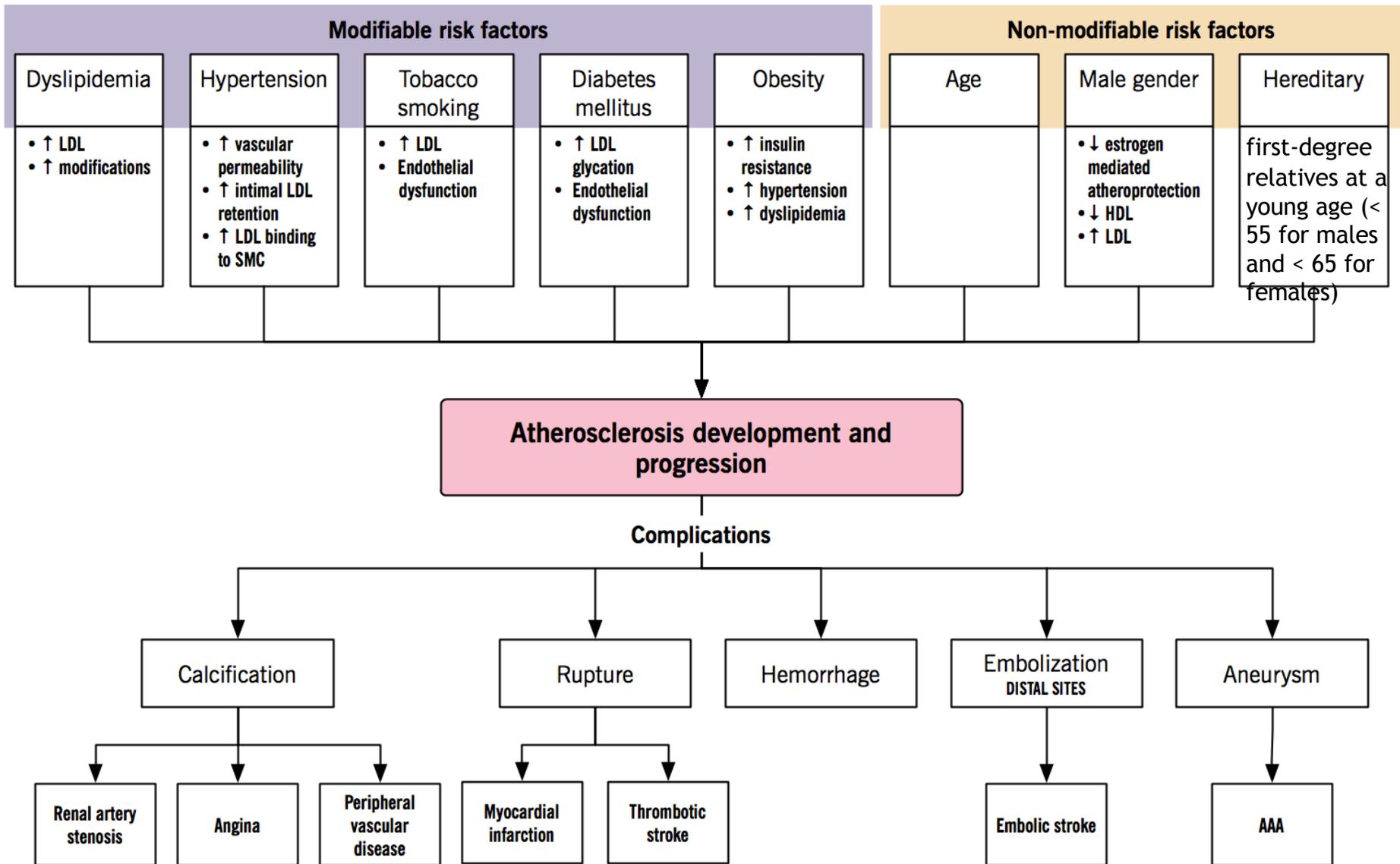
The main cause of CAD is atherosclerosis, which is characterized by the deposition of cholesterol and lipids primarily in the intimal wall of the artery



Artherosclerosis development



ATHEROSCLEROSIS | Risk factors and complications of atherosclerosis



Dyslipidemia - risk factor of CAD

Types of dyslipidemia disorders:

1. HYPERCHOLESTEROLEMIA -
 - ▶ LDL cholesterol ≥ 115 mg / dl (≥ 3 mmol / l)
 - ▶ total cholesterol ≥ 190 mg / dl (≥ 5.0 mmol / l);
2. HYPERTRIGLYCERIDEMIA -
 - ▶ TG concentration ≥ 150 mg / dl (≥ 1.7 mmol / l);
3. LOW HDL CHOLESTEROL -
 - ▶ HDL <40 mg / dl (1 mmol / l) in men
 - ▶ HDL <45 mg / dl (1.2 mmol / l) in women;
4. MIXED HYPERLIPIDEMIA

Statins in dyslipidemia treatment

Five-year observation of statins treatment showed reduction of LDL cholesterol on average 35%.

