Δυσλιπιδαιμίες: διάγνωση και αντιμετώπιση

Λιάμης Γεώργιος

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Ιατρικής Σχολής Παν/μίου Ιωαννίνων

ΠΡΟΣΟΧΗ ΣΤΙΣ ΣΥΝΘΗΚΕΣ ΠΡΟΣΔΙΟΡΙΣΜΟΥ ΤΩΝ ΛΙΠΙΔΑΙΜΙΚΩΝ ΠΑΡΑΜΕΤΡΩΝ

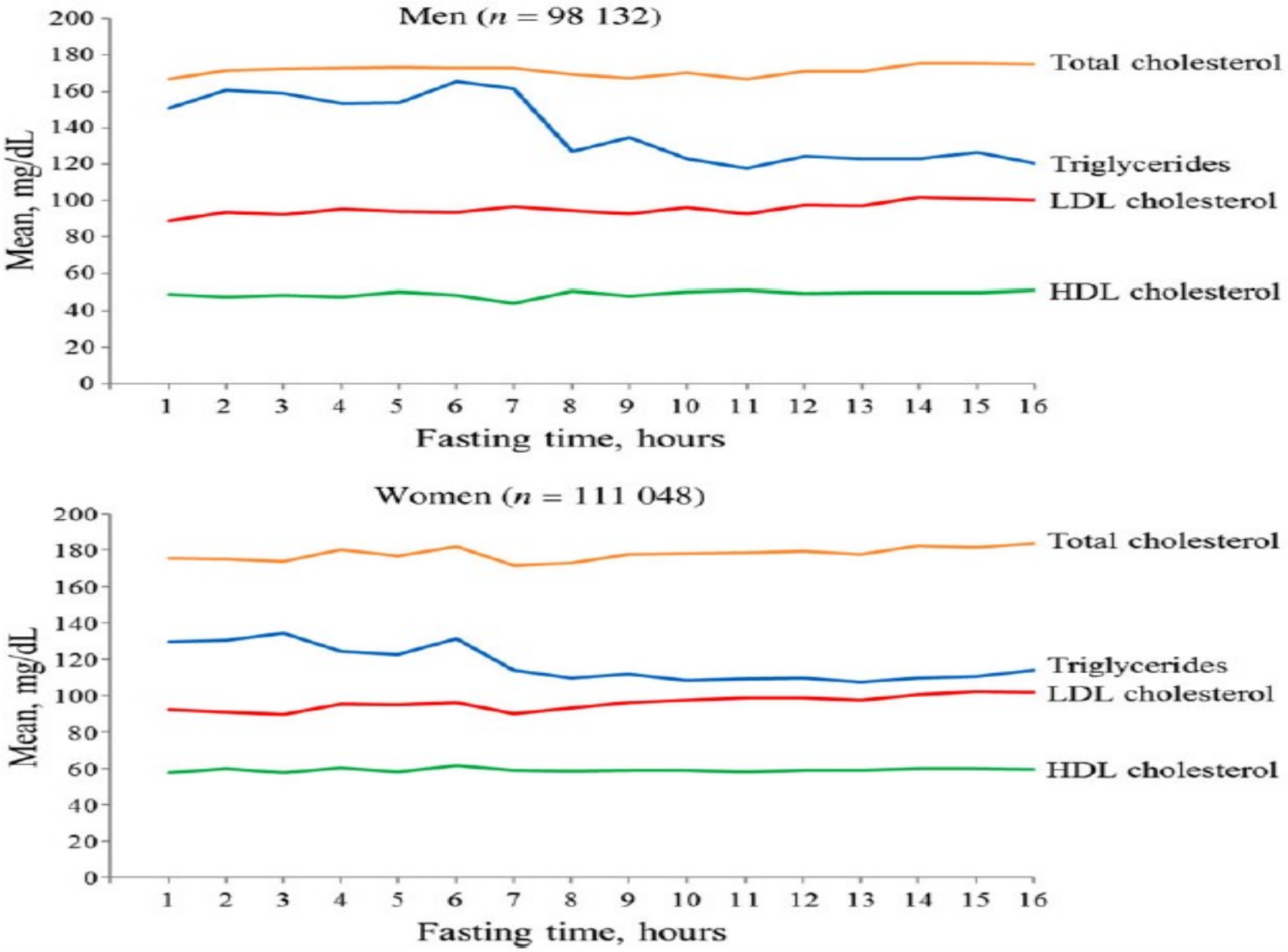
✓**2 μετρήσεις με απόσταση 1-12 εβδομάδες (εκτός από οξέα καρδιαγγειακά συμβάματα)**

✓Αναβολή του προσδιορισμού των λιπιδίων σε καταστάσεις stress (τραύματα, λοιμώξεις, χειρουργικές επεμβάσεις)

↓ T CHOL, ↓ LDL CHOL,

↓↓ HDL CHOL, ↑ TRG

✓**Νηστεία 12h ??**



ARCH INTERN MED 2012;172:1707

ΜΕΤΑΒΟΛΕΣ ΛΙΠΙΔΑΙΜΙΚΩΝ ΠΑΡΑΜΕΤΡΩΝ:

FASTING vs NON FASTING

ΔTRG	+26mg/dl
ΔTCHOL	-8mg/dl
Δ LDL CHOL	-8mg/dl
Δ REMNANT CHOLESTEROL	+8mg/dl
Δ non HDL CHOL	-8mg/dl

Table 4 When to use non-fasting and fasting blood sampling to assess the plasma lipid profile

Patients for lipid profile testing	
Non-fasting	In most patients, including: • Initial lipid profile testing in any patient • For cardiovascular risk assessment • Patients admitted with acute coronary syndrome[a] • In children • If preferred by the patient • In diabetic patients[b] (due to hypoglycaemic risk) • In the elderly • Patients on stable drug therapy
Fasting	Can sometimes be required if: • Non-fasting triglycerides >5 mmol/L (440 mg/dL) • Known hypertriglyceridaemia followed in lipid clinic • Recovering from hypertriglyceridaemic pancreatitis • Starting medications that cause severe hypertriglyceridaemia • Additional laboratory tests are requested that require fasting[c] or morning samples (e.g. fasting glucose[c], therapeutic drug monitoring)

Table I Key recommendations

- Fasting is not required routinely for assessing the plasma lipid profile
- When non-fasting plasma triglyceride concentration >5 mmol/L (440 mg/dL), consideration should be given to repeating the lipid profile in the fasting state
- Laboratory reports should flag abnormal values based on desirable concentration cut-points
- Life-threatening or extremely high concentrations should trigger an immediate referral to a lipid clinic or to a physician with special interest in lipids

Table 7 Definition of hypertriglyceridaemia by European Atherosclerosis Society consensus statement[24]

Severe hypertriglyceridaemia	>10 mmol/L	>880 mg/dL
Mild-to-moderate hypertriglyceridaemia	2–10 mmol/L	180–880 mg/dL

Separate referral to lipid specialist at

	Life-threatening concentrations	
Triglycerides	>10 mmol/L >880 mg/dL[a]	Pancreatitis risk?
LDL cholesterol	>13 mmol/L >500 mg/dL[a]	HoFH?
LDL cholesterol	>5 mmol/L >190 mg/dL[a]	HeFH?
LDL cholesterol in children	>4 mmol/L >155 mg/dL[a]	HeFH?

Nordestgaard et al. EAS EFLM joint Consensus Panel. Eur Heart J 2016; online April 26

LIFE – THREATENING EXTREMELY ABNORMAL LIPID CONCENTRATIONS – WHAT TO DO?:

ΠΑΡΑΠΟΜΠΗ ΣΕ ΕΝΑ ΕΞΕΙΔΙΚΕΥΜΕΝΟ ΚΕΝΤΡΟ

TRG	**>880mg/dl**	**ΧΥΛΟΜΙΚΡΟΝΑΙΜΙΑ – ΚΙΝΔΥΝΟΣ ΟΞΕΙΑΣ ΠΑΓΚΡΕΑΤΙΤΙΔΑΣ**
LDL CHOL	**>190mg/dl** **>155mg/dl** **(ΣΕ ΠΑΙΔΙΑ)**	**ΜΕΓΑΛΗ ΠΙΘΑΝΟΤΗΤΑ ΕΤΕΡΟΖΥΓΗΣ ΟΙΚΟΓΕΝΟΥΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑΣ**
LDL CHOL	**>500mg/dl**	**ΟΜΟΖΥΓΗ ΟΙΚΟΓΕΝΗΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ**
Lp(a)	**>150mg/dl**	**ΠΟΛΥ ΥΨΗΛΟΣ ΚΑΡΔΙΑΓΓΕΙΑΚΟΣ ΚΙΝΔΥΝΟΣ (ΟΕΜ/ΣΤΕΝΩΣΗ ΑΟΡΤΙΚΗΣ ΒΑΛΒΙΔΑΣ)**

Δυσλιπιδαιμίες

- Πρωτοπαθής
- Δευτεροπαθής

ΛΑΘΟΣ

Διάγνωση και θεραπεία δυσλιπιδαιμίας πριν τον αποκλεισμό των δευτεροπαθών δυσλιπιδαιμιών

Οι δευτεροπαθείς δυσλιπιδαιμίες

- Μπορεί να οδηγήσουν στη διάγνωση της υποκείμενης πρωτοπαθούς διαταραχής
- Στις περισσότερες περιπτώσεις η αντιμετώπιση της υποκείμενης διαταραχής οδηγεί στη διόρθωση των διαταραχών του μεταβολισμού των λιπιδίων
- Αποφυγή παρενεργειών από τη χορήγηση υπολιπιδαιμικών φαρμάκων
- Αποτελούν αναγνωρίσιμους παράγοντες επιδείνωσης ή ανθεκτικότητας στη θεραπεία μίας ήδη γνωστής δυσλιπιδαιμίας

ΚΑΤΗΓΟΡΙΕΣ ΔΥΣΛΙΠΙΔΑΙΜΙΩΝ

1.2 Δευτεροπαθείς δυσλιπιδαιμίες

Σε ασθενείς με παθολογικές τιμές των λιπιδαιμικών παραμέτρων πρέπει να αποκλεισθούν οι δευτεροπαθείς δυσλιπιδαιμίες, δηλαδή οι διαταραχές του μεταβολισμού των λιπιδίων που οφείλονται σε άλλα νοσήματα ή φάρμακα:

1. Σακχαρώδης διαβήτης
2. Υποθυρεοειδισμός
3. Χολόσταση
4. Χρόνια νεφρική νόσος-Νεφρωσικό σύνδρομο
5. Παχυσαρκία
6. Κατάχρηση οινοπνεύματος
7. Φάρμακα που προκαλούν δυσλιπιδαιμία
   - **α. προγεστερινοειδή**
   - **β. αναβολικά στεροειδή**
   - **γ. κορτικοστεροειδή**
   - **δ. θειαζιδικά διουρητικά σε υψηλές δόσεις**
   - **ε. κλασικοί β-αποκλειστές**
   - **στ. αντιρετροϊκά φάρμακα**
   - **ζ. ιντερφερόνη-α**
   - **η. ρετινοειδή**
   - **θ. οιστρογόνα-ταμοξιφαίνη**
   - **ι. κυκλοσπορίνη-everolimus-tacrolimus**

Hellenic Journal of Atherosclerosis 2014;5(3): 151-163

ΑΙΤΙΑ ΔΕΥΤΕΡΟΠΑΘΟΥΣ ΔΥΣΛΙΠΙΔΑΙΜΙΑΣ

Σακχαρώδης διαβήτης: ↑↑ TRG, ↓ HDL-C

Χρόνια νεφρική ανεπάρκεια: ↑↑ TRG, ↓ HDL-C

Νεφρωσικό σύνδρομο: ↑↑TCHOL, ↑↑LDL-C, ↑TRG

Υποθυρεοειδισμός: ↑↑ TCHOL, ↑↑ LDL-C, ↑ TRG

Πρωτοπαθής χολική κίρρωση: ↑↑ TCHOL

Φάρμακα

ΦΑΡΜΑΚΑ ΠΟΥ ΑΥΞΑΝΟΥΝ ΤΑ ΕΠΙΠΕΔΑ ΤΗΣ LDL-CHOL

- ✓ Διουρητικά
- ✓ Κυκλοσπορίνη
- ✓ Αμιοδαρόνη
- ✓ Αντιρετροϊκά φάρμακα

ΦΑΡΜΑΚΑ ΠΟΥ ΑΥΞΑΝΟΥΝ ΤΑ ΤΡΙΓΛΥΚΕΡΙΔΙΑ

- Ιντερφερόνη
- Ρητινοειδή
- Οιστρογόνα
- Ταμοξιφαίνη
- β-αποκλειστές

Συνιστώμενες εργαστηριακές εξετάσεις για τη διάγνωση των ασθενών με δυσλιπιδαιμία

Διάγνωση: Ολική χοληστερόλη, τριγλυκερίδια, HDL χοληστερόλη, υπολογισμός LDL χοληστερόλης, γλυκόζη, κρεατινίνη, υπολογισμός σπειραματικής διήθησης, αλκαλική φωσφατάση, AST, ALT, CK, TSH, Γενική ούρων

Hellenic Journal of Atherosclerosis 2014;5(3): 151-163

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,[a] or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.

High-risk	People with: Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage,[a] with DM duration ≥10 years or another additional risk factor. Moderate CKD (eGFR 30–59 mL/min/1.73 m^2). A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.

Cardiovascular risk categories in patients with diabetes

Very high risk	Patients with DM **and** established CVD **or** other target organ damage[b] **or** three or more major risk factors[c] **or** early onset T1DM of long duration (>20 years)
High risk	Patients with DM duration ≥10 years without target organ damage plus any other additional risk factor
Moderate risk	Young patients (T1DM aged <35 years or T2DM aged <50 years) with DM duration <10 years, without other risk factors

[b]Proteinuria, renal impairment defined as eGFR <30 mL/min/1.73 m^2, left ventricular hypertrophy, or retinopathy.

[c]Age, hypertension, dyslipidemia, smoking, obesity.

