



ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Εθνικόν και Καποδιστριακόν
Πανεπιστήμιον Αθηνών
— ΙΔΡΥΘΕΝ ΤΟ 1837 —

ΟΙΚΟΓΕΝΗΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ: ΔΙΑΓΝΩΣΗ-ΘΕΡΑΠΕΙΑ



Ευάγγελος Λυμπερόπουλος

Καθηγητής Παθολογίας-Μεταβολικών Νοσημάτων Ιατρικής Σχολής Εθνικού και Καποδιστριακού Πανεπιστημίου Αθηνών

Α΄ Προπαιδευτική Παθολογική Κλινική, ΓΝΑ 'Λαϊκό'

European Atherosclerosis Society Executive Committee member (2024-2027)



ΠΕΡΙΠΤΩΣΗ ΑΣΘΕΝΗ

- Ασθενής 48 ετών έρχεται με T-CHOL 350 mg/dL, TGs 100 mg/dL, HDL-CHOL 50 mg/dL & LDL CHOL 280 mg/dL

**1^ο ΒΗΜΑ: ΑΠΟΚΛΕΙΣΜΟΣ ΔΕΥΤΕΡΟΠΑΘΟΥΣ
ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑΣ**

ΑΠΟΚΛΕΙΣΜΟΣ ΔΕΥΤΕΡΟΠΑΘΟΥΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑΣ

✓ Υποθυρεοειδισμός (TSH)

✓ Χολόσταση (αλκαλική φωσφατάση)

✓ Νεφρωσικό σύνδρομο (λεύκωμα ούρων)

DIAGNOSTIC WORK-UP

➤ Εργαστηριακές εξετάσεις κ.φ.