Statins



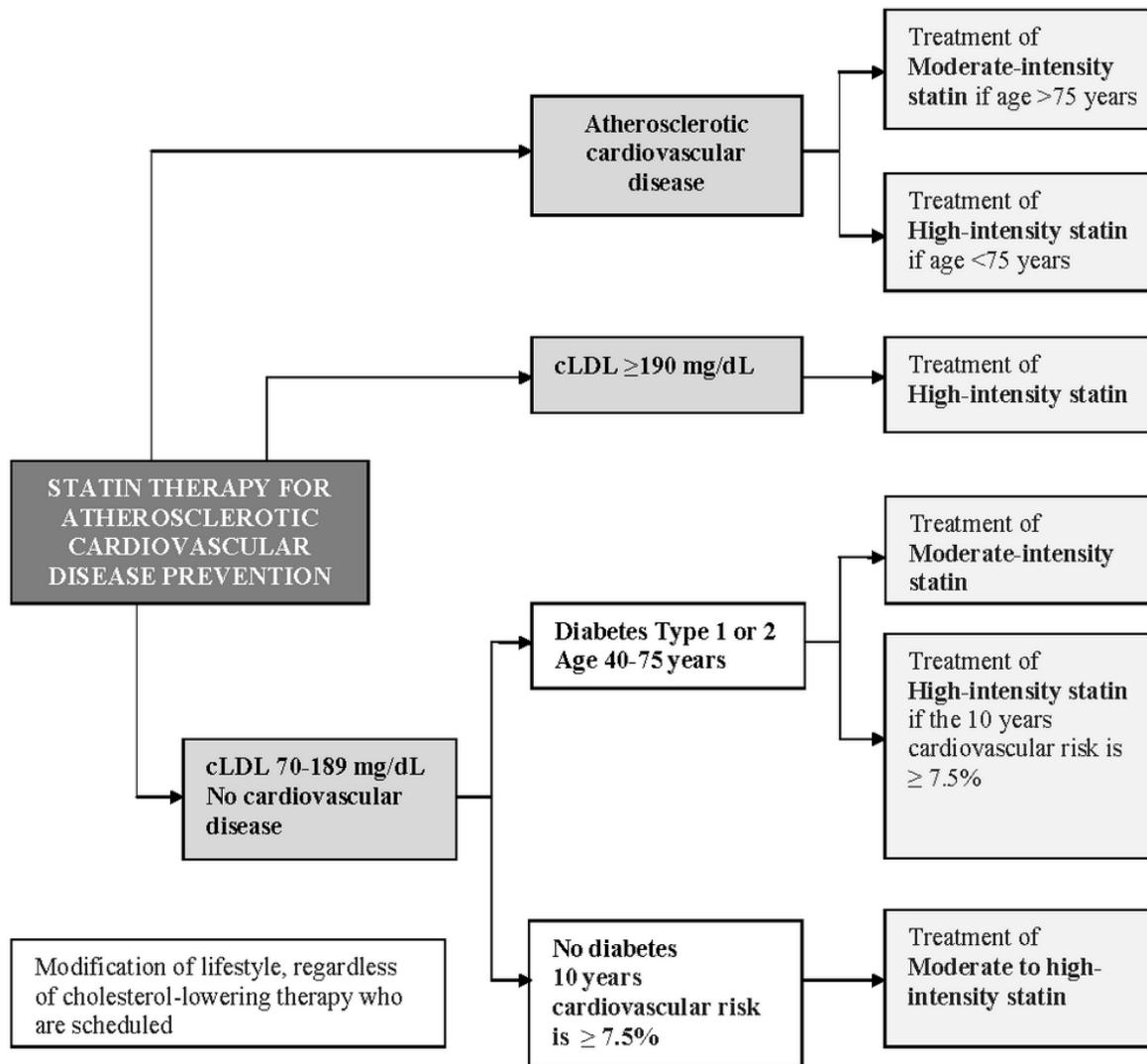
direct effect on the reduction of cholesterol, especially its LDL fraction



Pleiotropic effects:

- improve endothelial cell function,
- Stabilization atherosclerotic plaques,
- exhibit profibrinolytic,
- antiaggregative and anti-inflammatory effects,
- immunomodulatory, which is a consequence of the inhibitory effect effects on HMG-CoA reductase present in cells vascular endothelium, inflammatory cells and cells smooth muscle

Intensity of statins in dyslipidemia treatment



- ▶ Atorvastatin
- ▶ Cerivastatin
- ▶ Fluvastatin

- ▶ Lovastatin
(Primary prevention)
- ▶ Mevastatin
- ▶ Pitavastatin
- ▶ Pravastatin
- ▶ Rosuvastatin
- ▶ Simvastatin

The hypolipemetic effect of monacolin in primary prevention

Natural lovastatin - monacolin K - is found in fermented red rice, which arises in the fermentation process with *Monascus purpureus* fungus, called red yeast, and edible mushrooms - oyster mushroom

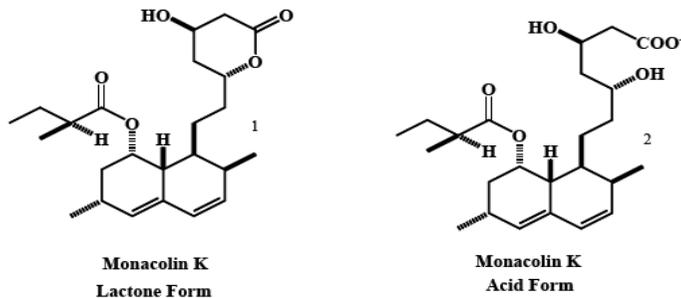


Figure 1: Structure of Monacolin K.



Pts with LDL 203,9 mg/dl

5.7 mg/day monacolin

For 8 weeks

Reduction of:

- Total cholesterol ↓ - 21.5% ,
- LDL cholesterol ↓ by 27.7,
- TG level ↓ by 15.8 %
- Apolipoprotein B ↓ by 26%

Increased

- HDL level by 0.9%
- Apolipoprotein A by 3.4%

Coronary artery disease prevention



Primary prevention

(group of pts with high risk of CAD developmet)



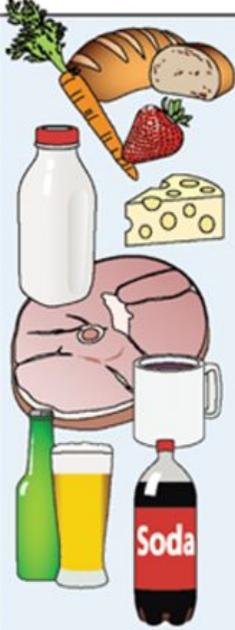
Secondary prevention

(e.g. pts with CAD, pts after PTCA, pts with PAD or after MI)

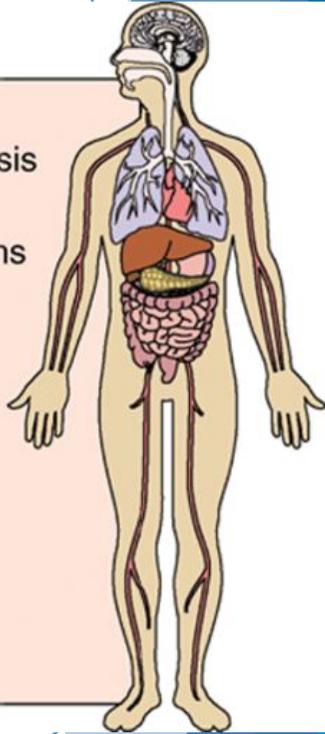
-
- Normalization of body weight
 - blood pressure,
 - Appropriate glucose tolerance,
 - Cholesterol levels

- all these cardiovascular risk factors are determined by nutrition habits

Nutrition influence on Cardiovascular System



- Refined grains, starches, sugars
- Fruits, vegetables, nuts
- Whole grains, legumes
- Yogurt, cheese, milk
- Fish, shellfish
- Processed meats, red meats
- Vegetable oils, specific fatty acids
- Coffee, tea, alcohol
- Sugary beverages, juice
- Minerals, antioxidants, phytochemicals
- Food-based dietary patterns
- Food processing, preparation methods