ESC European Society of Cardiology

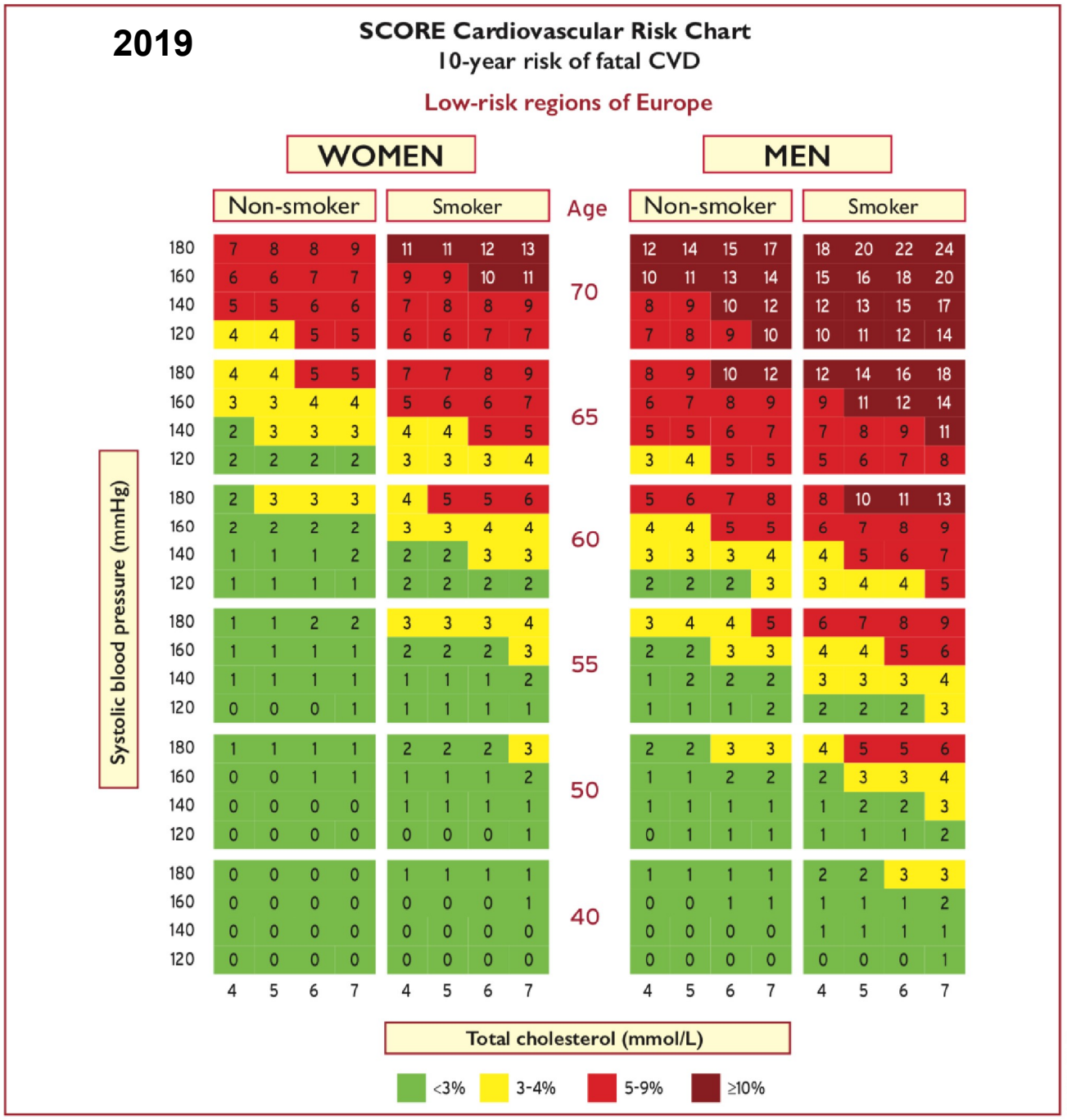
European Heart Journal (2019) **00**, 1–78
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

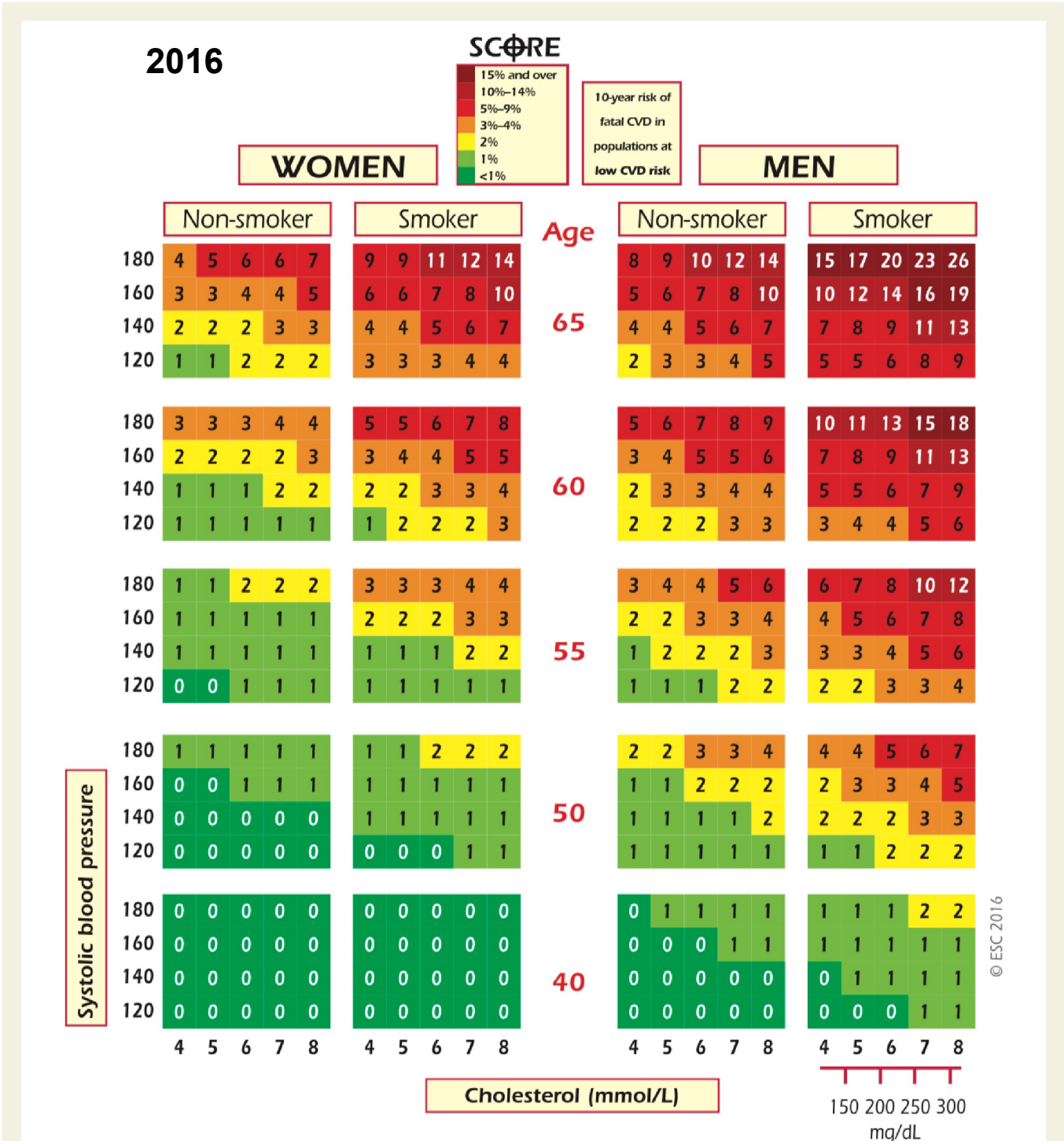
- ☑ The SCORE (Systematic Coronary Risk Estimation)



Total cholesterol (mmol/L)	Total cholesterol (mg/dL)
4	154
5	193
6	230
7	270

How to use the risk estimation charts

Risk is initially assessed on the level of TC and systolic BP before treatment, if known. The longer the treatment and the more effective it is, the greater the reduction in risk, but in general it will not be more than about one-third of the baseline risk. For example, for a person on antihypertensive drug treatment in whom the pre-treatment BP is not known, if the total CV SCORE risk is 6%, then the pre-treatment total CV risk may have been 9%.


2016
SCORE
15% and over
10%–14%
5%–9%
3%–4%
2%
1%
<1%
10-year risk of fatal CVD in populations at low CVD risk
WOMEN
MEN
Non-smoker
Smoker
Non-smoker
Smoker
Age
65
60
55
50
40
Systolic blood pressure
180 160 140 120
4 5 6 7 8
Cholesterol (mmol/L)
150 200 250 300
mg/dL
© ESC 2016

ΔΕΝ ΚΑΝΩ SCORE

- Ηλικία < 40 & > 70 έτη
- Εγκατεστημένη ΚΑΝ
- ΣΔ τύπου Ι: διάρκειας > 20 έτη
- ΣΔ τύπου ΙΙ: βλάβη οργάνων στόχου (ΒΟΣ)
- ΣΔ τύπου ΙΙ: χωρίς ΒΟΣ διάρκειας > 10 έτη ή με επιπρόσθετο παράγοντα κινδύνου
- Ολική χοληστερόλη ≥ 310 mg/dL
- LDL χοληστερόλη ≥ 190 mg/dL
- Αρτηριακή πίεση ≥ 180/110 mmHg
- eGFR < 60 mL/min/1,73 m^2

Η ΚΡΕΑΤΙΝΙΝΗ ΤΟΥ ΟΡΟΥ ΑΠΟ ΜΟΝΗ ΤΗΣ ΔΕΝ ΕΙΝΑΙ ΑΞΙΟΠΙΣΤΗ ΓΙΑ ΤΗΝ ΕΚΤΙΜΗΣΗ ΤΗΣ ΝΕΦΡΙΚΗΣ ΛΕΙΤΟΥΡΓΙΑΣ

CKD-EPI

MDRD-eGFR

Γυναίκα 60 ετών με Creat 1.1 mg/dL

→ e-GFR=55 mL/min/1.73 m^2

eGFR: CKD-EPI & MDRD

Γυναίκα 60 ετών με Creat 1.1 mg/dL
→ e-GFR=55 mL/min/1.73 m^2

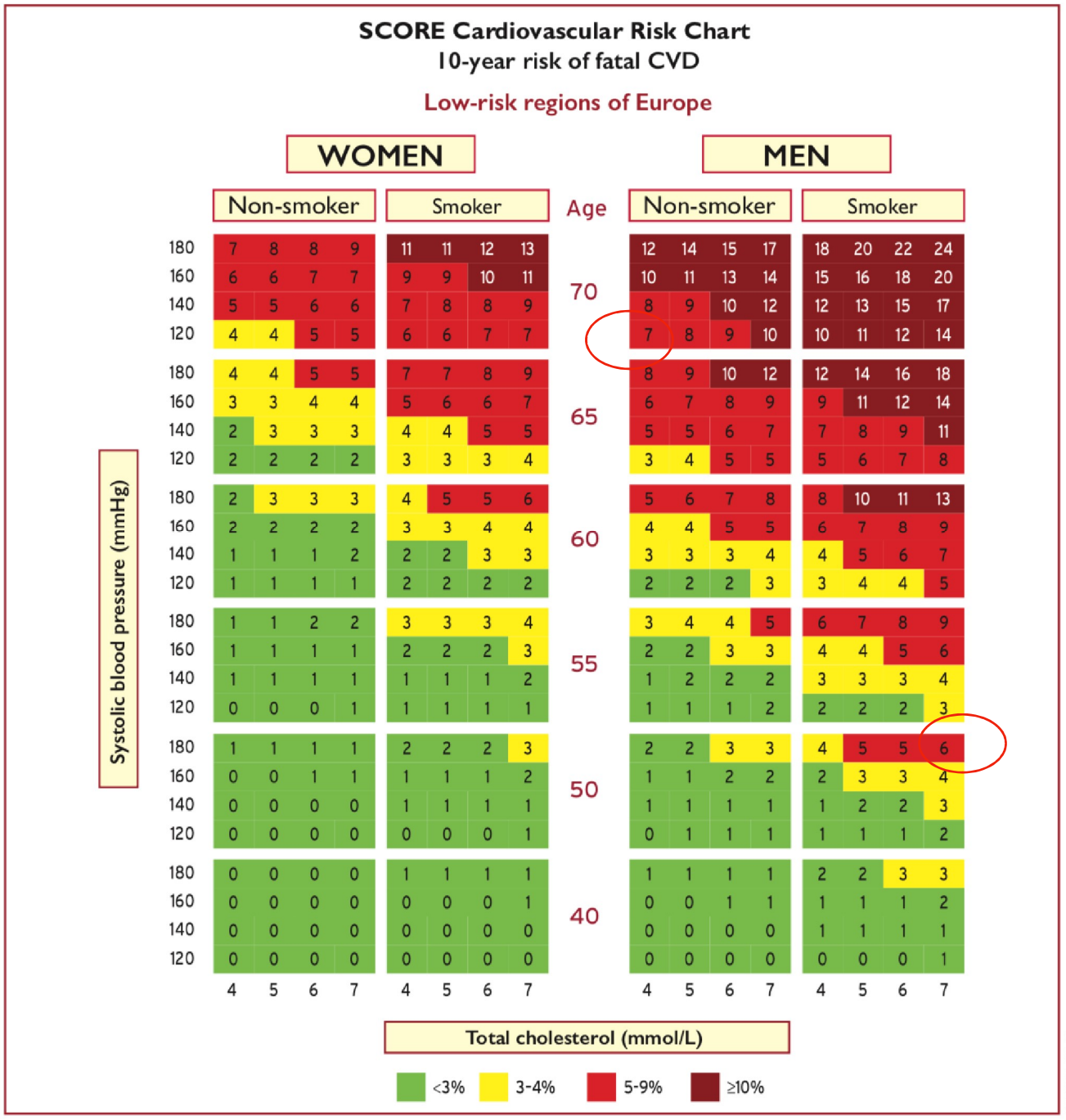
Recommendations for cardiovascular disease risk estimation

Recommendations	Class[a]	Level[b]
Total risk estimation using a risk estimation system such as SCORE is recommended for asymptomatic adults >40 years of age without evidence of CVD, DM, CKD, familial hypercholesterolaemia, or LDL-C >4.9 mmol/L (>190 mg/dL).	I	C
It is recommended that high- and very-high-risk individuals are identified on the basis of documented CVD, DM, moderate-to-severe renal disease, very high levels of individual risk factors, FH, or a high SCORE risk. It is recommended that such patients are considered as a priority for advice and management of all risk factors.	I	C
Risk scores developed for the general population are not recommended for CV risk assessment in patients with DM or FH.	III	C

Ο ρόλος της ηλικίας

- Άνδρας 70 ετών
- Μη καπνιστής
- ΣΑΠ = 120 mmHg
- TCHO = 150 mg/dL
- Χωρίς υπολιπιδαιμική & αντιυπερτασική αγωγή