➤ Μη καπνιστής

➤ BMI 25 Kg/m²

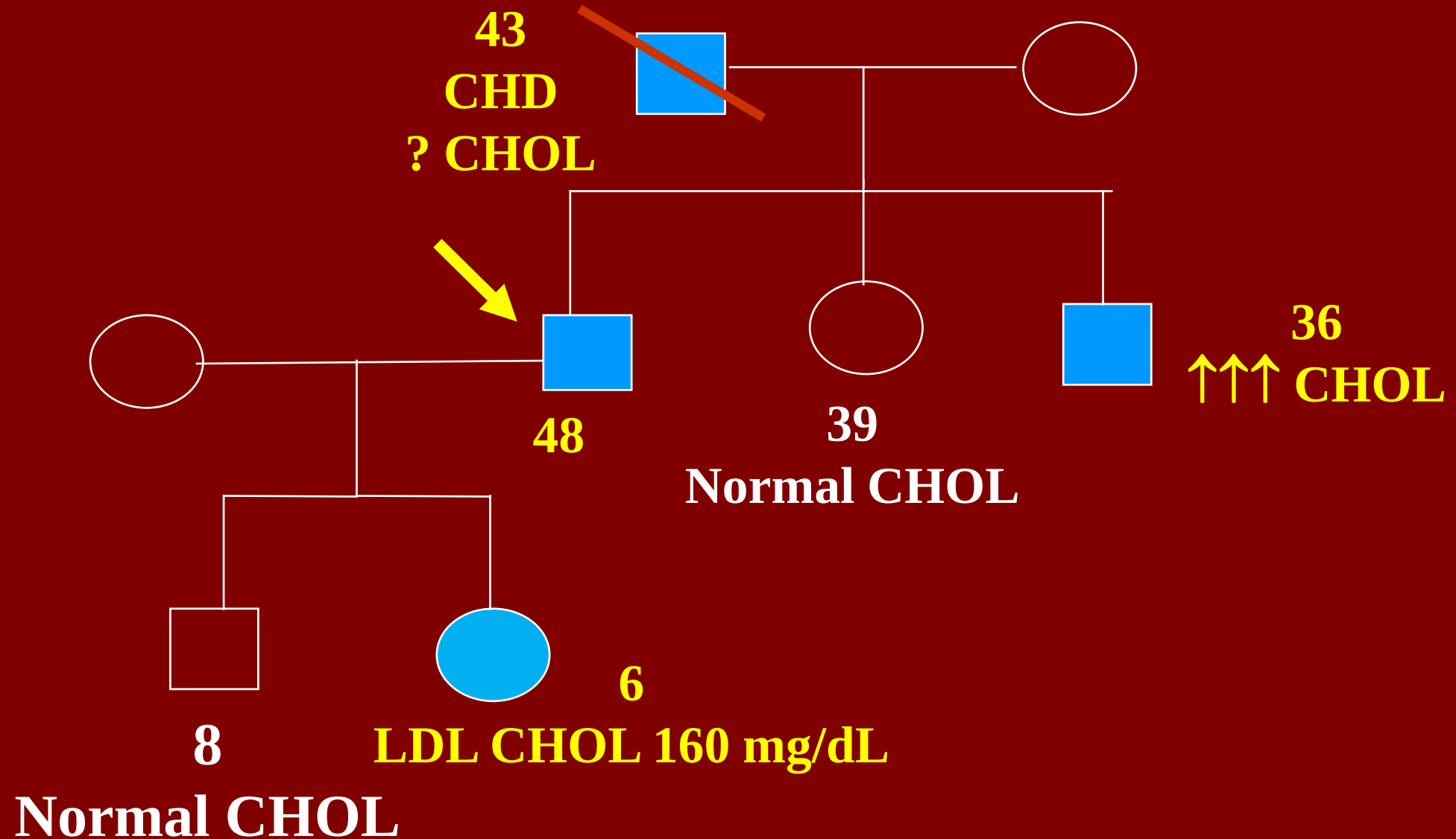
➤ ΑΤ 120/80 mmHg

2° ΒΗΜΑ: ΑΤΟΜΙΚΟ & ΟΙΚΟΓΕΝΕΙΑΚΟ ΙΣΤΟΡΙΚΟ

Διαγνωστικές ερωτήσεις

- 1) Έχει ο ασθενής ατομικό ιστορικό CVD;
- 2) Τι LDL χοληστερόλη και ιστορικό CVD έχουν οι γονείς;
- 2) Τι LDL χοληστερόλη και ιστορικό CVD έχουν τα αδέλφια του;
- 3) Τι LDL χοληστερόλη και ιστορικό CVD έχουν τα παιδιά του;

FAMILY TREE



3^ο ΒΗΜΑ: ΦΥΣΙΚΗ ΕΞΕΤΑΣΗ

Consider

FH

Clinical evidence of:



- Corneal Arcus



- Xanthelasma

- Tendon xanthomas in the hands and Achilles tendons





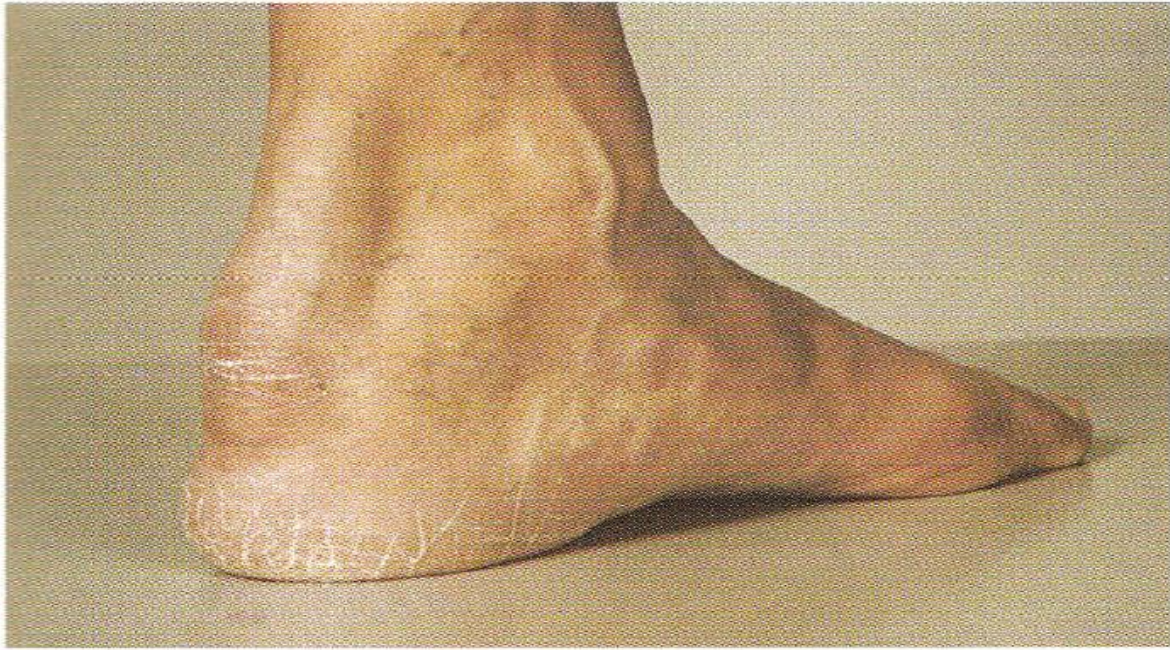


Plate 1 *Achilles tendon xanthoma (heterozygous familial hypercholesterolaemia)*

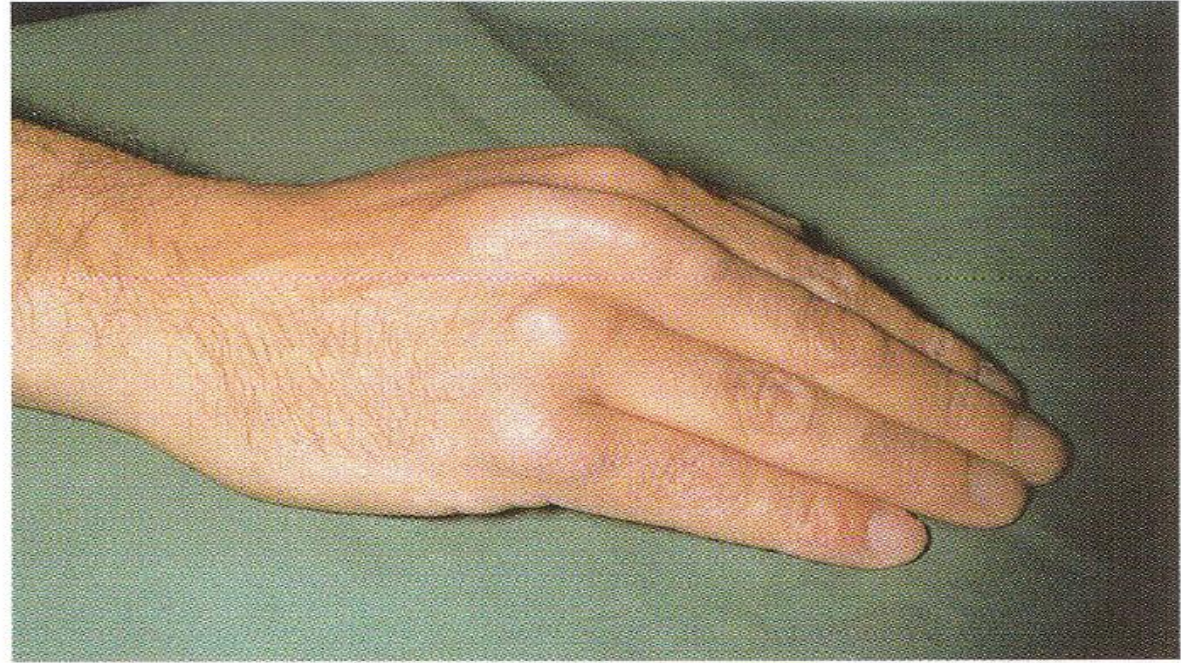


Plate 3 *Tendon xanthomata on dorsum of hand (heterozygous familial hypercholesterolaemia) (courtesy of Dr J. Barth)*