- Blood pressure
- Glucose-insulin homeostasis
- Liver fat synthesis
- Blood lipids, apolipoproteins
- Endothelial function
- Systemic inflammation
- Brain reward, craving
- Gut microbiome
- Satiety, hunger, obesity
- Adipocyte function
- Cardiac function
- Thrombosis, coagulation
- Vasular adhesion

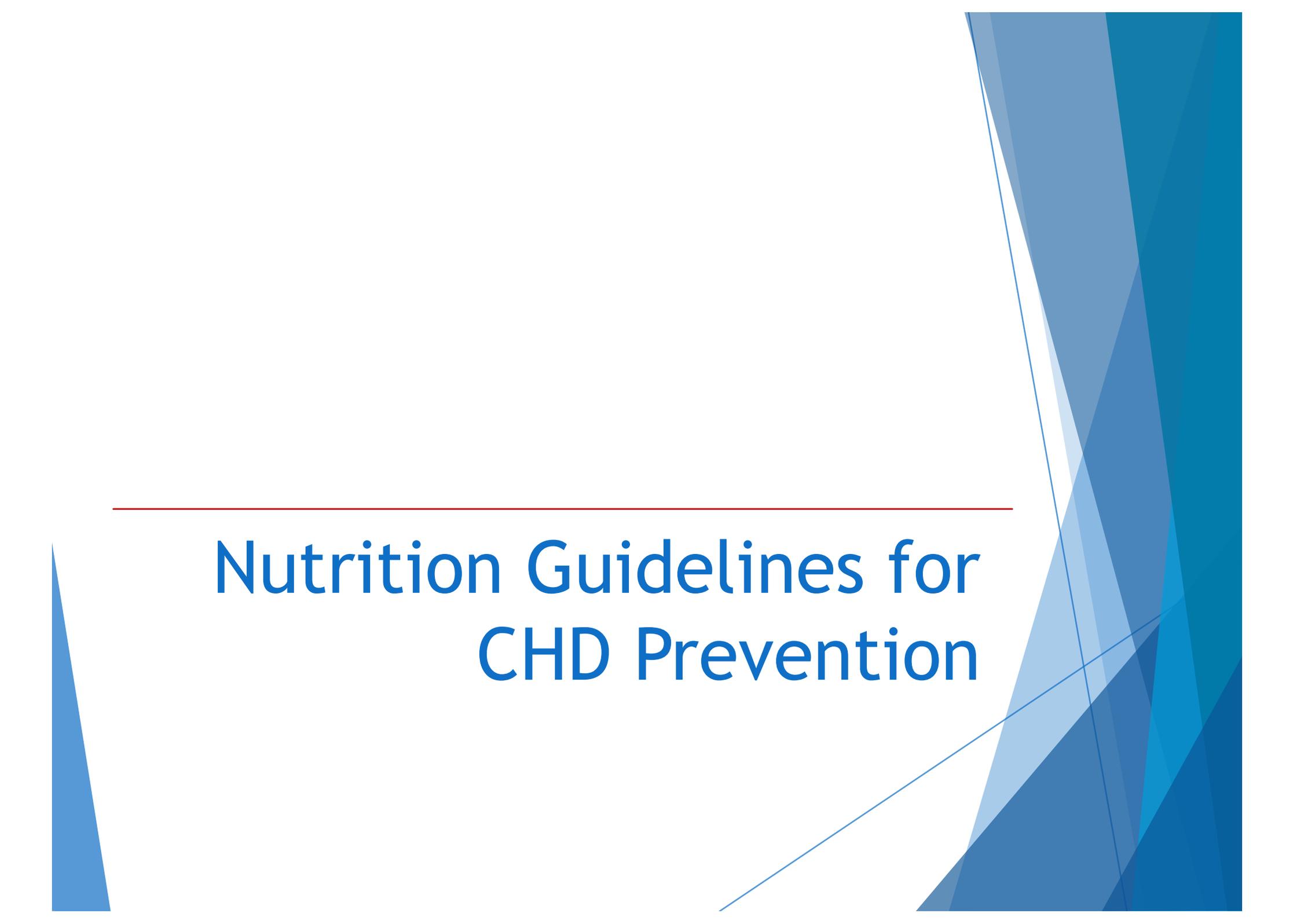
<https://doi.org/10.1161/CIRCULATIONAHA.115.018585>
Circulation. 2016;133:187-225 Originally published January 11, 2016

CHD nutrition intervention

- ▶ Nutritional interventions are aimed at neutralizing nutrition-related risk factors, including:
 - ▶ dyslipidemia,
 - ▶ hypertension,
 - ▶ overweight or obesity,
 - ▶ as well as disturbing the balance of carbohydrate metabolism

- ▶ Due to the reduction of excessive body weight and improved nutrition, regular physical activity and the cessation of smoking →
 - ▶ reduction in blood pressure,
 - ▶ lipid profile normalization
 - ▶ an increase in glucose tolerance

Nutrition Guidelines for CHD Prevention

The slide features a white background with several blue geometric shapes. On the left, there is a solid blue triangle pointing upwards. On the right, there is a large, complex shape composed of overlapping translucent blue triangles and rectangles, creating a layered effect. A thin red horizontal line is positioned above the main title text.



Instytut
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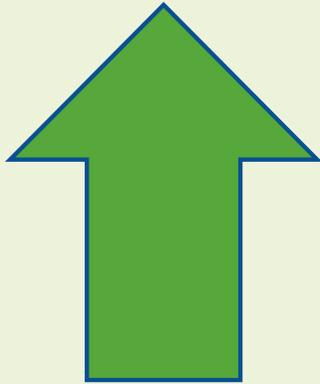
Ranges of population nutrient intake goals (WHO data)



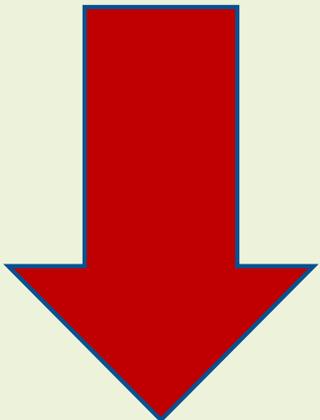
Dietary factor	
Total fat	15-30%
•Saturated fatty acids	< 10%
•Polyunsaturated fatty acids (PUFAs)	6-10%
•n-6 PUFAs	5-8%
•N-3 PUFAs	1-2%
•Trans unsaturated fatty acids	<1%
•Monounsaturated fatty acids (MUFAs)	by difference
Total carbohydrate	55-75%
•Free sugars	<10%
Protein	10 - 15%
Cholesterol	< 300 mg per day
Sodium Chloride	<5g per day (<2g per day)
Fruits and vegetables	≥400 g per day
Total dietary fibre	27 - 40g per day



Based on the principles of healthy nutrition, the diet in ischemic heart disease with atherosclerotic features:



- Fruits and Vegetables;
- Wholegrain cereal; products;
- Legumes;
- Nuts;
- Fibre-rich products
- Plants oil;
- Fatty fish;
- Antioxidants;
- Folates;



- Cholesterol-rich products;
- Saturated fatty acids;
- Red meat;
- Sugar and salt;
- Highly processed food;
- Alcohol;
- Strong tea and coffee;
- Cheese, e.g. parmesan

Impact of specific lifestyle changes on lipid levels (1)

	Magnitude of the effect	Level of evidence	References
Lifestyle interventions to reduce TC and LDL-C levels			
Reduce dietary trans fat	+++	A	136, 139
Reduce dietary saturated fat	+++	A	136, 137
Increase dietary fibre	++	A	140, 141
Use functional foods enriched with phytosterols	++	A	142, 143
Use red yeast rice supplements	++	A	144–146
Reduce excessive body weight	++	A	147, 148
Reduce dietary cholesterol	+	B	149
Increase habitual physical activity	+	B	150
Use soy protein products	+/-	B	151

Saturated fatty acids

„Saturated fatty acids are the main factor increasing the concentration of cholesterol in the blood serum”.

Seven Countries Study, 1958-1964

However newest meta-analysis:

the cardioprotective effect results not so much from reducing the consumption of saturated acids as from the increased supply of polyunsaturated acids in the daily diet.

- Replacing 5% of the energy obtained from SFAs with energy from PUFAs reduces the risk of CHD by 42%.
- No need to reduce the consumption of SFAs below 9% of the daily energy demand

Trans-unsaturated fatty acid isomers and food cholesterol

1. Trans-unsaturated Fatty Acids:

- ▶ correlation between the mortality rate CHD and the intake of eridinic acid (trans oleic fatty acid isomer)

increase LDL cholesterol in the blood serum
lower HDL cholesterol

- ▶ **Source:** naturally in small amounts in butter, milk, beef or mutton; however, their main source is partially hydrogenated fats, i.e. hard margarines, bakery and kitchen fats
- ▶ **OUTCOME:** recommended to significantly reduce, and sometimes completely eliminate

Trans-unsaturated fatty acid isomers and food cholesterol

2. Cholesterol

- ▶ increased cholesterol intake from food products by 100mg leads to an **increase in total cholesterol by 0.05-0.51 mmol/l** on average
- ▶ According to the American Heart Association recommendations:

food intake of dietary cholesterol should not exceed 300mg per day

Unsaturated fatty acids

- ▶ **PUFAs (Polyunsaturated Fatty Acids):**
 - ▶ enrichment of phospholipids of cell membranes with eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA),
 - ▶ which demonstrate antiarrhythmic, hypotensive and anti-inflammatory effects against antiplatelet agents
- ▶ **Increase in daily PUFA consumption by 1g resulted in a decrease in triglycerides by 8mg / dl**

Functional food enriched with n-3 PUFA fatty acids

Table 1: Omega-3 fatty acid content (EPA and DHA) of selected fish and seafood, functional foods and fish oil supplements

Product	Concentration of sum of EPA and DHA*
Fish or seafood	
Mackerel	2500 mg/100 g
Herring	1700 mg/100 g
Salmon	1200 mg/100 g
Trout	500 mg/100 g
Halibut	400 mg/100 g
Tuna	400 mg/100 g
Shrimp	300 mg/100 g
Cod	300 mg/100 g
Functional foods	
Liquid eggs (Omega Pro)†	900 mg/180 mL
Fish oil supplements	
Standard	300 mg/capsule
Specialty (Omega 600)‡	600 mg/capsule

Note: EPA = eicosapentaenoic acid, DHA = docosahexaenoic acid.

*The EPA and DHA content of the fish and seafood will vary somewhat according to the species, source and other factors.

†Naturegg (Burnbrae Farms Ltd., Lyn, Ont.).

‡Ocean Essentials (Ocean Nutrition Canada Ltd., Halifax, NS).



Rich sources of α -linolenic acid are **vegetable oils, especially oils: linseed, rapeseed and soybean oils**, and EPA and DHA acids - greasy sea fish.

The n-3 PUFA fatty acid preparations used in functional foods are obtained from **fish oils**. They are most often enriched with margarines for spreading bread and milk.

Total fat intake

- ▶ It is recommended that polyunsaturated fatty acids account for 13-21% of total energy (with total fat: around 35% of total energy), thus contributing to a significant reduction the risk of coronary events.

According to the results of a study by The Finnish Mental Hospital, Los Angeles Veterans and The Oslo Diet Heart

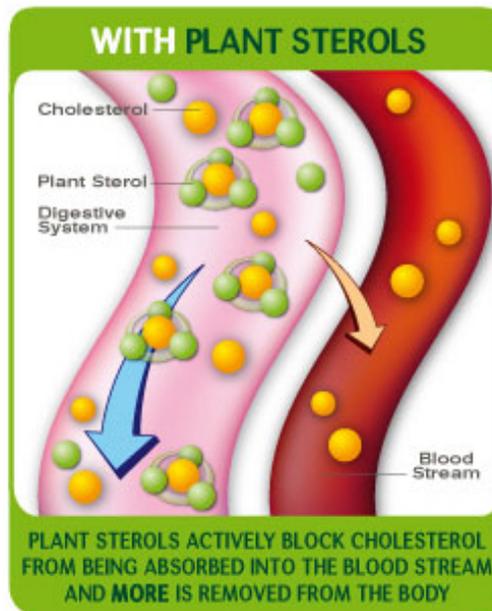
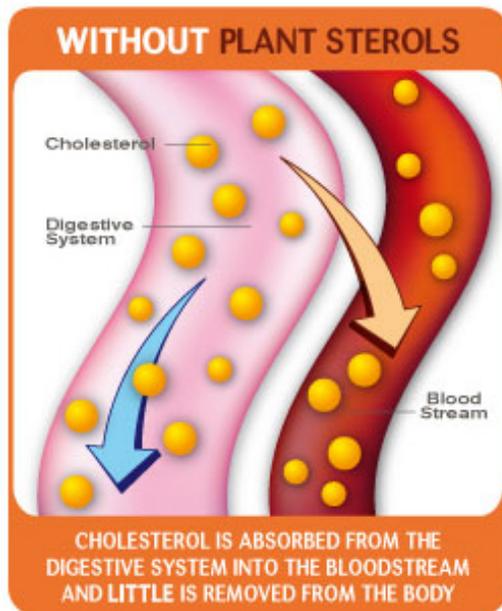
UNSATURATED FATTY ACIDS - SOURCES:

1. **Nuts** → Almonds, hazelnuts, walnuts and macadamia nuts
2. **Vegetables** → **Avocado**
3. **Plants olis** → olive oil; linseed oil, sunflower oil, rapeseed oil
4. **Fish** → mackerel, herring, salmon, halibut
5. **Seeds** → sunflower seeds, pumpkin seeds, sesame

Functional food enriched with stanols and plant sterols

Plant sterols/stanols (when taken at 2 g/day) cause significant inhibition of cholesterol absorption and lower LDL-C levels by between 8 and 10%

PLANT STEROLS WORK TO ACTIVELY LOWER YOUR CHOLESTEROL ABSORPTION



Functional food enriched with stanols and plant sterols

functional foods with plant sterols/stanols may be considered

- 1) in individuals with high cholesterol levels at intermediate or low global cardiovascular risk who do not qualify for pharmaco-therapy,
- 2) as an adjunct to pharmacologic therapy in high and very high risk patients who fail to achieve LDL-C targets on statins or are statin-intolerant,
- 3) and in adults and children (>6 years) with familial hypercholesterolaemia,



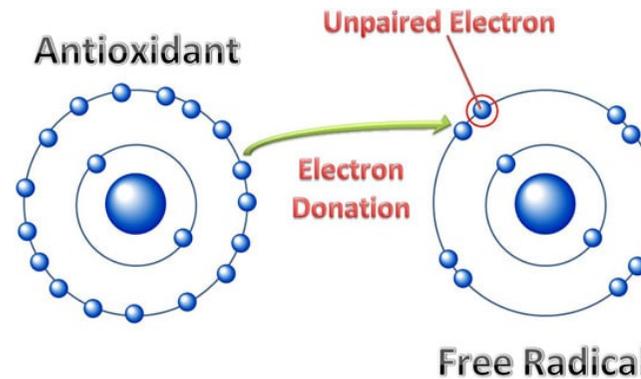
Natural source: e.g. sesame and sunflowerseeds

Food enriched with stanols and sterols: margarines, yoghurts and cheese

Oil	Total sterols (mg/100g)
Coconut	40-120
Olive	221-440
Palm	30-70
Groundnut	90-290
Rapeseed	450-1130
Soybean	180-450
Sunflower	240-500

Antioxidants

- ▶ The essence of using antioxidants in atherosclerosis therapy and prevention is based on the common statement that low-density lipoprotein LDL acquires atherosclerotic features only under the influence of free oxygen radicals.



https://www.healthline.com/hlcmsresource/images/AN_images/antioxidants-vs-free-radicals-diagram_0.jpg

- ▶ The goal of antioxidants is to protect the LDL lipoprotein molecule from oxidative modification
- ▶ Source: (vitamin A, vitamin C, vitamin E, carotenoids, folic acid and flavonoids) vegetables and fruits, cereal seeds, legume seeds, tea, wine and some herbs and spices

Antioxidants



Fiber

- ▶ food fibers lower the total cholesterol level by 1.1 mg / dl per 1g of fiber consumed and LDL cholesterol by 1.13mg / dl per 1g of fiber consumed

- ▶ WHO data:

the average intake of dietary fiber should oscillate between 27 and 40 g / day, of which about 15g should be a soluble fraction (pectin).

- ▶ The richest sources of dietary fiber are cereal products (especially bran - 42g / 100g), vegetables (especially dry beans, peas and soybeans) and fruits (especially dried plums, currants or raspberries)

THE TOP 12 HIGH-FIBER FOODS

-  **SPLIT PEAS**
1 cup cooked : 16.3 grams
-  **LENTILS**
1 cup cooked : 15.6 grams
-  **BLACK BEANS**
1 cup cooked : 15 grams
-  **MUNG BEANS**
1 cup cooked : 15 grams
-  **FIGS**
1 cup dried : 14.6 grams
-  **LIMA BEANS**
1 cup cooked : 13.2 grams
-  **COCONUT FLOUR**
1/4 cup : 10 grams
-  **ARTICHOKE**
1 artichoke : 8.7 grams
-  **ACORN SQUASH**
1 cup cooked : 9 grams
-  **GREEN PEAS**
1 cup cooked : 8.8 grams
-  **RASPBERRIES**
1 cup : 8 grams
-  **BLACKBERRIES**
1 cup : 7.6 grams

Minerals

POTASSIUM

- ▶ Meta-analysis by McGregor & Cappucio
**higher potassium intake reduces SBP by 5.9 mm Hg,
and DBP by 3.4 mm Hg**
- ▶ American Heart Association recommends to increase potassium daily intake to **4,7g (120mmol) per day**

SODIUM

- ▶ Dietary Approaches to Stop Hypertension (DASH Trials):
**reduction in sodium intake of 1g/day reduces SBP by 3.1 mm Hg in
hypertensive patients and 1.6 mm Hg in normotensive pts.**
- ▶ Salt reduction by:
 - ▶ Elimination of highly processed food;
 - ▶ Lowering salt content
 - ▶ Replacing salt with herbs and spices