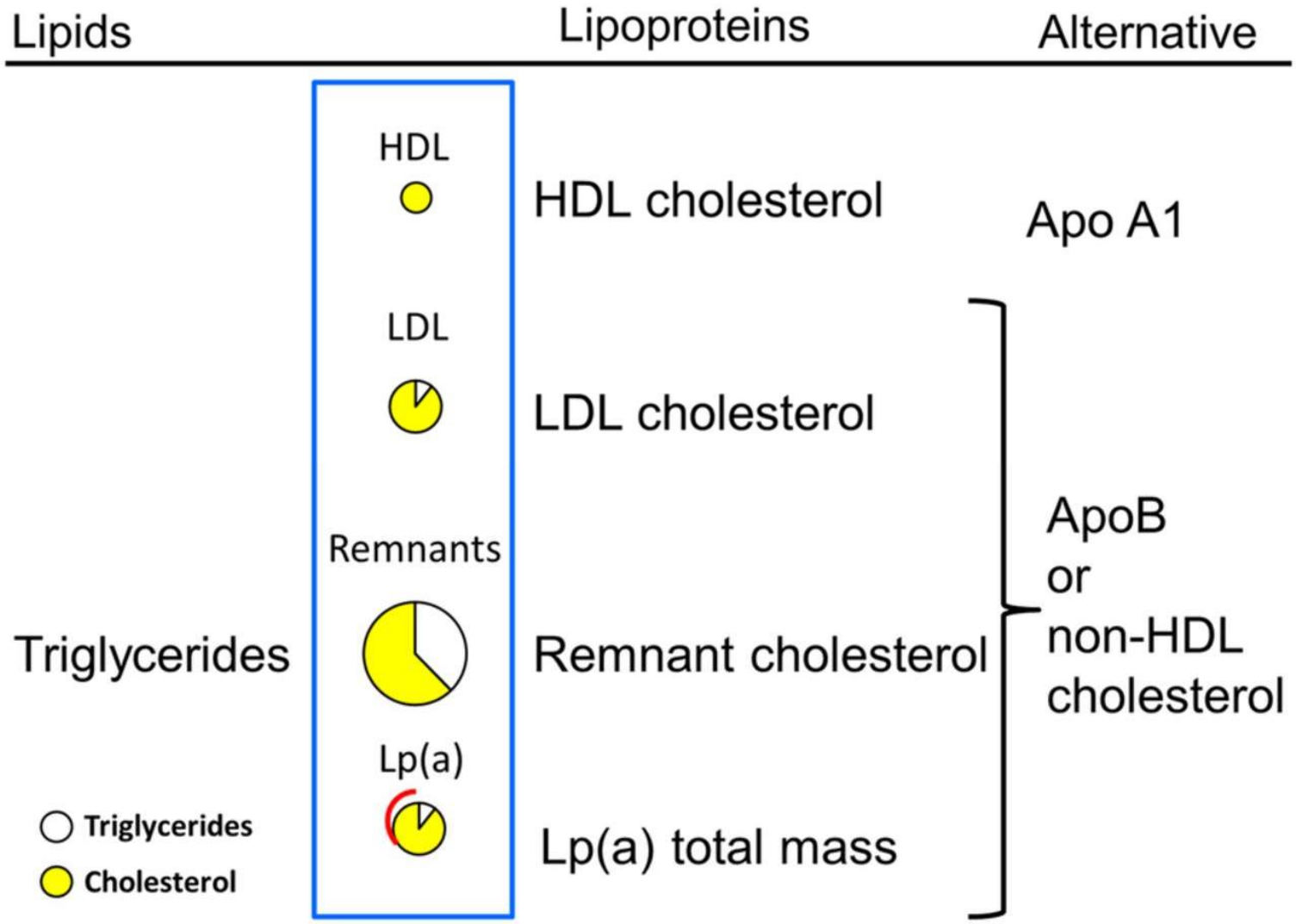
- Άνδρας 50 ετών
- Καπνιστής
- ΣΑΠ = 180 mmHg
- TCHO = 250 mg/dL



Total cholesterol (mmol/L)	Total cholesterol (mg/dL)
4	154
5	193
6	230
7	270

Μόνο ολική χοληστερόλη ?

Lipids, lipoproteins, and apolipoproteins as part of standard and expanded lipid profiles.



Børge G. Nordestgaard et al. Eur Heart J 2016;eurheartj.ehw152

European Heart Journal

Recommendations for lipid analyses for cardiovascular disease risk estimation

Recommendations	Class[a]	Level[b]
TC is to be used for the estimation of total CV risk by means of the SCORE system.	I	C
HDL-C analysis is recommended to further refine risk estimation using the online SCORE system.	I	C
LDL-C analysis is recommended as the primary lipid analysis method for screening, diagnosis, and management.	I	C
TG analysis is recommended as part of the routine lipid analysis process.	I	C
Non-HDL-C evaluation is recommended for risk assessment, particularly in people with high TG levels, DM, obesity, or very low LDL-C levels.	I	C
ApoB analysis is recommended for risk assessment, particularly in people with high TG levels, DM, obesity, metabolic syndrome, or very low LDL-C levels. It can be used as an alternative to LDL-C, if available, as the primary measurement for screening, diagnosis, and management, and may be preferred over non-HDL-C in people with high TG levels, DM, obesity, or very low LDL-C levels.	I	C
Lp(a) measurement should be considered at least once in each adult person's lifetime to identify those with very high inherited Lp(a) levels >180 mg/dL (>430 nmol/L) who may have a lifetime risk of ASCVD equivalent to the risk associated with heterozygous familial hypercholesterolaemia.	IIa	C
Lp(a) should be considered in selected patients with a family history of premature CVD, and for reclassification in people who are borderline between moderate and high-risk.	IIa	C

Apo = apolipoprotein; ASCVD = atherosclerotic cardiovascular disease; CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; Lp(a) = lipoprotein(a); SCORE = Systematic Coronary Risk Estimation; TC = total cholesterol; TG = triglyceride.

ΠΡΟΣΔΙΟΡΙΣΜΟΣ ΛΙΠΙΔΑΙΜΙΚΩΝ ΠΑΡΑΜΕΤΡΩΝ

T CHOL, HDL CHOL, TRG

LDL CHOL=T CHOL - HDL CHOL - TRG/5
(όταν TRG<400mg/dl)

ΑΝΕΞΑΡΤΗΤΑ ΑΠΟ ΤΑ ΕΠΙΠΕΔΑ ΤΩΝ ΛΙΠΙΔΙΩΝ

ΒΑΣΙΚΟΣ ΣΤΟΧΟΣ ΤΗΣ ΑΓΩΓΗΣ:

Η ΜΕΙΩΣΗ ΤΗΣ LDL CHOL

ΣΕ ΑΤΟΜΑ ΜΕ TRG >200 mg/dL

ΚΥΡΙΟΣ ΣΤΟΧΟΣ: Η μείωση της LDL CHOL

ΔΕΥΤΕΡΕΥΩΝ ΣΤΟΧΟΣ :

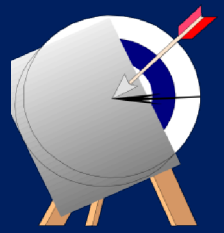
Η μείωση της non HDL CHOL

TC = HDL-C + LDL-C + VLDL-C

non HDL-C = TC – HDL-C

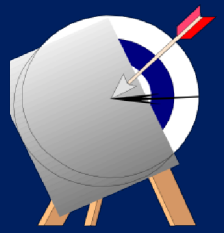
TC = HDL-C + LDL-C + VLDL-C

non HDL-C = TC – HDL-C = LDL-C + VLDL-C



non HDL-C

=

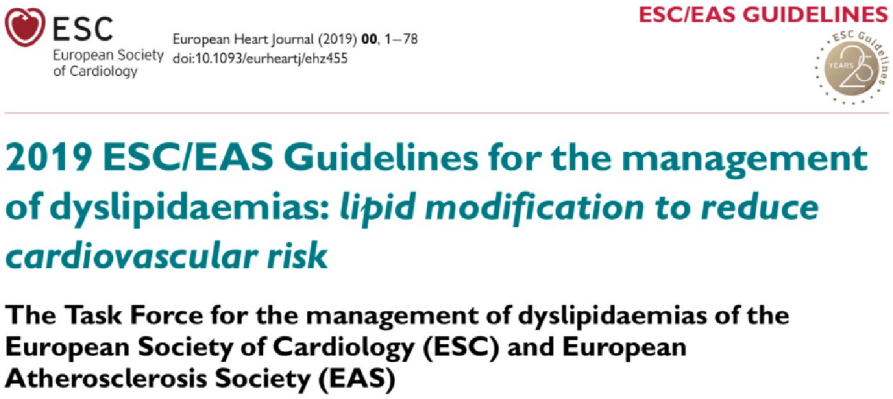


LDL-C

+ 30mg/dl

HDL-C

- HDL-C can be used to increase the accuracy of the risk evaluation.
- The electronic version of SCORE includes HDL-C
- Extremely high values > 90 mg/dL of HDL-C cannot be used as a risk predictor (increased risk of ASCVD)



Ο ρόλος της HDL-C

- Άνδρας 50 ετών
- Καπνιστής
- ΣΑΠ = 180 mmHg
- TCHO = 250 mg/dL
- HDL-C= 30 mg/dL
- SCORE= 7%

- Άνδρας 50 ετών
- Καπνιστής
- ΣΑΠ = 180 mmHg
- TCHO = 250 mg/dL
- HDL-C= 60 mg/dL
- SCORE= 4%

Factors modifying Systematic Coronary Risk Estimation risks

Social deprivation: the origin of many of the causes of CVD.
Obesity and central obesity as measured by the body mass index and waist circumference, respectively.
Physical inactivity.
Psychosocial stress including vital exhaustion.
Family history of premature CVD (men: <55 years and women: <60 years).
Chronic immune-mediated inflammatory disorder.
Major psychiatric disorders.
Treatment for human immunodeficiency virus infection.
Atrial fibrillation.
Left ventricular hypertrophy.
Chronic kidney disease.
Obstructive sleep apnoea syndrome.
Non-alcoholic fatty liver disease.

Risk will also be higher than indicated in the charts in:

- Those with a family history of premature CVD, which is considered to increase the risk by 1.7-fold in women and by 2.0-fold in men.

- The presence of additional risk factors increases the risk (such as low HDL-C, high TG).

European Heart Journal (2011) **32**, 1769–1818

ΚΑΝ & φλεγμονή

- Atherosclerosis is undoubtedly a multifactorial disease in which chronic inflammation plays a key role
- CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study): 10,061 patients with previous myocardial infarction and a high-sensitivity C-reactive protein level (> 2 mg/L)

- Antiinflammatory therapy targeting the interleukin-1β innate immunity pathway with canakinumab at a dose of 150 mg every 3 months led to a significantly lower rate of recurrent cardiovascular events than placebo, independent of lipid-level lowering.
- Canakinumab was associated with a higher incidence of fatal infection than was placebo.

- Recent guidelines from the European League Against Rheumatism (EULAR) recommend aggressive management of traditional risk factors in addition to RA disease activity control to decrease the CVD risk.
- Several CVD risk calculators are available for clinical use to stratify a patients' risk of developing a CVD event.
- Most of these calculators do not account for RA as a risk factor
- **A multiplication factor of 1.5 is recommended to predict the risk more accurately.**

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

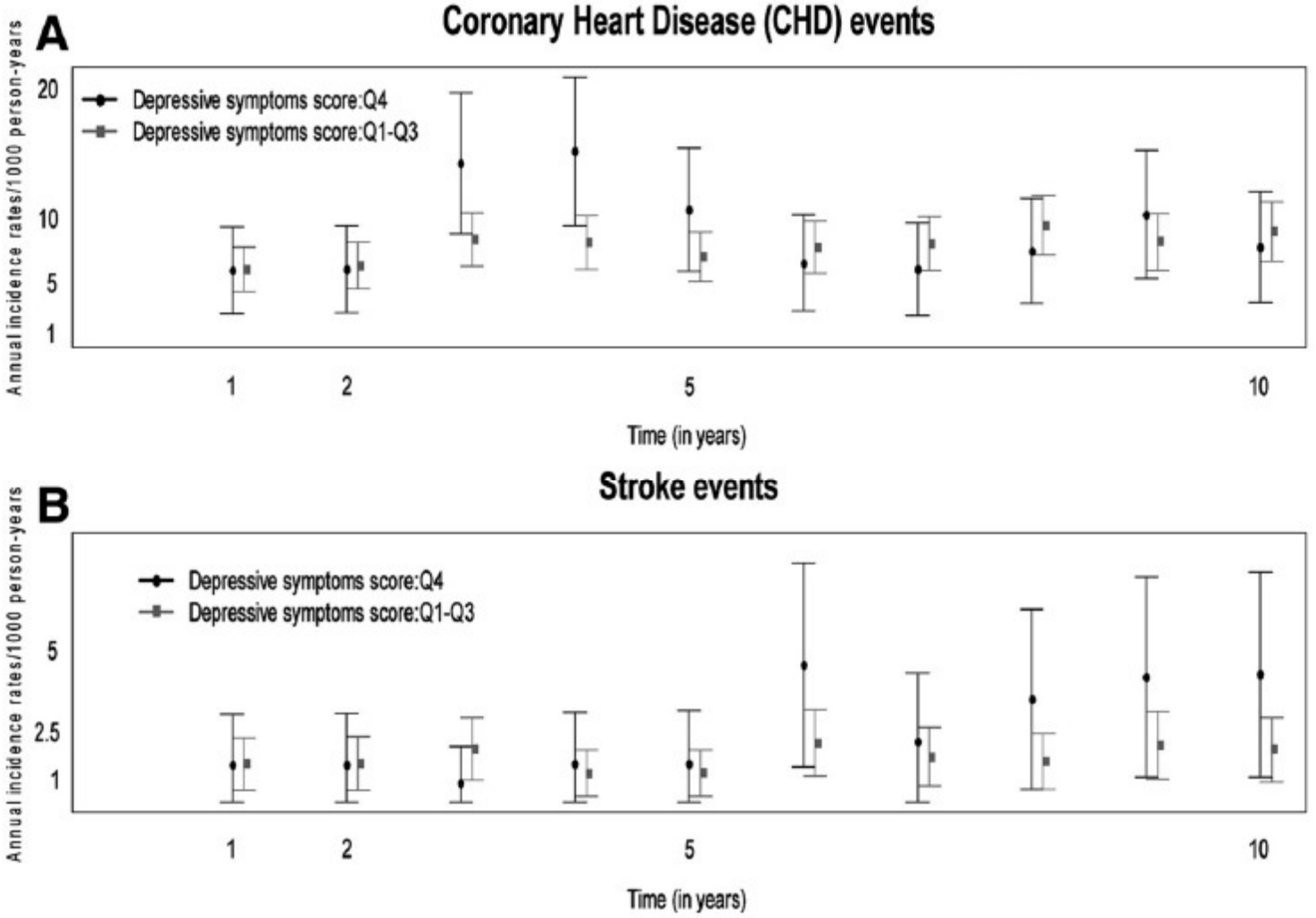
Caren G. Solomon, M.D., M.P.H., *Editor*

Depression in the Primary Care Setting

Lawrence T. Park, M.D., and Carlos A. Zarate, Jr., M.D.

In the United States, the estimated lifetime risk of a major depressive episode now approaches 30%.