ΦΥΣΙΚΗ ΕΞΕΤΑΣΗ ΗοFH



Homozygous FH

A horrible inherited metabolic disease



Case report:

- 5-year-old boy with HoFH
- Treated with colestyramine
- LDL 26 mmol/L (2314 mg/dl)



Follow-up:

- Acute ischaemic cardiac event; complete obstruction of the left coronary artery
- Died from second MI after three months



4^ο ΒΗΜΑ: ΔΙΑΓΝΩΣΗ

ΟΙΚΟΓΕΝΗΣ (50% των 1^{ου} βαθμού συγγενών)

+

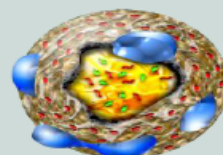
ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ (LDL-C >190
mg/dL ενήλικοι ή >160 mg/dL παιδιά)

=

ΟΙΚΟΓΕΝΗΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ (FH)

DUTCH FH CRITERIA

Feature	Score
Family history	
First-degree relative with known premature coronary and/or vascular disease (men <55 years, females <60 years) OR First-degree relative with known LDL-C above the 95th percentile for age and sex	1
First-degree relative with tendinous xanthomata and/or arcus cornealis OR Children aged less than 18 years with LDL-C above the 95th percentile for age and sex	2
Clinical history	
Premature coronary artery disease (men <55 years, females < 60 years)	2
Premature cerebral or peripheral vascular disease (men <55 years, females <60 years)	1
Physical examination	
Tendinous xanthomata	6
Arcus cornealis prior to age 45 years	4
LDL-C (mmol/L)	
– 9.0 or higher	8
– 6.5 to 8.4	5
– 5.0 to 6.4	3
– 4.0 to 4.9	1
DNA analysis: functional mutation in the <i>LDLR</i> , <i>APOB</i> or <i>PCSK9</i> gene	8
Stratification of familial hypercholesterolaemia (FH), as determined by total score using the Dutch Lipid Clinic Network Criteria: • Definite FH = total score greater than 8 • Probable FH = total score between 6 and 8 • Possible FH = total score between 3 and 5 • Unlikely FH = total score of less than 3	



Family History + Hypercholesterolemia = FH in Children*

- Cholesterol testing should be used to make a phenotypic diagnosis
 - 5 mmol/L (190 mg/dL), 2 successive occasions over 3 months
 - 4 mmol/L (160 mg/dL) AND family history of premature CVD ± baseline high cholesterol in one parent
 - 3.5 mmol/L (130 mg/dL) AND positive genetic diagnosis in the family
- Rule out secondary causes (thyroid, liver or renal dysfunction, concomitant medication, obesity)
- Genetic testing confirms the diagnosis (after parental testing)
- If a parent died from CHD, a child even with moderate hypercholesterolaemia should be tested genetically for FH and inherited elevation in Lp(a).

Box 2 Updated criteria for the diagnosis of homozygous familial hypercholesterolaemia

Clinical criteria

- LDL-C criteria:
Untreated LDL-C >10 mmol/L (>~400 mg/dL) is suggestive of HoFH requiring further investigation to confirm the diagnosis.
- Additional criteria:
Cutaneous or tendon xanthomas before age of 10 years and/or
untreated elevated LDL-C levels consistent with heterozygous FH in both parents*
*In digenic form, one parent may have normal LDL-C levels and the other may have LDL-C levels consistent with HoFH.