The Mediterranean Diet

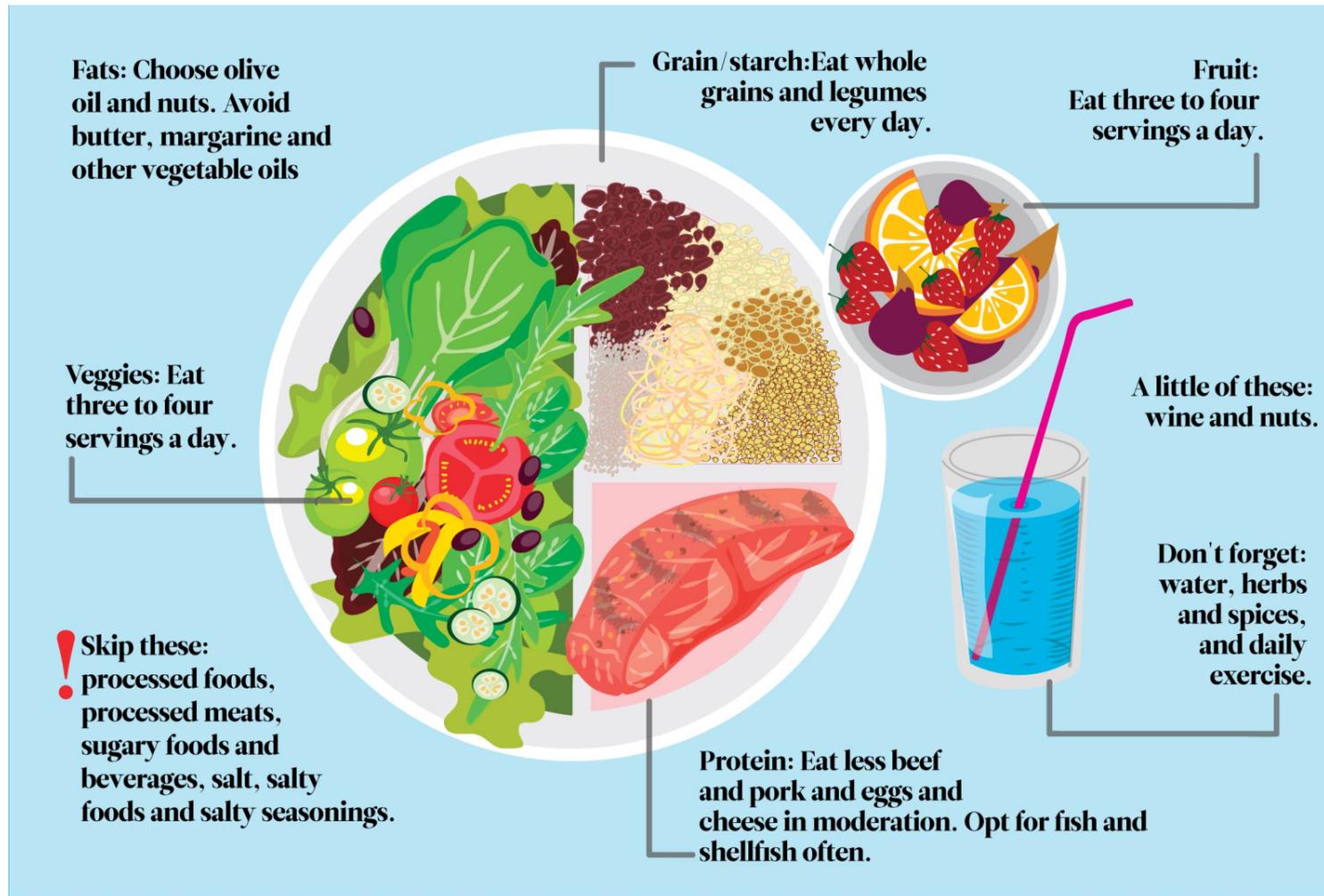
A meta-analysis of prospective cohort studies:

1. The Mediterranean Diet is associated with 10% reduction in CV incidence and an 8% reduction in all-cause mortality
 2. Following Mediterranean Diet for 5 years could lower the risk of CVD by 29%.
-

The Mediterranean Diet

- Guidelines based on results of many clinical trials and meta-analysis of individual diet's component (**Evidence-Based Medicine**):
- High intake of fruits and vegetables, legumes, wholegrain products, fish and unsaturated fatty acids (olive oil);
- Lower consumption of meat (mostly red), dairy products and saturated fatty acids, sugars and highly processed food.

The Mediterranean Diet

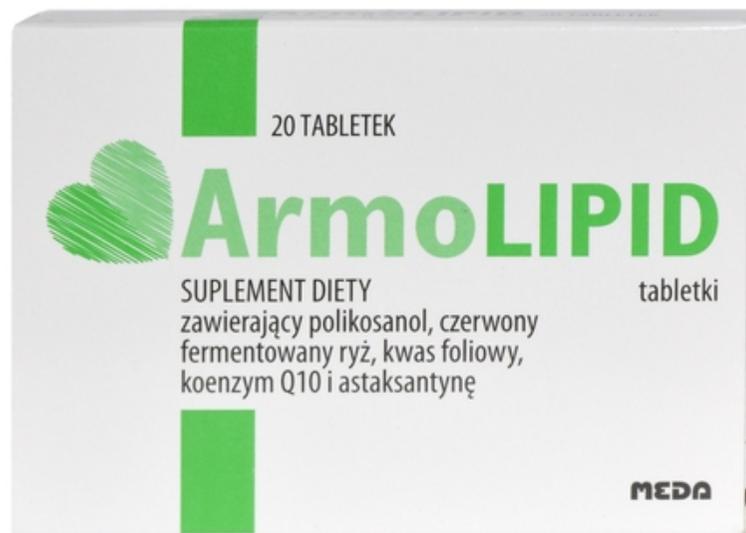


<https://www.rd.com/wp-content/uploads/2017/08/02-This-Infographic-Is-Your-Mediterranean-Diet-Cheat-Sheet.jpg>

A nutraceutical approach (Armolid Plus) to reduce total and LDL cholesterol in individuals with mild to moderate dyslipidemia

Investigated in several RCTs,:

- ▶ 7 of which were placebo-controlled,
- ▶ 2 were ezetimibe comparators
- ▶ 4 were “real life” studies comparing diet and Armolid Plus to diet alone.



- red yeast rice
- policosanol
- Berberine,
- folic acid,
- astaxanthin,
- coenzyme Q10
(Armolid Plus®)

A nutraceutical approach (Armolidip Plus) to reduce total and LDL cholesterol in individuals with mild to moderate dyslipidemia

Investigated in several RCTs:

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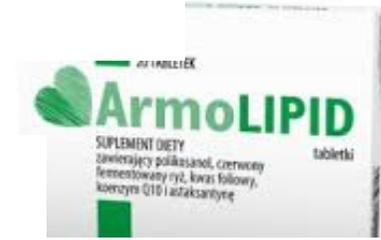


Pts with **mild to moderate dyslipidemia**
and in whom **statins** were contraindicated or who could **not tolerate** them