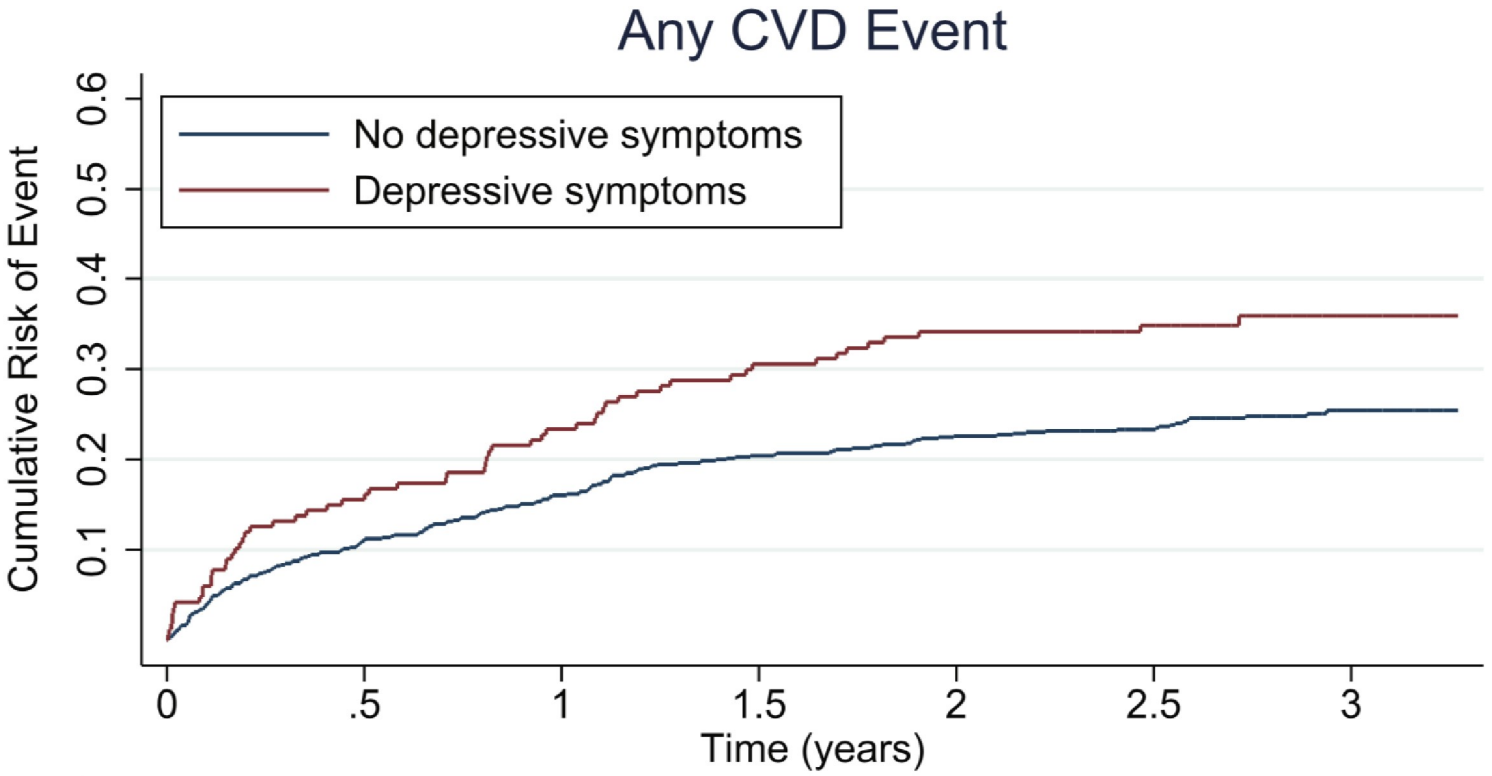
PRIME STUDY



Conclusions—The current study suggests that in healthy, European, middle-aged men, baseline depressive symptoms are associated with an increased risk of coronary heart disease in the short-term, and for stroke in the long-term.

Stroke. **2012;43:1761-1767**

Cumulative Incidence of Cardiovascular Event, or All-cause Mortality



Circulation

AHA/ACC SPECIAL REPORT

Use of Risk Assessment Tools to Guide Decision-Making in the Primary Prevention of Atherosclerotic Cardiovascular Disease

A Special Report From the American Heart Association and American College of Cardiology

Risk-Enhancing Factors
Family history of premature ASCVD (males, age <55 y; females, age <65 y)
Primary hypercholesterolemia (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L); non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*
Metabolic syndrome (increased waist circumference, elevated triglycerides [>150 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis)
Chronic kidney disease (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
Chronic inflammatory conditions such as psoriasis, RA, or HIV/AIDS
History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia
High-risk race/ethnicities (eg, South Asian ancestry)
Lipid/biomarkers: Associated with increased ASCVD risk
Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dL);
If measured:
Elevated high-sensitivity C-reactive protein (≥2.0 mg/L)
Elevated Lp(a): A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor especially at higher levels of Lp(a).
Elevated apoB ≥130 mg/dL: A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C ≥160 mg/dL and constitutes a risk-enhancing factor.
ABI <0.9

Risk-Enhancing Factors for Primary Prevention*

Family history of premature ASCVD

- Males, age < 55 years
- Females, age < 65 years

Primary hypercholesteremia†

- LDL-C 160-189 mg/dL (4.1-4.8 mmol/L)
- Non-HDL-C 190-219 mg/dL (4.9-5.6 mmol/L)

Metabolic syndrome (total: 3)

- Increased waist circumference
- Triglycerides > 150 mg/dL
- Low HDL-C (< 40 mg/dL [men], < 50 mg/dL [women])
- Elevated BP
- Elevated glucose

Conditions specific to women

- Premature menopause (before age 40 years)
- Preeclampsia

Chronic kidney disease

- eGFR 15-59 mL/min/1.73 m^2 with or without albuminuria
- Not treated with dialysis or transplant

Chronic inflammatory conditions

- Psoriasis, rheumatoid arthritis, HIV/AIDS

High-risk race/ethnicities

- South Asian

Lipid/Biomarkers

- hs-CRP ≥ 2.0 mg/L
- Lp(a) ≥ 50 mg/dL (≥ 125 nmol/L)
- apoB ≥ 130 mg/dL
- ABI < 0.9

Presence of risk-enhancing factors may affect the threshold for nonstatin intensification.

*No established ASCVD or diabetes. †Optimally, 3 determinations.

Grundy SM, et al. *J Am Coll Cardiol*. 2018. [Epub ahead of print]

Recommendations for cardiovascular imaging for risk assessment of atherosclerotic cardiovascular disease

Recommendations	Class[a]	Level[b]
Arterial (carotid and/or femoral) plaque burden on arterial ultrasonography should be considered as a risk modifier in individuals at low or moderate risk.[29,30]	IIa	B
CAC score assessment with CT should be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.[14–16,24,26]	IIa	B

CAC = coronary artery calcium; CT = computed tomography; CV = cardiovascular.

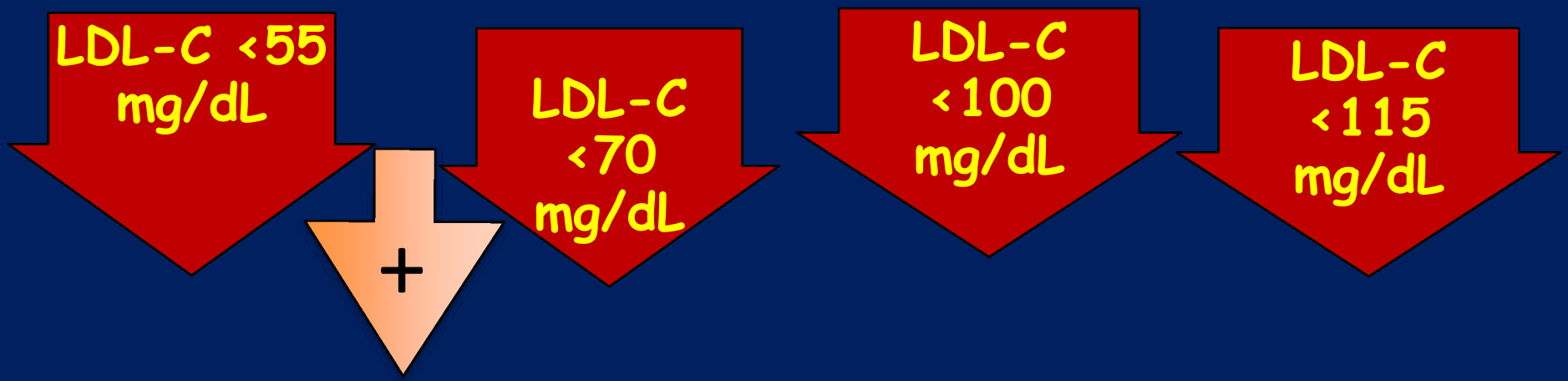
Εκτίμηση του καρδιαγγειακού κινδύνου

- The SCORE (Systematic Coronary Risk Estimation)
- Ηλικία: 40 - 70 έτη
- ΟΧΙ σε άτομα που είναι ήδη πολύ υψηλού ή υψηλού κινδύνου
- ΠΡΟΣΟΧΗ: eGFR < 60 mL/min/1,73 m^2
- SCORE: ΣΑΠ, κάπνισμα, T-CHO
- Άλλες λιπιδαιμικές παράμετροι
- Ιστορικό: κληρονομικότητα πρώιμης ΚΑΝ, αυτοανοσία, παχυσαρκία, καταθλιπτικά συμπτώματα ……

Treatment targets and goals for cardiovascular disease prevention

Smoking	No exposure to tobacco in any form.
Diet	Healthy diet low in saturated fat with a focus on wholegrain products, vegetables, fruit, and fish.
Physical activity	3.5–7 h moderately vigorous physical activity per week or 30–60 min most days.
Body weight	BMI 20–25 kg/m^2, and waist circumference <94 cm (men) and <80 cm (women).
Blood pressure	<140/90 mmHg.[a]

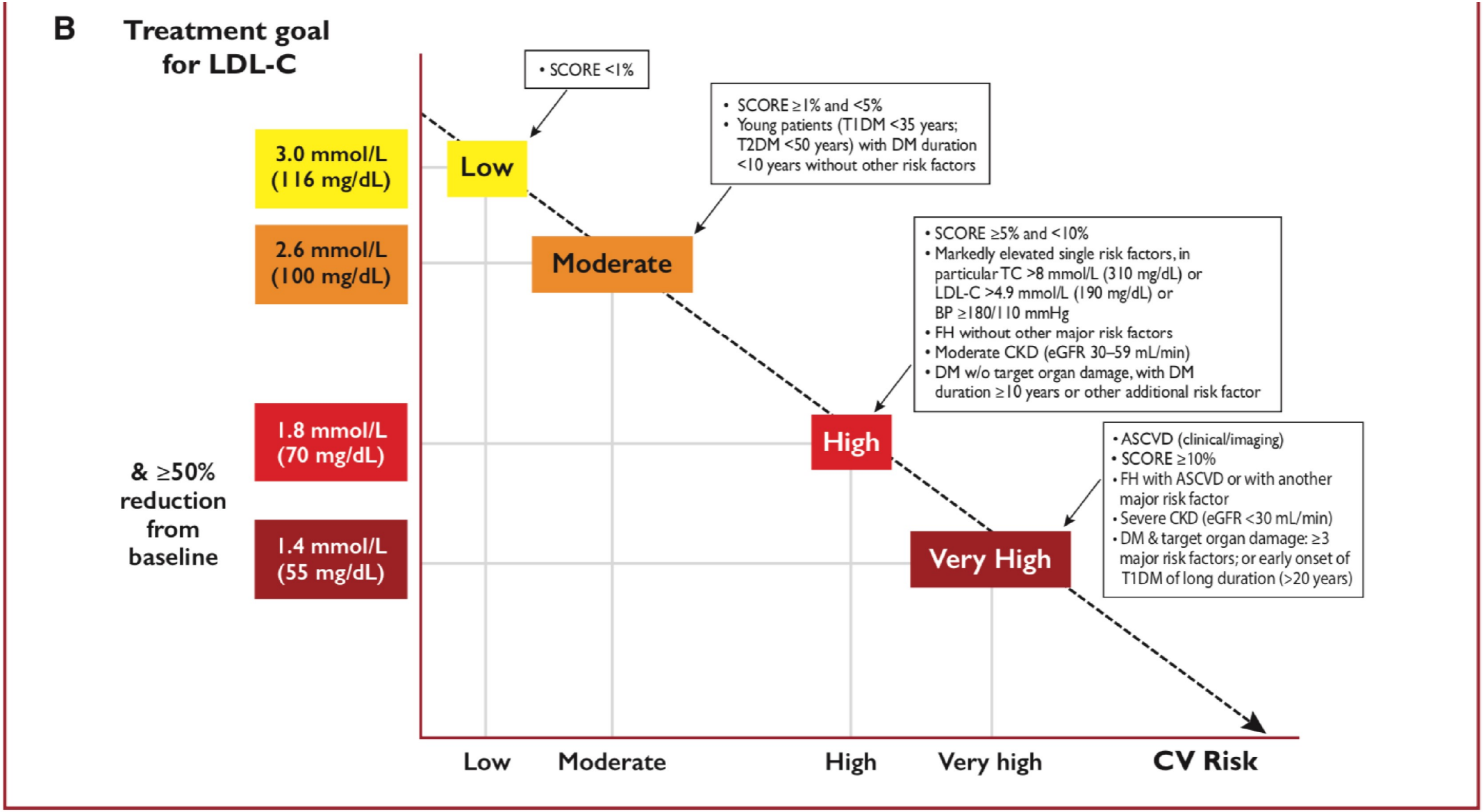
ΘΕΡΑΠΕΥΤΙΚΟΙ ΣΤΟΧΟΙ ΤΗΣ LDL-C



Μείωση τουλάχιστον 50%

Recommendations for treatment goals for low-density lipoprotein cholesterol

Recommendations	Class[a]	Level[b]
In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]	I	A
In primary prevention for individuals at very-high risk but without FH,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[34–36]	I	C
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A


B
Treatment goal for LDL-C
• SCORE <1%
• SCORE ≥1% and <5%
• Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors
• SCORE ≥5% and <10%
• Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg
• FH without other major risk factors
• Moderate CKD (eGFR 30–59 mL/min)
• DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor
• ASCVD (clinical/imaging)
• SCORE ≥10%
• FH with ASCVD or with another major risk factor
• Severe CKD (eGFR <30 mL/min)
• DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)
Low
Moderate
High
Very High
3.0 mmol/L (116 mg/dL)
2.6 mmol/L (100 mg/dL)
1.8 mmol/L (70 mg/dL)
1.4 mmol/L (55 mg/dL)
& ≥50% reduction from baseline
Low
Moderate
High
Very high
CV Risk

- For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.