Genetic criteria

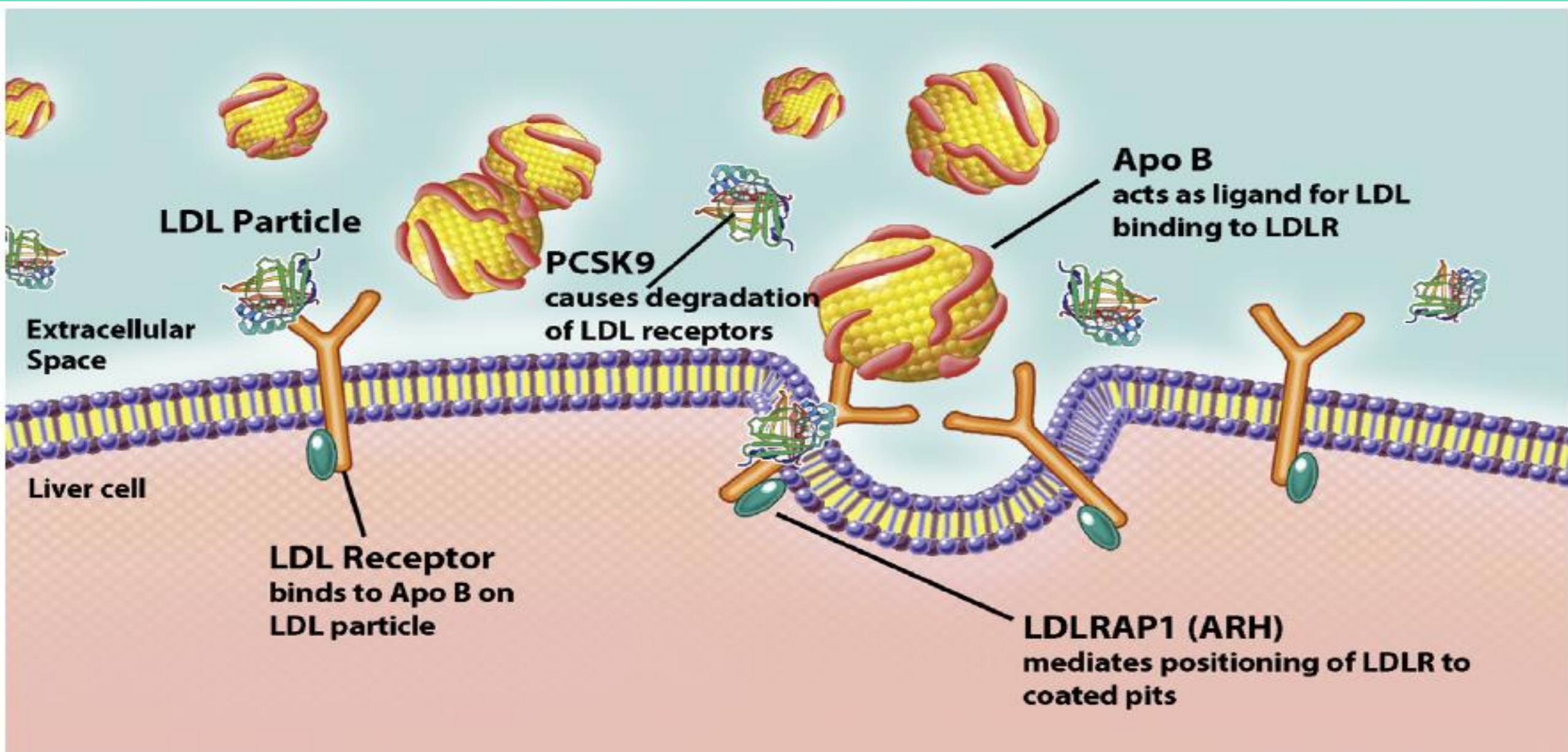
- Genetic confirmation of bi-allelic pathogenic/likely pathogenic variants on different chromosomes at the *LDLR*, *APOB*, *PCSK9*, or *LDLRAP1* genes or ≥ 2 such variants at different loci