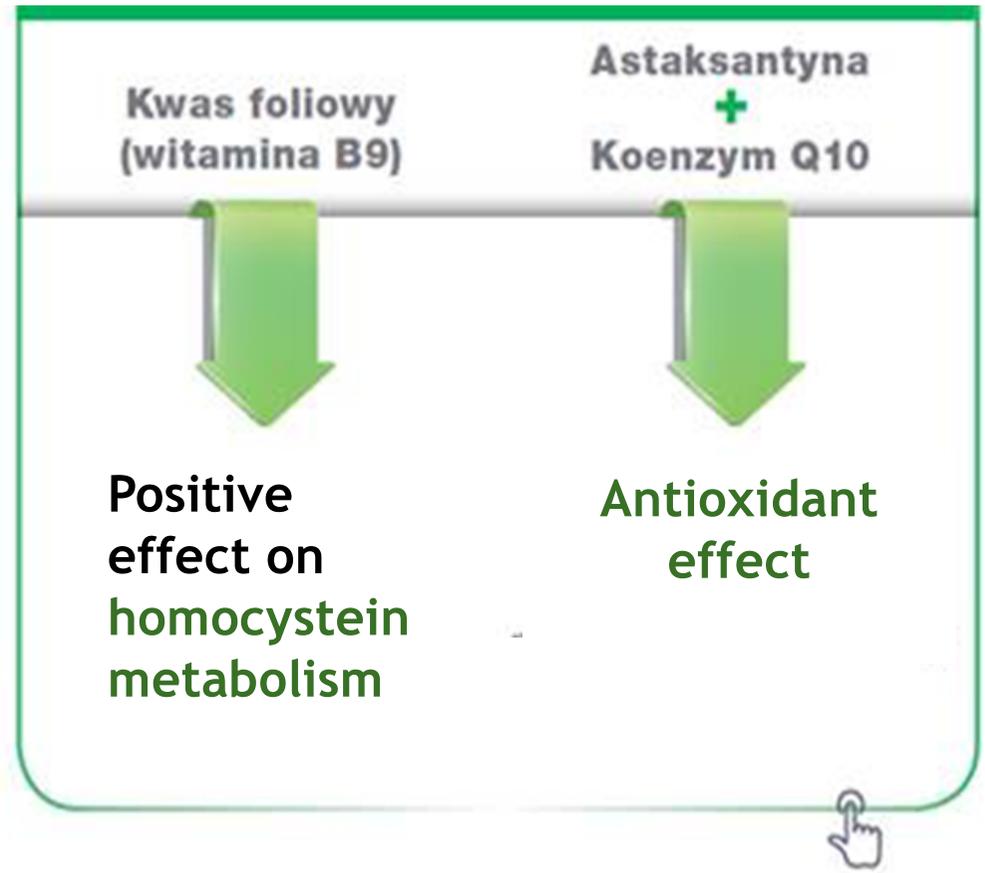
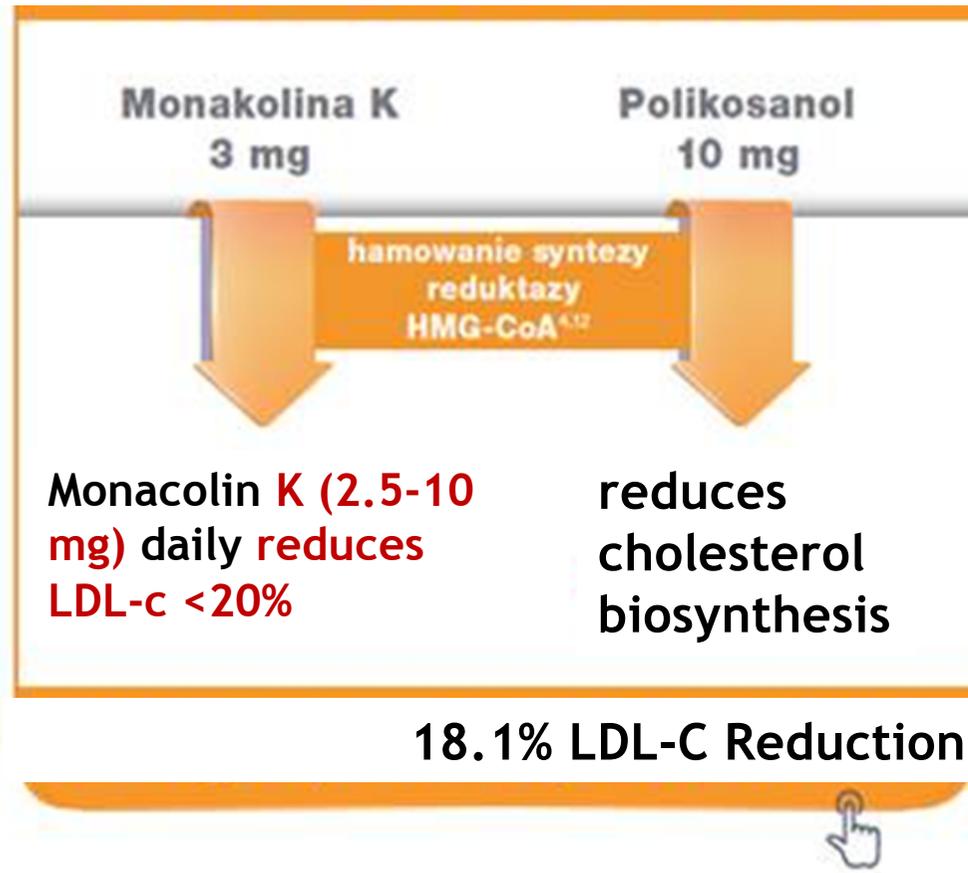
A nutraceutical approach (Armolipid Plus) to reduce total and LDL cholesterol in individuals with mild to moderate dyslipidemia

Results of clinical trials:

- ▶ Armolipid Plus has proved to achieve
 - reductions in TC (↓ by 11-21%)**
 - reductions in LDL-C (↓ by 15-31%),**which is equivalent to expectations from low dose statins.
- ▶ In patients intolerant to statins , who are taking ezetimibe, Armolipid Plus can achieve
 - a further 10% reduction in TC and LDL-C.**
- ▶ Dietary interventions with Armolipid Plus supplementation :
 - ↓ for
 - pts with mild to moderate hyperlipidemia
 - dyslipidemic pts in statins intolerance