Non-HDL-C	Non-HDL-C secondary goals are <2.2, 2.6, and 3.4 mmol/L (<85, 100, and 130 mg/dL) for very-high-, high-, and moderate-risk people, respectively.
ApoB	ApoB secondary goals are <65, 80, and 100 mg/dL for very-high-, high-, and moderate-risk people, respectively.
Triglycerides	No goal, but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
Diabetes	HbA1c: <7% (<53 mmol/mol).

Non HDL= LDL +30

Recommendations for pharmacological low-density lipoprotein cholesterol lowering

Recommendations	Class[a]	Level[b]
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.[32,34,38]	I	A
If the goals[c] are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.[33]	I	B
For primary prevention patients at very-high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.	IIb	C
For secondary prevention, patients at very-high risk not achieving their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.[119,120]	I	A
For very-high-risk FH patients (that is, with ASCVD or with another major risk factor) who do not achieve their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.	I	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), ezetimibe should be considered.[197,265,353]	IIa	C
If a statin-based regimen is not tolerated at any dosage (even after rechallenge), a PCSK9 inhibitor added to ezetimibe may also be considered.[197,265,353]	IIb	C
If the goal[c] is not achieved, statin combination with a bile acid sequestrant may be considered.	IIb	C

Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%

High intensity statin: Rosuvastatin 20 -40 mg - Atorvastatin 40-80 mg

Recommendations for drug treatment of patients with hypertriglyceridaemia

Recommendations	Class[a]	Level[b]
Statin treatment is recommended as the first drug of choice to reduce CVD risk in high-risk individuals with hypertriglyceridaemia [TG levels >2.3 mmol/L (>200 mg/dL)].[355]	I	B
In high-risk (or above) patients with TG levels between 1.5–5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2×2 g/day) should be considered in combination with a statin.[194]	IIa	B
In primary prevention patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356]	IIb	B
In high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356]	IIb	C

Summary of recommendations for monitoring lipids and enzymes in patients, before and on lipid-lowering therapy

Testing lipids
How often should lipids be tested?
• Before starting lipid-lowering drug treatment, at least two measurements should be made, with an interval of 1–12 weeks, with the exception of conditions where prompt drug treatment is suggested, such as ACS and very high-risk patients.
How often should a patient's lipids be tested after starting lipid-lowering treatment?
• After starting treatment: 8 (±4) weeks. • After adjustment of treatment: 8 (±4) weeks until the goal is achieved.
How often should lipids be tested once a patient has achieved the target or optimal lipid level?
• Annually (unless there are adherence problems or other specific reasons for more frequent reviews).

Monitoring liver and muscle enzymes

How often should liver enzymes (ALT) be routinely measured in patients on lipid-lowering drugs?

- Before treatment.
- Once, 8–12 weeks after starting a drug treatment or after dose increase.
- Routine control of ALT thereafter is not recommended during statin treatment, unless symptoms suggesting liver disease evolve. During treatment with fibrates, control of ALT is still recommended.

What if liver enzymes become elevated in a person taking lipid-lowering drugs?

If ALT <3× ULN:

- Continue therapy.
- Recheck liver enzymes in 4–6 weeks.

If ALT rises to ≥3× ULN

- Stop lipid-lowering therapy or reduce dose and recheck liver enzymes within 4–6 weeks.
- Cautious reintroduction of therapy may be considered after ALT has returned to normal.
- If ALT remains elevated check for the other reasons.

How often should CK be measured in patients taking lipid-lowering drugs?

Pre-treatment

- Before starting therapy.
- If baseline CK is >4× ULN, do not start drug therapy; recheck.

Monitoring:

- Routine monitoring of CK is not necessary.
- Check CK if patient develops myalgia.

What if CK becomes elevated in a person taking lipid-lowering drugs?

Re-evaluate indication for statin treatment.

If ≥4× ULN:

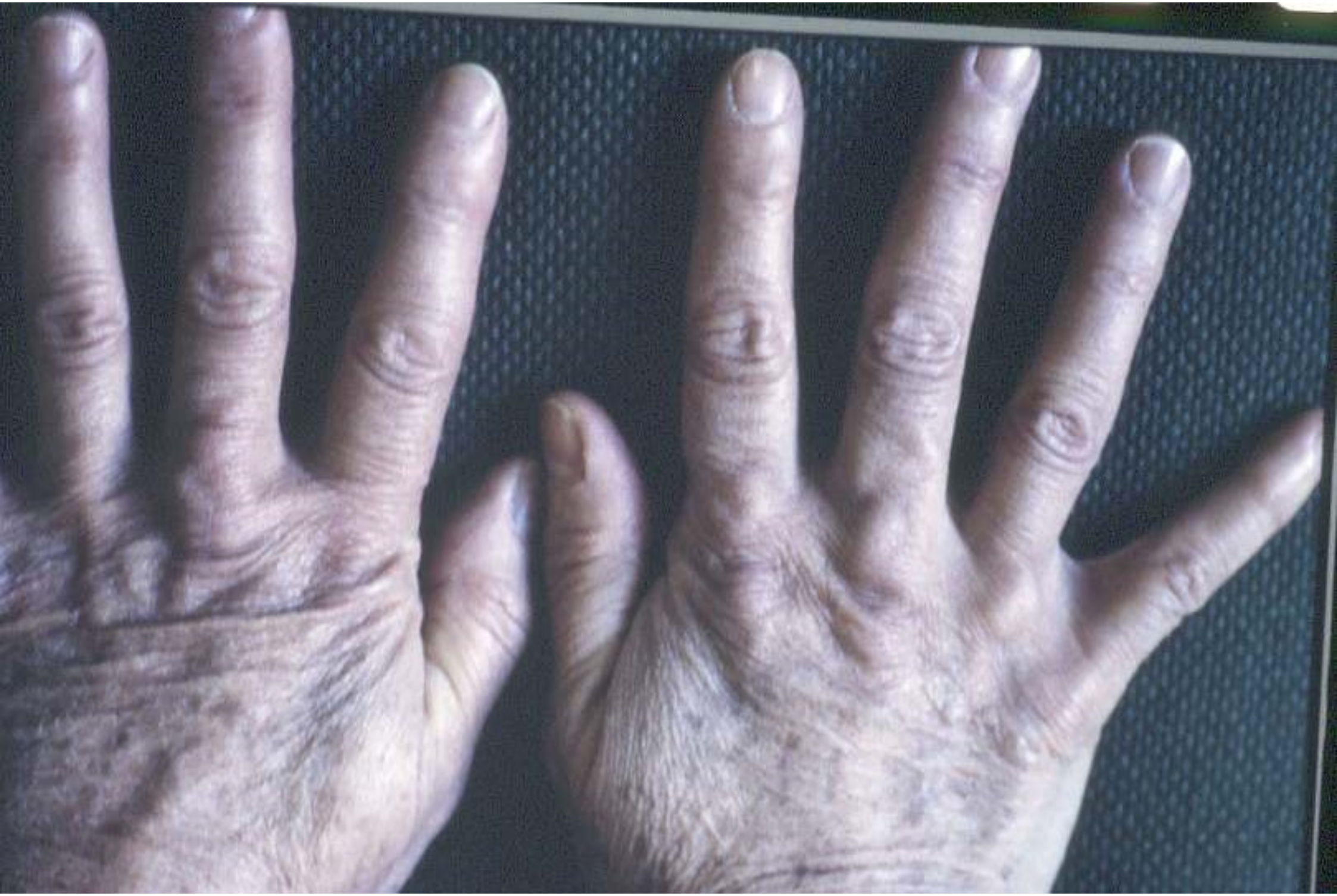
- If CK >10× ULN: stop treatment, check renal function, and monitor CK every 2 weeks.
- If CK <10× ULN: if no symptoms, continue lipid-lowering therapy while monitoring CK between 2 and 6 weeks.
- If CK <10× ULN: if symptoms present, stop statin and monitor normalization of CK, before rechallenge with a lower statin dose.
- Consider the possibility of transient CK elevation for other reasons such as exertion.
- Consider myopathy if CK remains elevated.
- Consider combination therapy or an alternative drug.

If <4× ULN:

- If no muscle symptoms, continue statin (patient should be alerted to report symptoms; check CK).
- If muscle symptoms, monitor symptoms and CK regularly.
- If symptoms persist, stop statin and re-evaluate symptoms after 6 weeks; re-evaluate indication for statin treatment.
- Consider rechallenge with the same or another statin.
- Consider low-dose statin, alternate day or once/twice weekly dosing regimen, or combination therapy.

In which patients should HbA1c or blood glucose be checked?

- Regular checks of HbA1c or glucose should be considered in patients at high-risk of developing diabetes, and on high-dose statin treatment.
- Groups to be considered for glucose control are the elderly and patients with metabolic syndrome, obesity, or other signs of insulin resistance.



ΑΙΤΙΑ ΔΕΥΤΕΡΟΠΑΘΟΥΣ ΔΥΣΛΙΠΙΔΑΙΜΙΑΣ

Σακχαρώδης διαβήτης:	γλυκόζη νηστείας
Υποθυρεοειδισμός:	TSH
Νεφρωσικό σύνδρομο:	γενική ούρων
Χρόνια νεφρική ανεπάρκεια:	κρεατινίνη ορού, eGFR
Πρωτοπαθής χολική κίρρωση:	αλκαλική φωσφατάση

Διαθέσιμα φάρμακα για την αντιμετώπιση της δυσλιπιδαιμίας

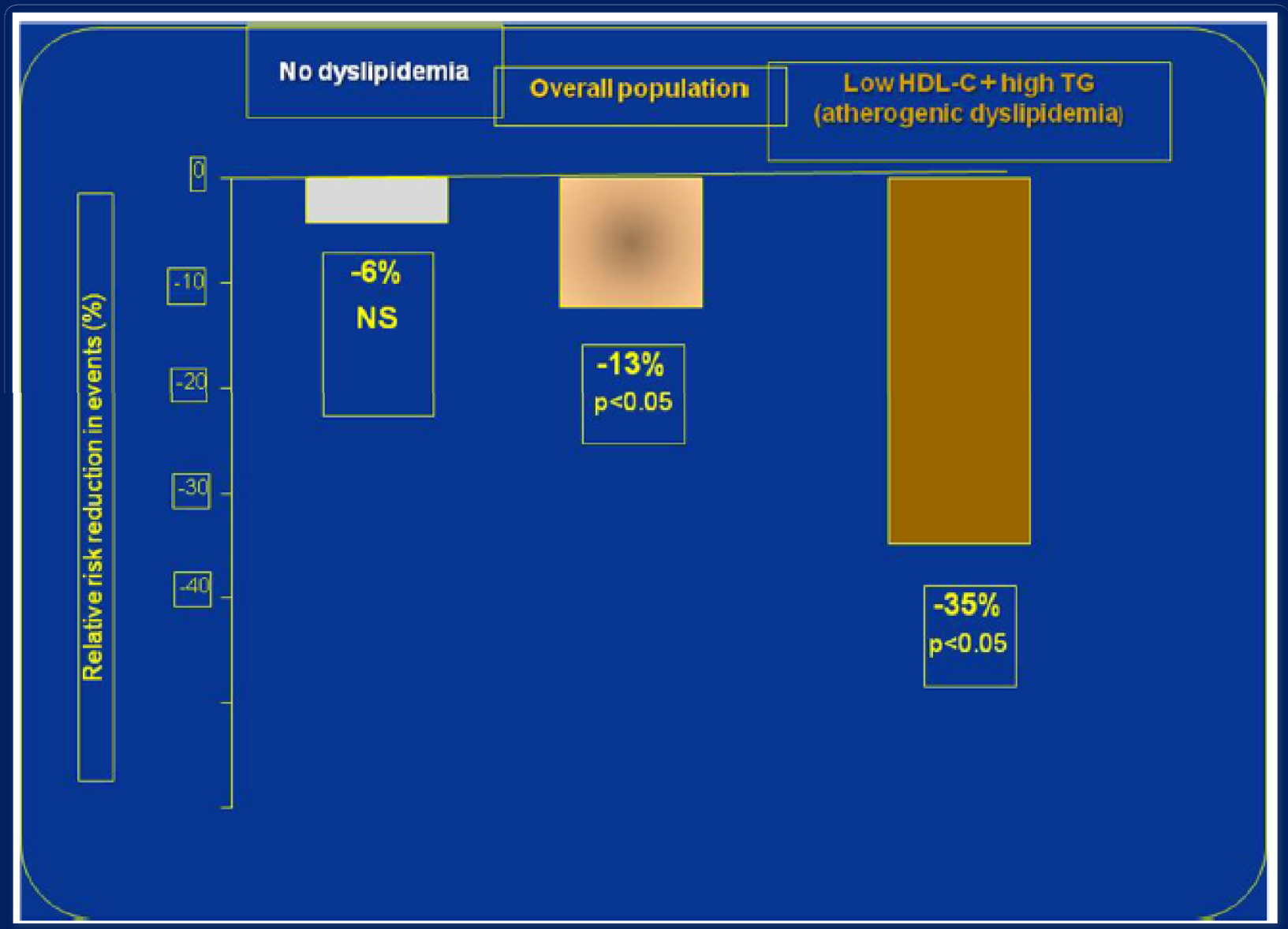
EZETIMIBE

- Παρεμποδίζει την απορρόφηση της χοληστερόλης (τροφών και χολής) στο έντερο
- LDL: ↓ ~ 15-20% (ως μονοθεραπεία)
- Συνδυασμός με στατίνη (όταν δεν έχει επιτευχθεί ο στόχος θεραπείας)
- Μείωση των καρδιαγγειακών συμβαμάτων (μελέτη IMPROVE-IT)

ΦΙΜΠΡΑΤΕΣ

- Δρουν σε πυρηνικούς υποδοχείς PPAR-α (peroxisome proliferator-activated receptor gamma): μεταβολές στη μεταγραφή γονιδίων που κωδικοποιούν πρωτείνες, οι οποίες επηρεάζουν το μεταβολισμό των λιπιδίων
- μείωση TG ~ 20-50% & LDL: ~ 10-20%
- Αύξηση HDL: ~ 10-20%
- **Αντενδείξεις**: νεφρική νόσος (eGFR < 60 ml/min)
- **Ανεπιθύμητες ενέργειες**: παρόμοιες των στατινών & χολολιθίαση
- Ένδειξη: TRG > 500 mg/dl (κίνδυνος παγκρεατίτιδας)