European Heart Journal (2023) **44**, 2277–2291

5° ΒΗΜΑ: ΓΕΝΕΤΙΚΗ ΔΙΑΓΝΩΣΗ
[ΟΧΙ ΑΠΑΡΑΙΤΗΤΗ]

Figure 2

Major Molecular Causes of Familial Hypercholesterolemia



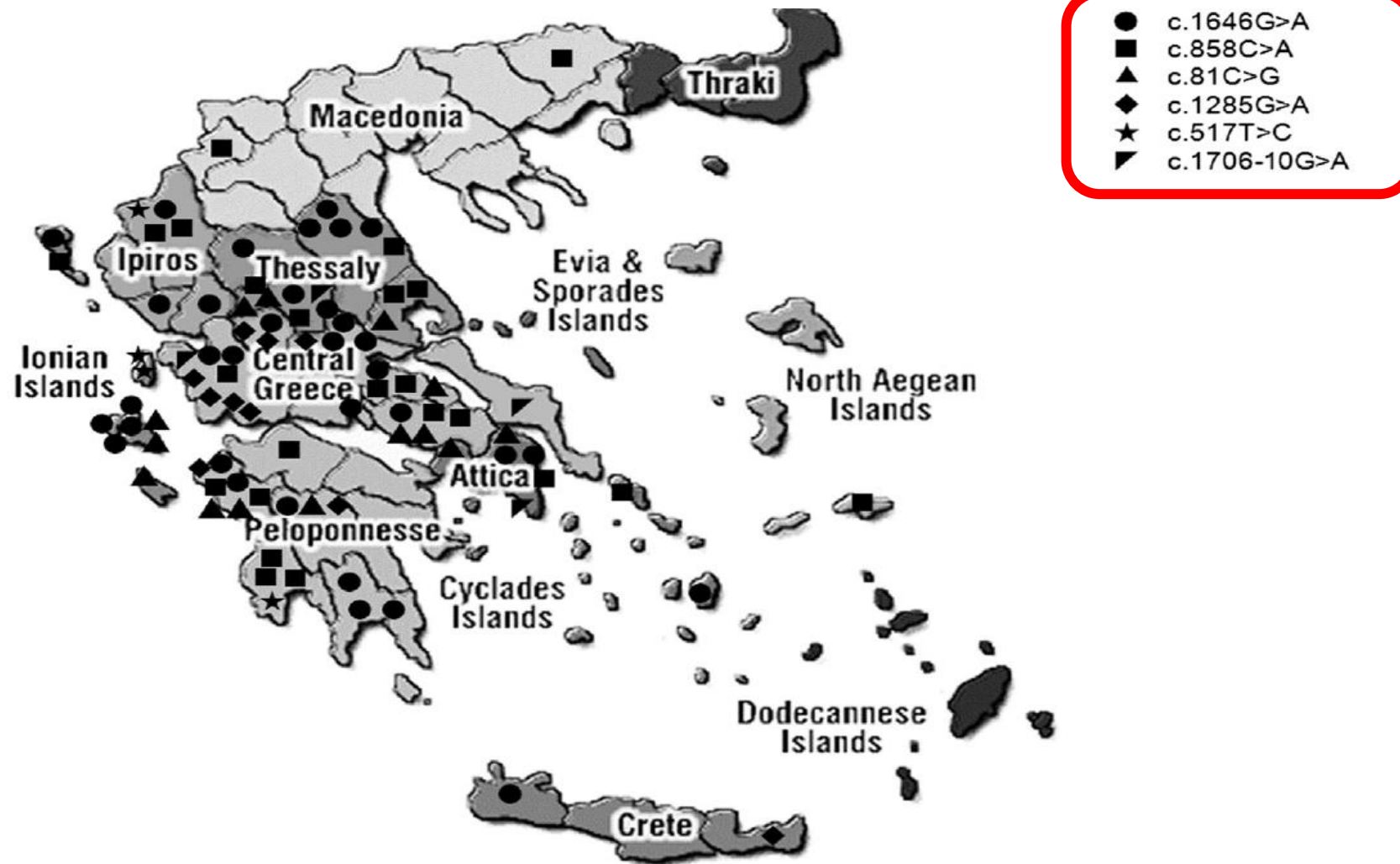
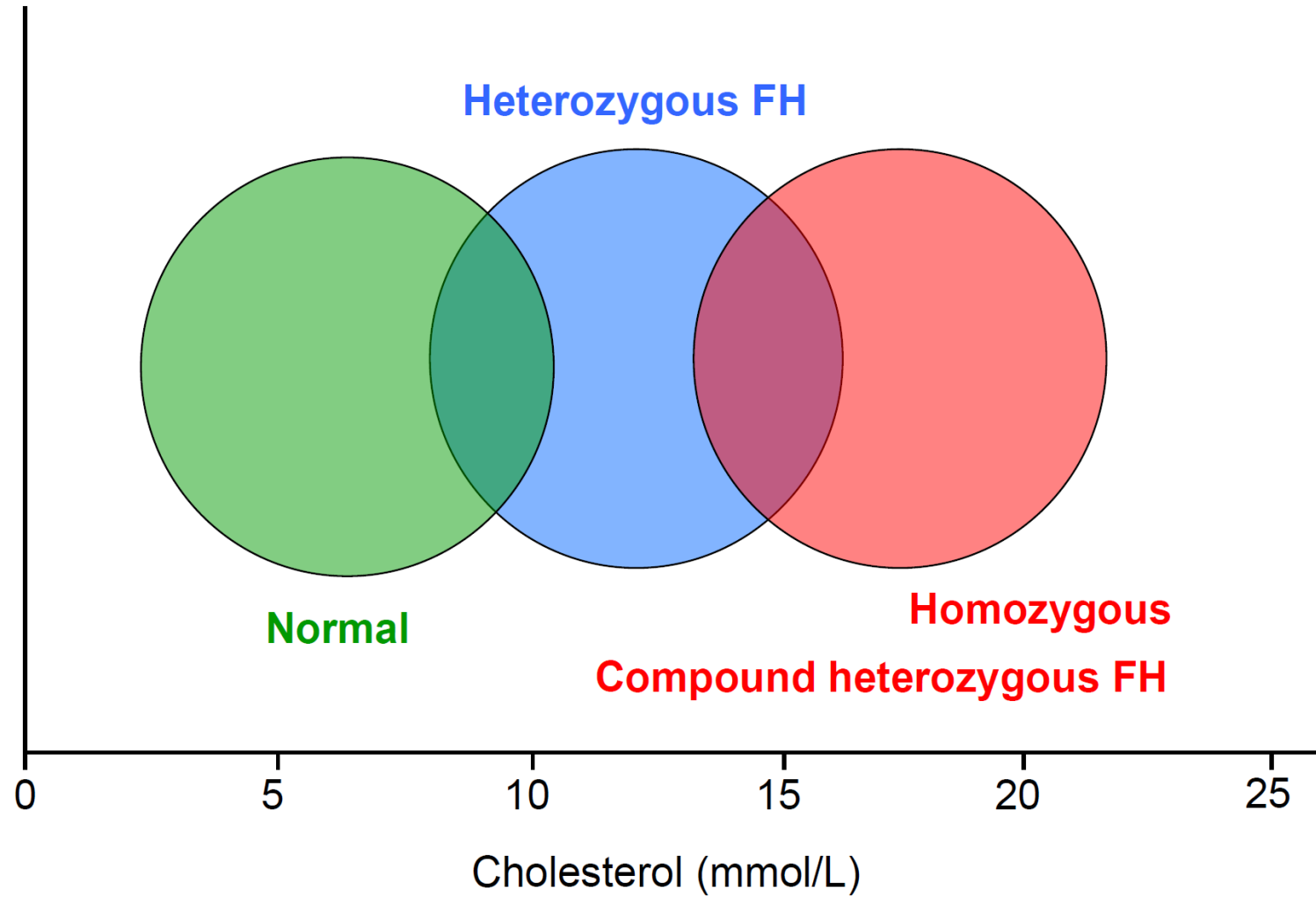