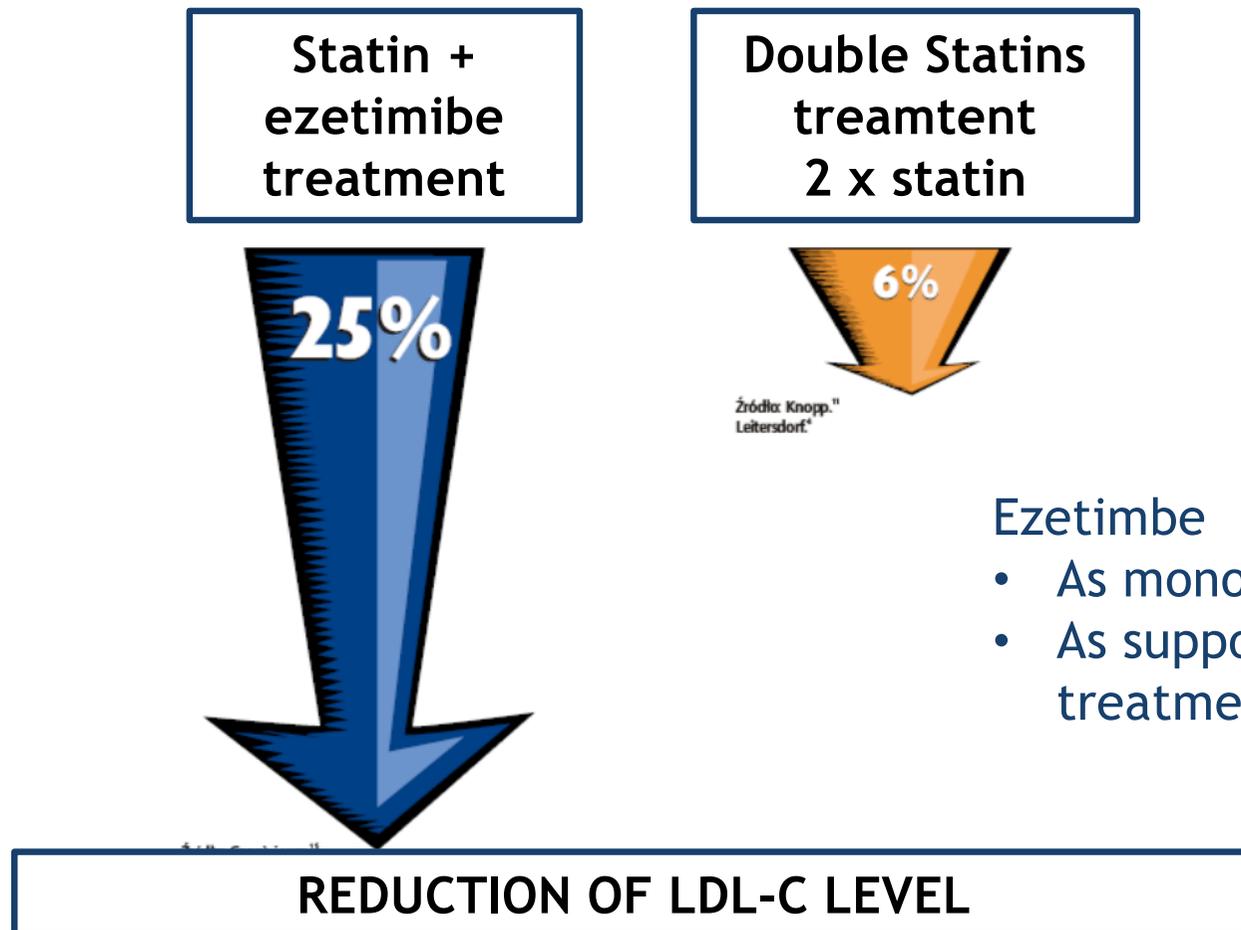


SYNERGY EFFECT OF COMPONENTS:



Ezetimibe - higher reduction of LDL level than statin's monotherapy.

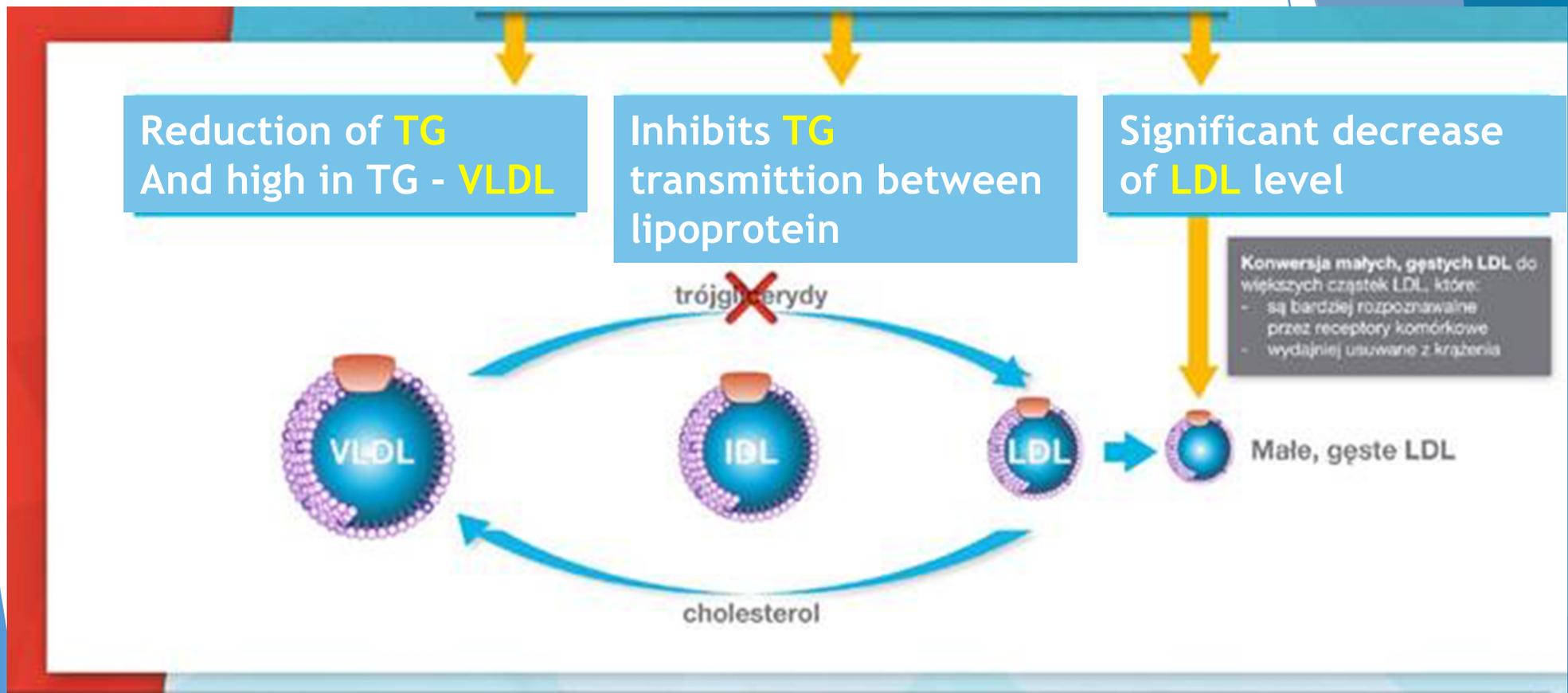
- Action in digestive system → by blocking cholesterol absorption in intestine
- Usage in monotherapy in pts with statins intolerance and combination therapy with a statin



Ezetimibe

- As monotherapy
- As support for statin treatment

FIBRATE Treatment for Atherogenic Dyslipidemia



Additional **35%** Reduction of Heart Attack and Stroke Risk Factors

FIBRATE treatment for Atherogenic Dyslipidemia

Improve the Quality of LDL-C



Cardiovascular



Statyna⁽³⁾

LDL-c ↓ 100 mg/dl

od 22 do 35%

FIBRATE

↓ 35%⁽⁴⁾

TG > 200 mg/dl
HDL ≤ 34 mg/dl



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Thank you for your attention