Fibrates trials



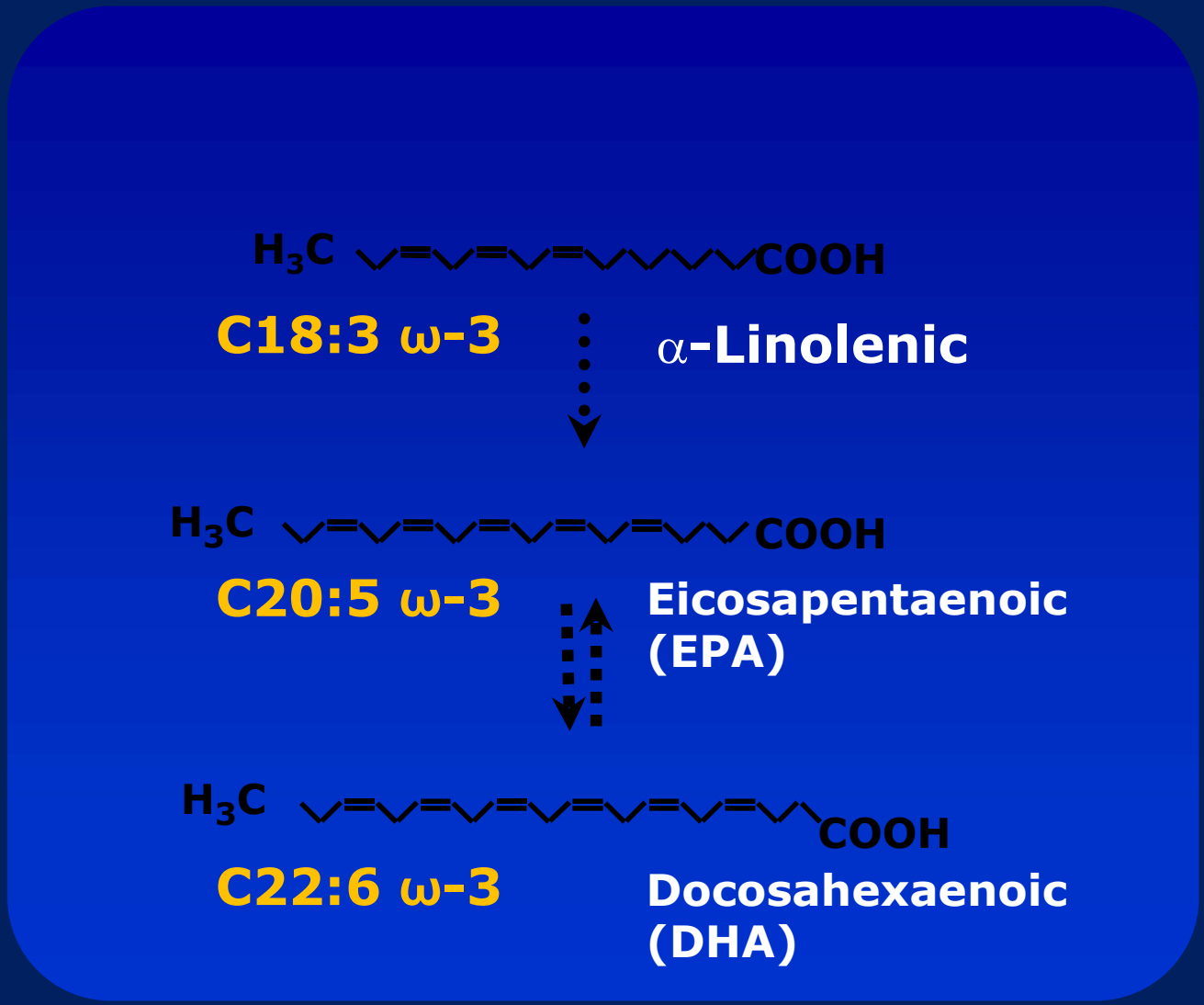
ΦΑΙΝΟΦΙΜΠΡΑΤΗ ΚΑΙ ΟΜΟΙΟΣΤΑΣΙΑ ΤΟΥ ΟΥΡΙΚΟΥ ΟΞΕΟΣ

n=64 ασθενείς με δυσλιπιδαιμία

	Πριν τη χορήγηση	Μετά τη χορήγηση	p
Ουρικό οξύ (mg/dL)	6.8±1.2	4.9±1.4 (↓ κατά 27.9%)	0.001
FEUA (%)	8±313±4	(↑ κατά 62.5%)	0.01

Liamis G et al. Am J Kidney Dis 1999;34:594

ω-3 λιπαρά οξέα



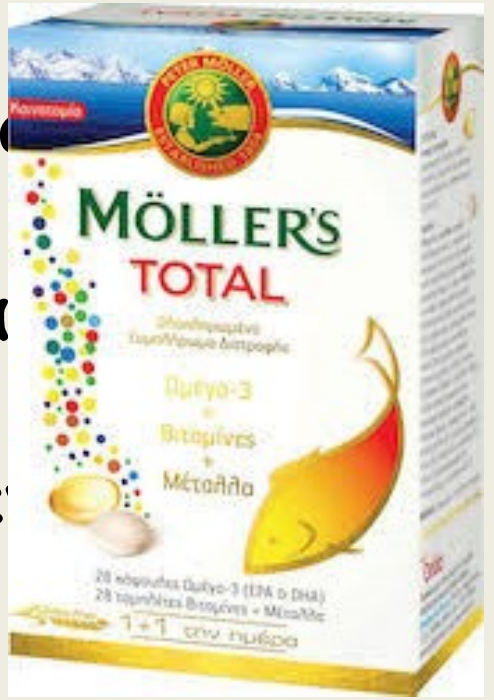
α-λινολενικό οξύ: Περιέχεται στα φυτά και είναι απαραίτητο για το σχηματισμό μεγαλύτερης αλυσίδας ω-3 λιπαρών οξέων που βρίσκονται στα ψάρια.

Ω - 3 ΛΙΠΑΡΑ ΟΞΕΑ

- Πολυακόρεστα λιπαρά οξέα ιχθύων (EPA & DHA)
- Προκαλούν σημαντική μείωση των τριγλυκεριδίων

ΠΛΕΙΟΤΡΟΠΙΚΕΣ ΔΡΑΣΕΙΣ ΤΩΝ ω-3 ΛΙΠΑΡΩΝ ΟΞΕΩΝ

- Αντιαρρυθμικές δράσεις
- Μείωση της συσσώρευσης των
- Μείωσ
- Βελτίω ς του α
- Αγγειο
- Βελτίω ς του ε
- Αντιφλ εις
- Αντιαθ
- Μείωση της συσσώρευσης κολλαγόνου
- Σταθεροποίηση των αθηρωματικών πλακών



JACC 2009;54: 585-594,
Lancet 2010;375: 540-550, J Nutr Biochem 2010;21: 781-792

JAMA Cardiology | Original Investigation

Associations of Omega-3 Fatty Acid Supplement Use With Cardiovascular Disease Risks

Meta-analysis of 10 Trials Involving 77 917 Individuals

JAMA Cardiol. 2018;3(3):225-234.

CONCLUSIONS AND RELEVANCE This meta-analysis demonstrated that omega-3 fatty acids had no significant association with fatal or nonfatal coronary heart disease or any major vascular events. It provides no support for current recommendations for the use of such supplements in people with a history of coronary heart disease.

(eicosapentaenoic acid dose range, 226-1800 mg/d)

DHA: αύξηση LDL

Ω - 3 ΛΙΠΑΡΑ ΟΞΕΑ

- Δεν συνταγογραφούνται/Όχι μείωση καρδιαγγειακών συμβαμάτων
- Πιθανή χρήση: υπετριγλυκαιριδιαμία σε ασθενείς με νεφρική νόσο (αντένδειξη λήψης φιμπράτης)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

CONCLUSIONS

Among patients with elevated triglyceride levels despite the use of statins, the risk of ischemic events, including cardiovascular death, was significantly lower among those who received 2 g of icosapent ethyl twice daily than among those who received placebo. (Funded by Amarin Pharma; REDUCE-IT ClinicalTrials.gov number, NCT01492361.)

Μείωση συμβαμάτων και σε ασθενείς χωρίς υψηλά τριγλυκερίδια

LDL-C and Lipid Changes

IMPROVE-IT

1 Yr Mean	LDL-C	TC	TG	HDL	hsCRP
Simva	69.9	145.1	137.1	48.1	3.8
EZ/Simva	53.2	125.8	120.4	48.7	3.3
Δ in mg/dL	-16.7	-19.3	-16.7	+0.6	-0.5

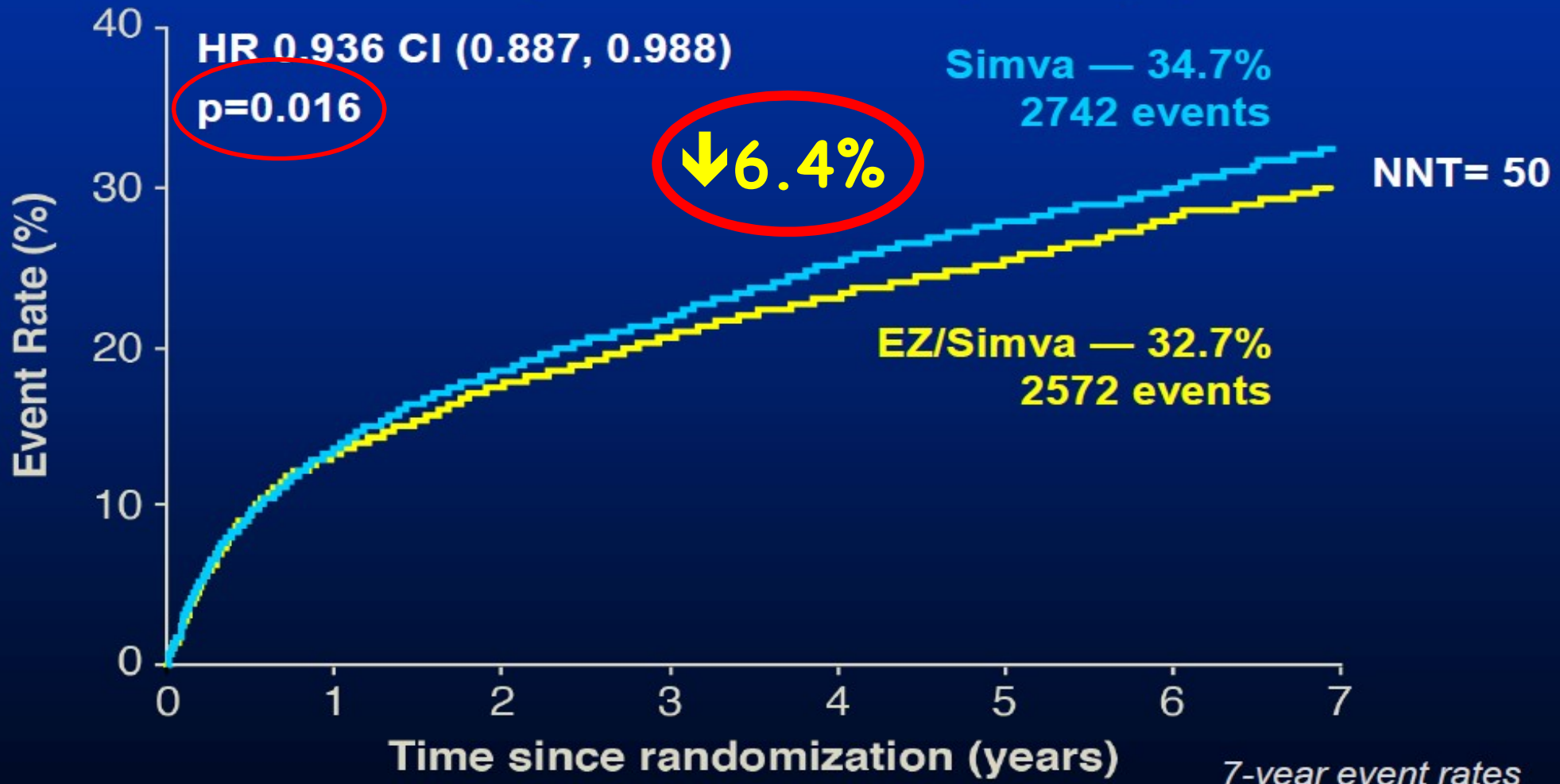
Number at risk:

EZ/Simva	8990	8889	8230	7701	7264	6864	6583	6256	5734	5354	4508	3484	2608	1078
Simva	9009	8921	8306	7843	7289	6939	6607	6192	5684	5267	4395	3387	2569	1068

Primary Endpoint — ITT

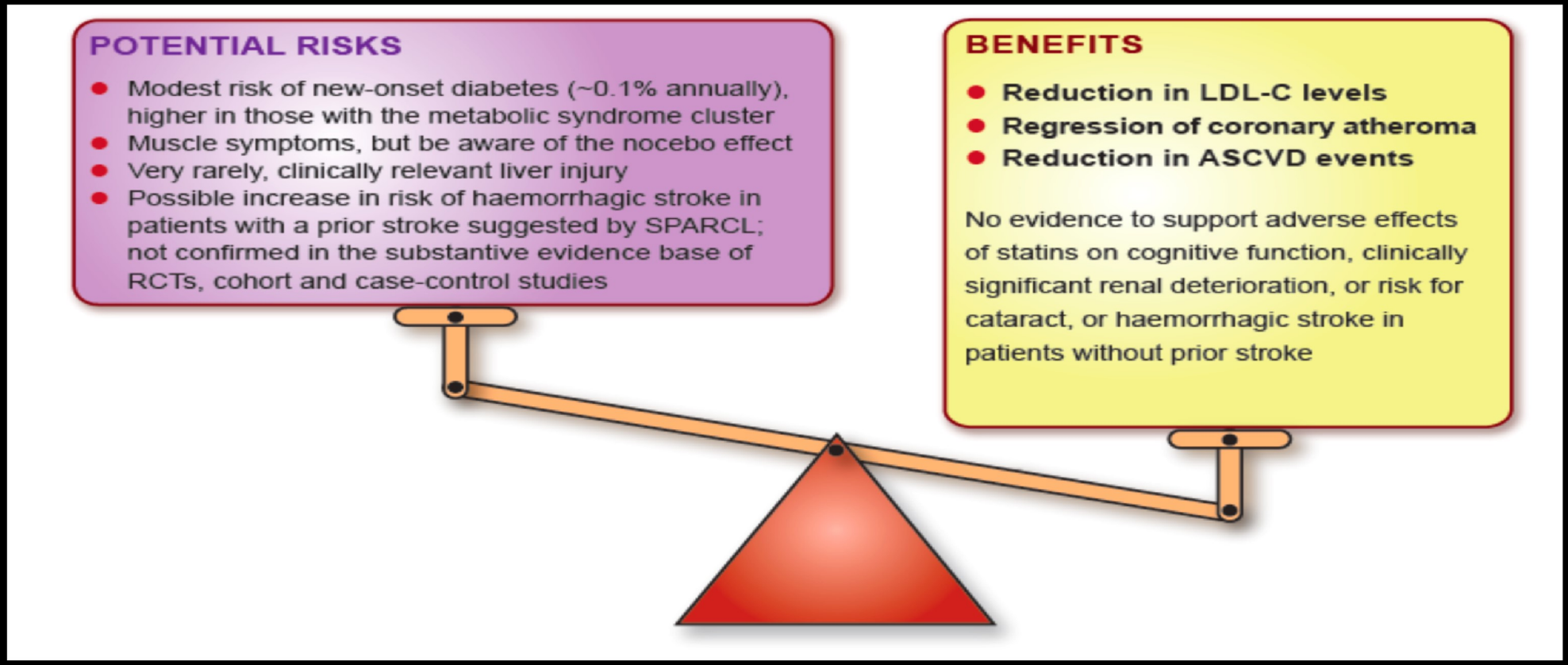
IMPROVE-IT

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥30 days), or stroke



7-year event rates

Statins: Highly Favourable Benefit vs. Risk Ratio



..' the Panel emphasizes that the established cardiovascular benefits of statin therapy far outweigh the risk of any such adverse effects '

Mach F et al. Eur Heart J 2018;

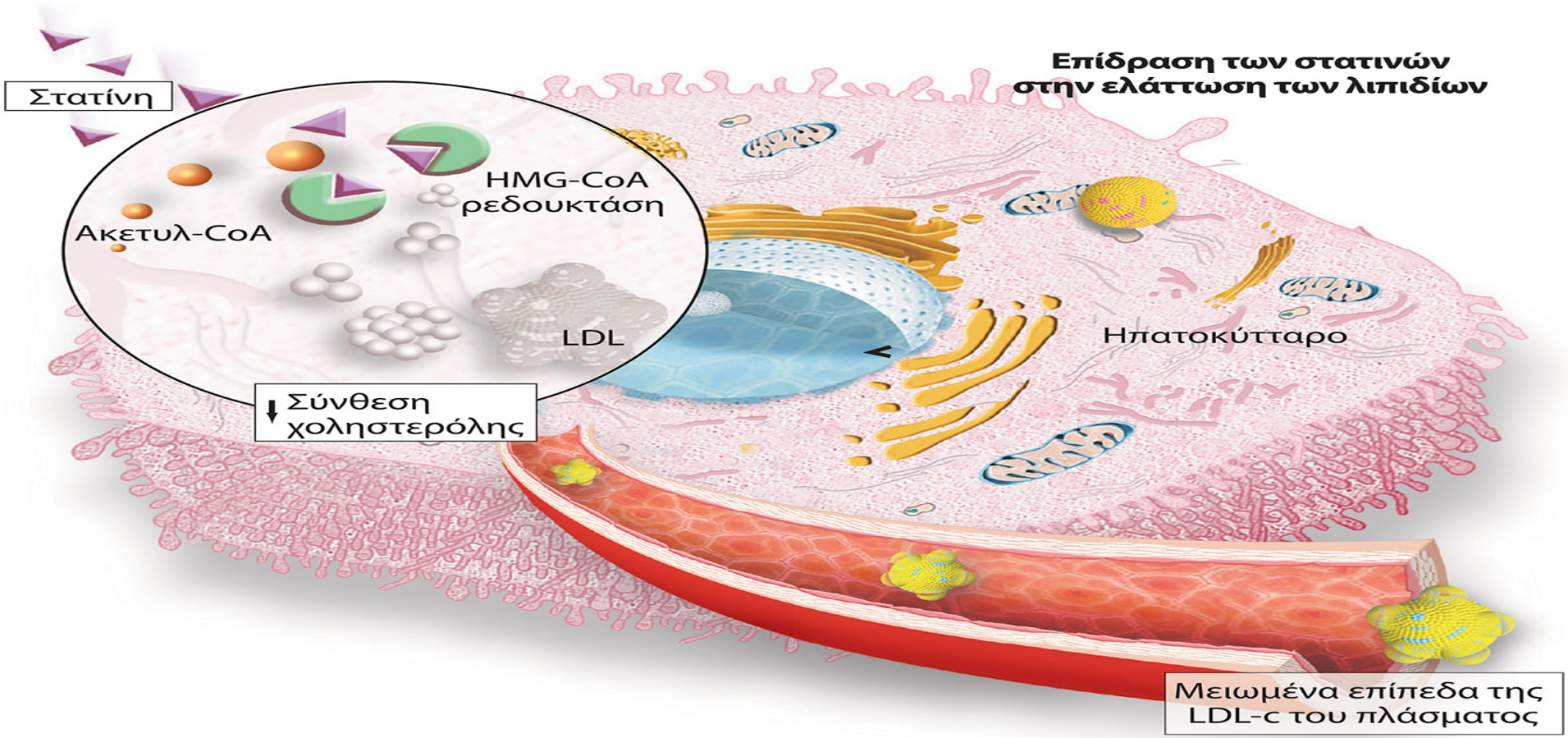
EAS

ΣΤΑΤΙΝΕΣ

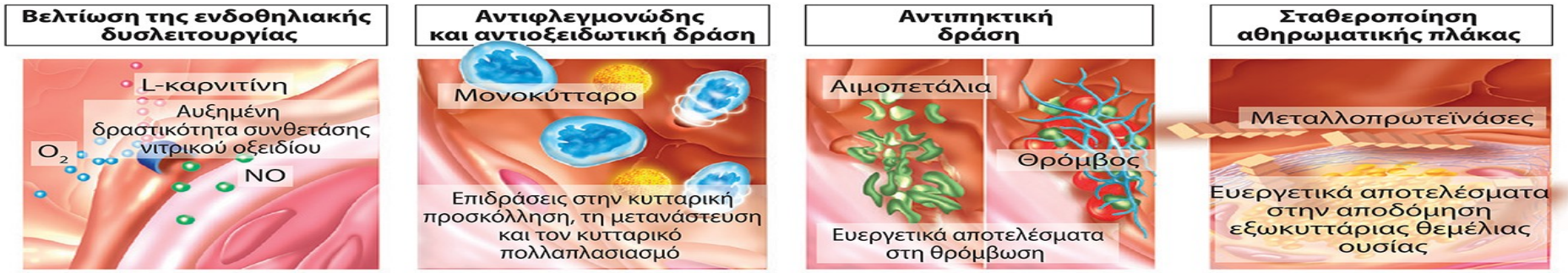
- Αναστολείς της HMG Co αναγωγάσης: της ενδογενούς σύνθεσης χοληστερόλης, των υποδοχέων της LDL & κατά συνέπεια παραλαβή της χοληστερόλης από το πλάσμα
- Είναι πιο αποτελεσματικές όταν χορηγούνται βράδυ (ενδογενής σύνθεση χοληστερόλης γίνεται κυρίως τη νύχτα).
- Οι μακράς δράσης στατίνες (ατορβα/ροσουβαστατίνη) χορηγούνται και το πρωί
- LDL: 20-50, HDL: μικρή ↑ & TG: μικρή

Πλειοτροπικές δράσεις

- Εκτός των υπολιπιδαιμικών δράσεων οι στατίνες έχουν και πλειοτροπικές δράσεις
- Αυτές είναι ευεργετικές δράσεις (αντιφλεγμονώδεις, αντιθρομβωτικές και αντιοξειδωτικές δράσεις και βελτίωση της λειτουργίας του ενδοθηλίου)
- Ως ένα βαθμό είναι ανεξάρτητες από τις δράσεις στο μεταβολισμό των λιπιδίων και συμβάλουν σημαντικά στην επίτευξη του ευεργετικού κλινικού αποτελέσματος των στατινών



Πλειοτροπικές επιδράσεις των στατινών



ΣΤΑΤΙΝΕΣ: Ανεπιθύμητες ενέργειες

- Από τα πιο ασφαλή φάρμακα
- Μυαλγίες/μυοσκελετικά άλγη

- μυλαγίες, κόπωση, αδυναμία, κράμπες, δυσκαμψία
- Τα συμπτώματα είναι συνήθως συμμετρικά, αφορούν μεγάλες μυϊκές ομάδες και εμφανίζονται συχνότερα σε άτομα με αυξημένη σωματική δραστηριότητα.
- Η βελτίωση των συμπτωμάτων με τη διακοπή της στατίνης (συνήθως εντός 2 εβδομάδων) και η επανεμφάνισή τους με την επαναχορήγηση της ίδιας ή διαφορετικής στατίνης (συνήθως εντός 4 εβδομάδων) ενισχύουν τη διάγνωση της δυσανεξίας στις στατίνες.

Αποκλεισμός άλλων αιτίων:

έντονη άσκηση-μυϊκή καταπόνηση, αλκοολισμός, υποθυρεοειδισμός, λοιμώξεις, υποκαλιαιμία, μεταβολικές μυοπάθειες, φλεγμονώδεις και αυτοάνοσες μυοσίτιδες

αλληλεπίδραση με συγχορηγούμενα φάρμακα

γεμφιμπροζίλη, κυκλοσπορίνη, μακρολίδια (κλαριθρομυκίνη), ιτρακοναζόλη και άλλα αντιμυκητιασικά φάρμακα, αντικαταθλιπτικά φάρμακα (nefazodone)

Φαινόμενο nocebo

Θεραπευτικές δυνατότητες σε ασθενείς με δυσανεξία στις στατίνες

1	• Επιθετική υγιεινοδιαιτητική αγωγή
2	• Χορήγηση εζετιμίμπης (10 mg/ημέρα)
3	• Χορήγηση συνδυασμού εζετιμίμπης (10 mg/ ημέρα) με κολεσεβελάμη (3.8 g/ ημέρα). Η αναμενόμενη μείωση της LDL χοληστερόλης είναι ~30%. Εναλλακτικά μπορεί να χορηγηθεί ο συνδυασμός εζετιμίμπης με φαινοφιμπράτη
4	• Ενδεχόμενη προσεκτική χορήγηση πραβαστατίνης 20 mg/ημέρα ή φλουβαστατίνης 40 mg/ημέρα
5	• Χορήγηση ροσουβαστατίνης 5 mg ή ατορβαστατίνης 10 mg ανά δεύτερη ημέρα ή δύο φορές την εβδομάδα ή μια φορά την εβδομάδα, σε συνδυασμό με εζετιμίμπη
6	• Προσδιορισμός των επιπέδων της βιταμίνης 25(OH)D3 και υποκατάστασή της σε περιπτώσεις μειωμένων επιπέδων
7	• Χορήγηση τροφοφαρμάκων (ARMOLIPID®, 1 δισκίο ημερησίως) σε ασθενείς που εμφανίζουν δυσανεξία στις στατίνες (ή δεν επιθυμούν να πάρουν αγωγή με στατίνη). Τα δισκία αυτά περιέχουν μεταξύ των άλλων κυρίως αντιοξειδωτικών ουσιών, μαγιά του κόκκινου ρυζιού (red yeast rice) που περιέχει μονακολίνες, ουσίες οι οποίες συσχετίζονται με τις στατίνες. Τα τροφοφάρμακα πρέπει να χορηγούνται με ιατρική συνταγή και υπό ιατρική παρακολούθηση

Hellenic Journal of Atherosclerosis 2014;5(3): 151-163

Statin-Associated Autoimmune Myopathy

- muscle weakness,
- evidence of muscle-cell necrosis on biopsy
- presence of autoantibodies against 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase.
- In contrast to most patients who have side effects from statin therapy, those with statin-associated autoimmune myopathy may have progressive weakness that must be controlled with immunosuppressive therapy. (similarly to those with other forms of autoimmune muscle disease)

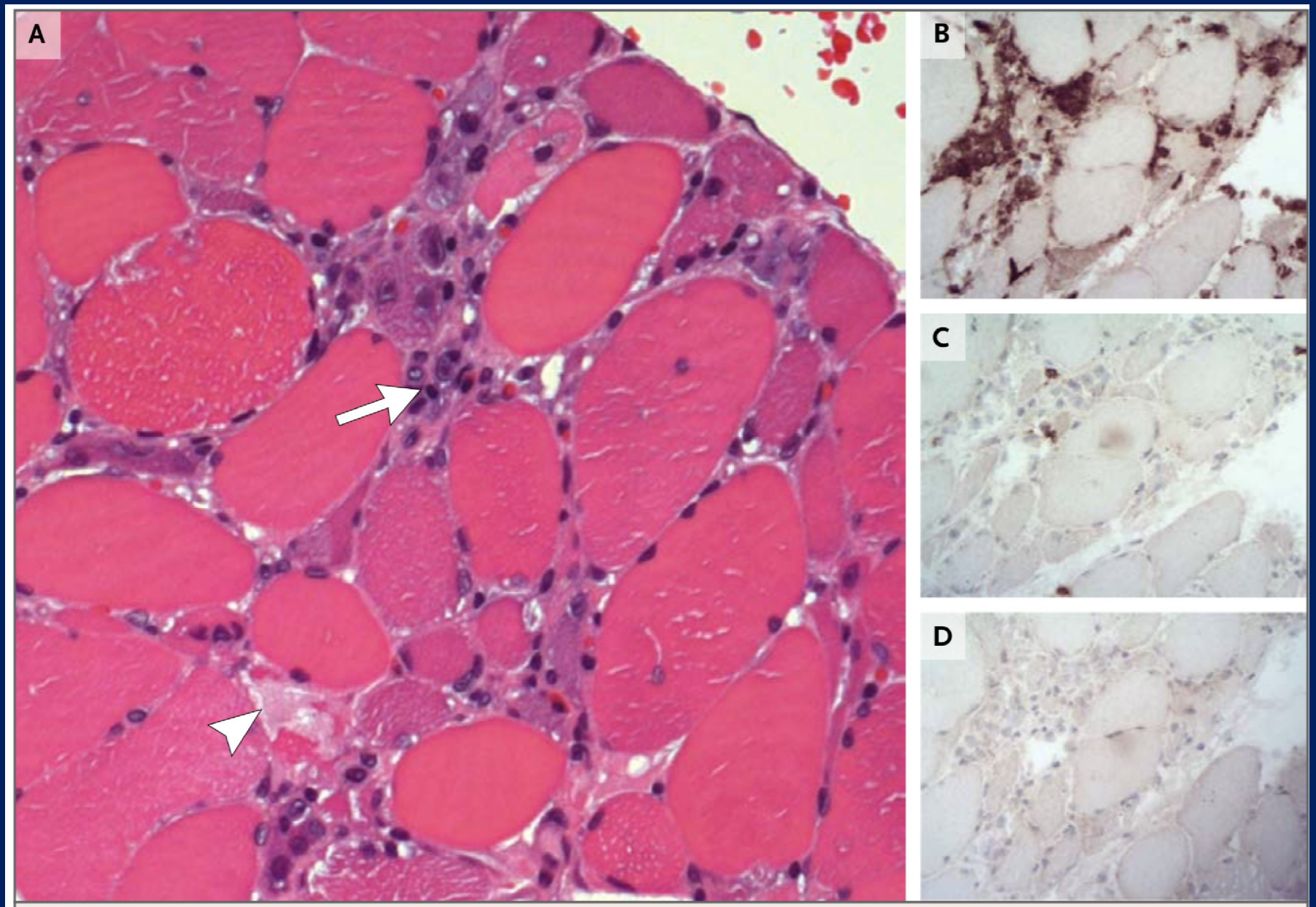
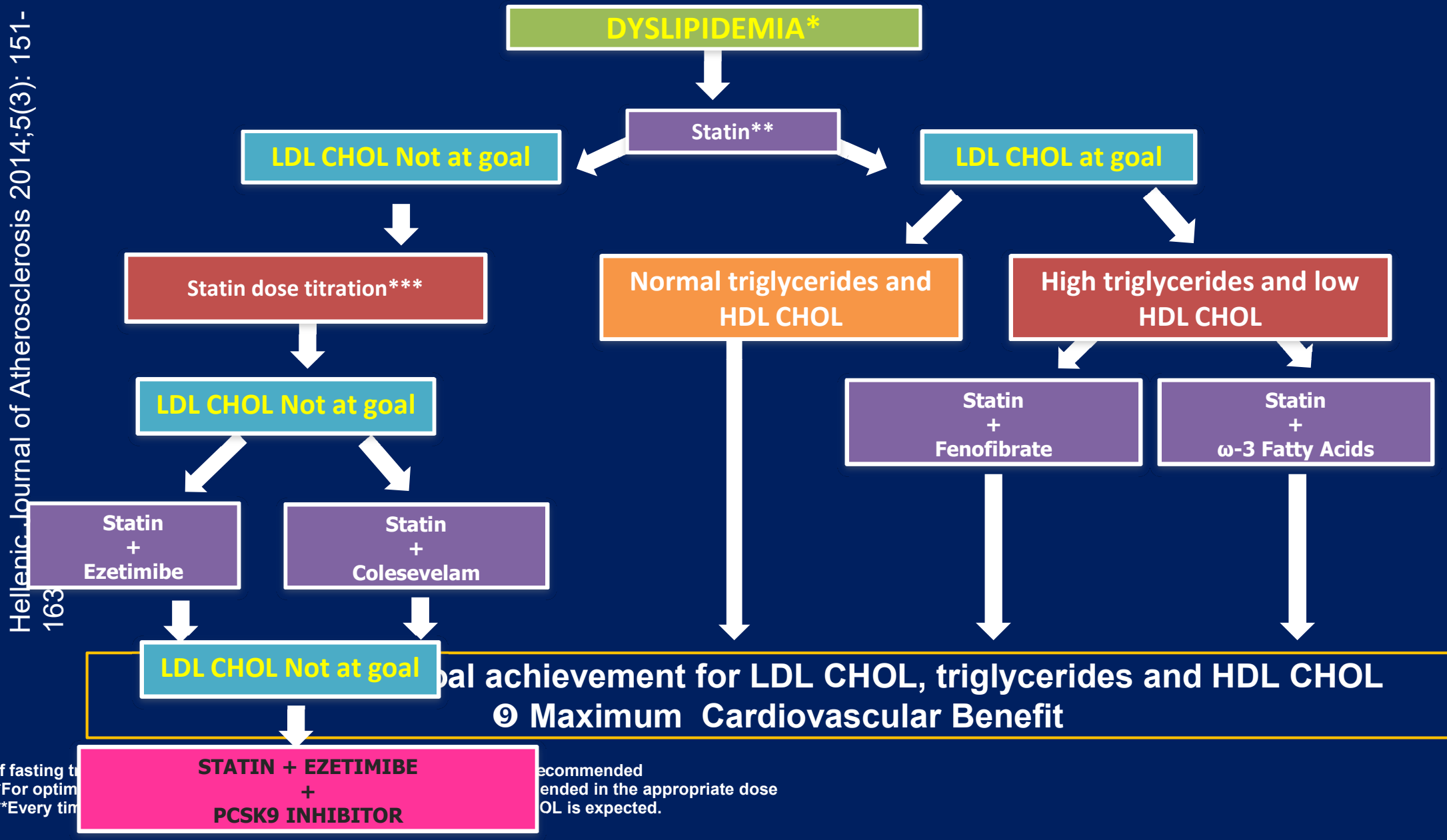


Figure 1. Muscle-Cell Necrosis and Macrophage Infiltration in Statin-Associated Autoimmune Myopathy.

Treatment Algorithm for Patients with Dyslipidemia



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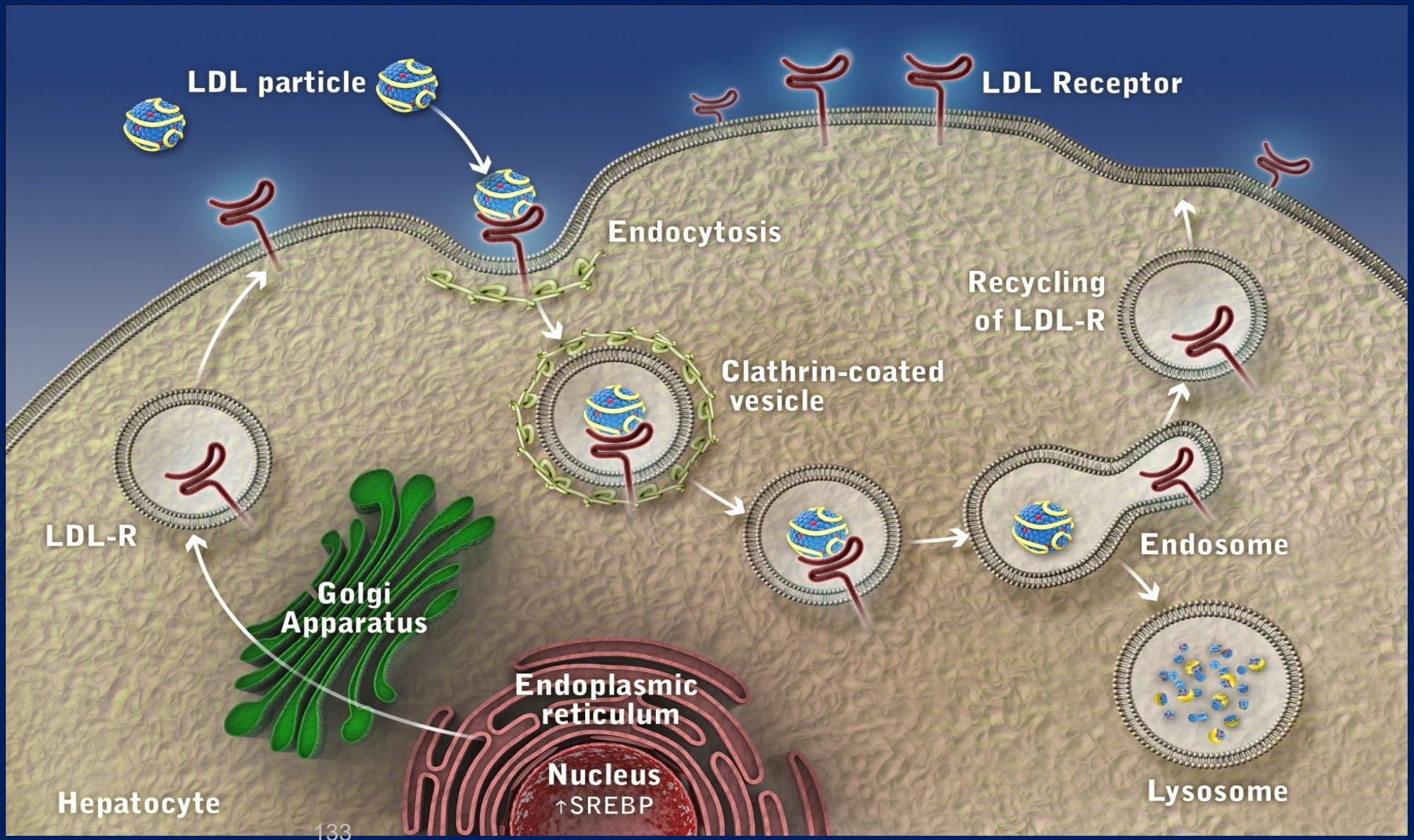
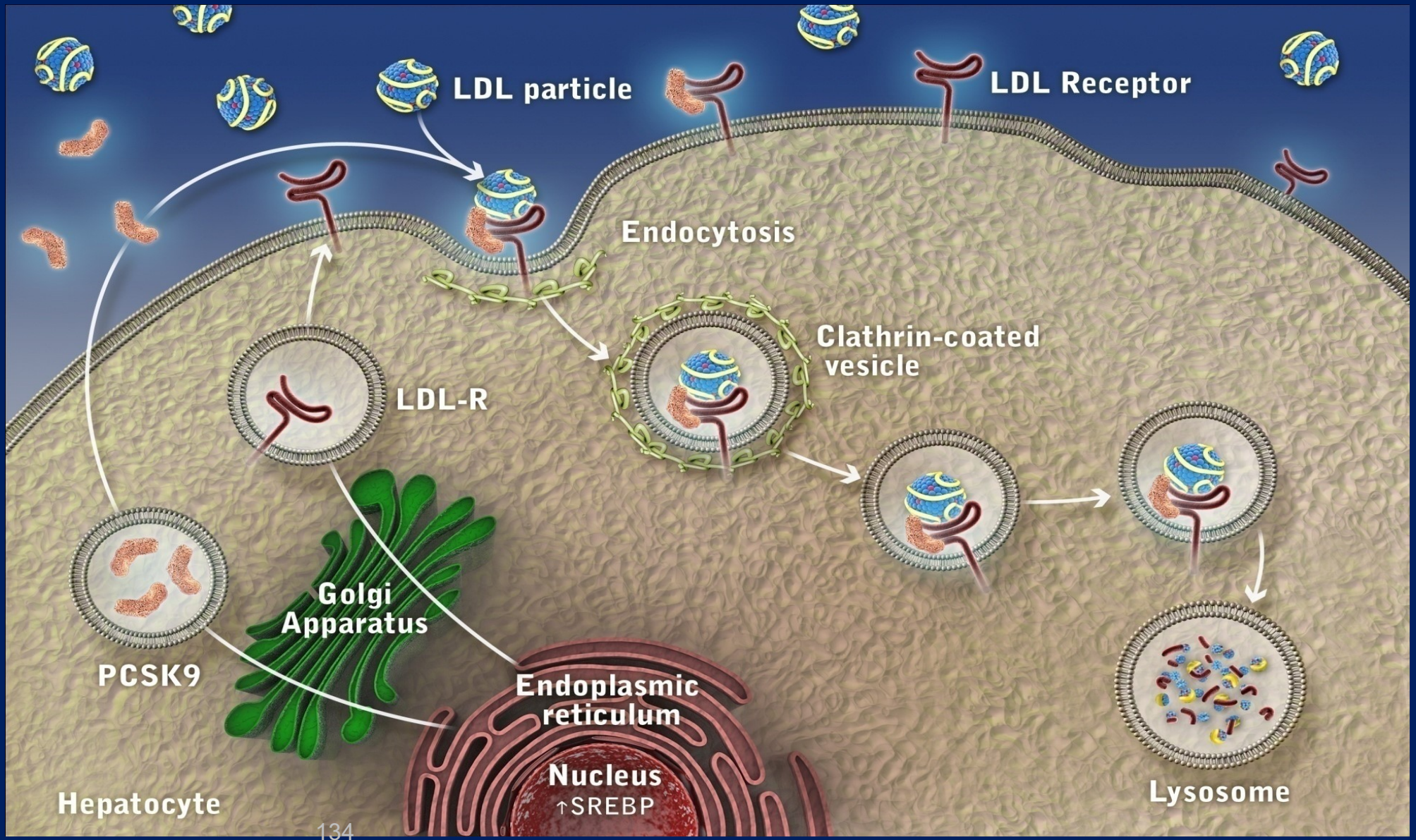
*If fasting tr ecommended
**For optim ended in the appropriate dose
***Every tim OL is expected.

LDL Receptor Function and Life Cycle



The Role of PCSK9 in the Regulation of LDL Receptor Expression



ΑΝΑΣΤΟΛΕΙΣ ΤΗΣ PCSK9 (EVOLOCUMAB /ALIROCUMAB)

Μείωση της PCSK9

Αύξηση του αριθμού και της δραστηριότητας των LDLR

Αύξηση του καταβολισμού των LDL

Μείωση της LDL CHOL (> 60%), Lp(a) (30%)

Evolocumab/Alirocumab

- ✓ Πολύ καλά ανεκτά
- ✓ Επίτευξη των στόχων στην πλειοψηφία των ασθενών
- ✓ Εξαιρετικό προφίλ ασφάλειας
- ✓ Χωρίς αλληλεπιδράσεις με άλλα φάρμακα
- ✓ Όχι τροποποίηση με βάση τη νεφρική λειτουργία
- ✓ Επίπτωση ΣΔ και νευρογνωσιακών διαταραχών ? (απαιτούνται μελέτες με μεγαλύτερη διάρκεια παρακολούθησης)
- ✓ Μείωση καρδιαγγειακών συμβαμάτων (μελέτες Fourier & Odyssey)

HDL ?

- Επιδημιολογικές μελέτες: αντίστροφη συσχέτιση HDL με ΚΑΝ (προστατευτική δράση)
- Φάρμακα για αύξηση της HDL (CETP inhibitors): αύξηση των ΚΑΝ !!!
- Λειτουργικότητα της HDL
- Βελτίωση της ποιότητας της HDL και όχι της ποσότητας μπορεί να αποτελέσει θεραπευτικό στόχο στο μέλλον

ΚΑΝ & φλεγμονή ?

- Atherosclerosis is undoubtedly a multifactorial disease in which chronic inflammation plays a key role
- CANTOS (Canakinumab Anti-inflammatory Thrombosis Outcomes Study): 10,061 patients with previous myocardial infarction and a high-sensitivity C-reactive protein level (> 2 mg/L)

- Antiinflammatory therapy targeting the interleukin-1β innate immunity pathway with canakinumab at a dose of 150 mg every 3 months led to a significantly lower rate of recurrent cardiovascular events than placebo, independent of lipid-level lowering.
- Canakinumab was associated with a higher incidence of fatal infection than was placebo.

The NEW ENGLAND JOURNAL of MEDICINE

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ORIGINAL ARTICLE

Low-Dose Methotrexate for the Prevention of Atherosclerotic Events

- low-dose methotrexate (at a target dose of 15 to 20 mg weekly) or matching placebo in 4786 patients with previous myocardial infarction or multivessel coronary disease who additionally had either type 2 diabetes or the metabolic syndrome. All participants received 1 mg of folate daily.

CONCLUSIONS

Among patients with stable atherosclerosis, low-dose methotrexate did not reduce levels of interleukin-1β, interleukin-6, or C-reactive protein and did not result in fewer cardiovascular events than placebo. (Funded by the National Heart, Lung, and Blood Institute; CIRT ClinicalTrials.gov number, NCT01594333.)