Fig. 2. Geographic distribution of the six most common *LDLR* mutations in Greece. The distribution of mutations is only shown for the index cases with determined exact origin. Four patients originating from Minor Asia carried the mutations c.1646G > A ($n = 2$), and c.81C > G ($n = 2$), and one patient originating from Cyprus carried the mutation c.1646G > A (data not shown in figure).

FH

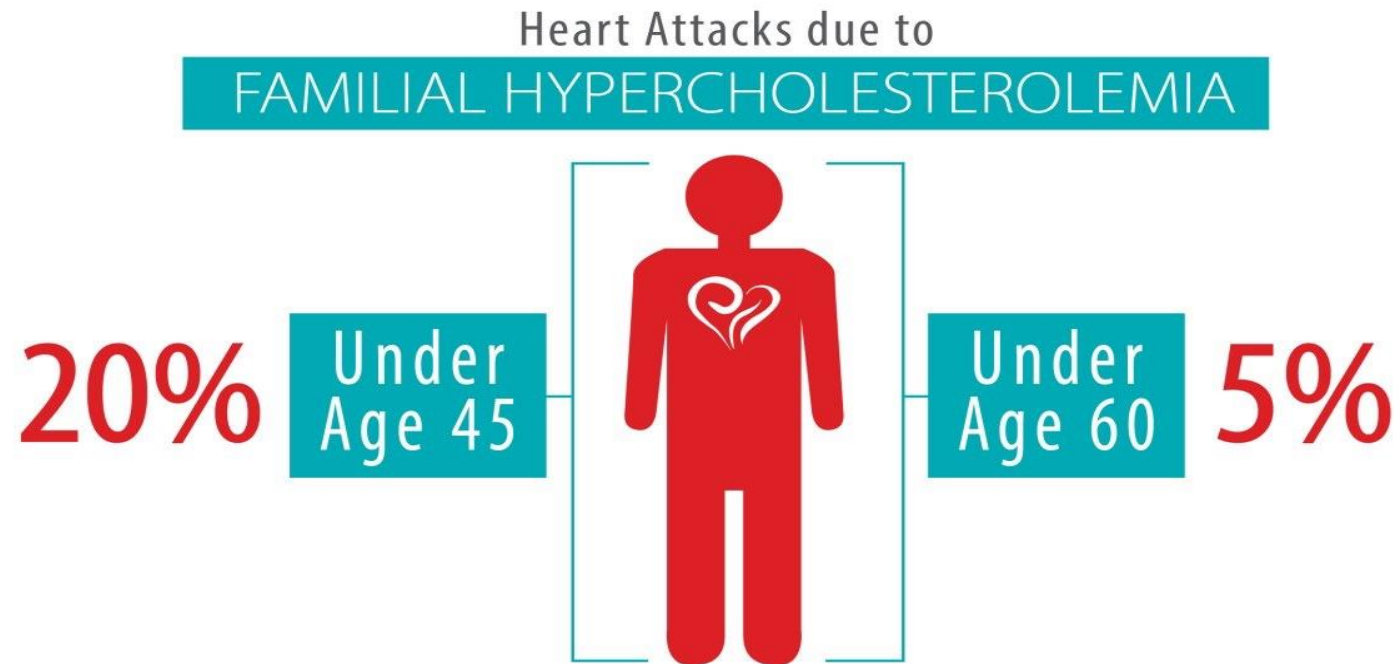


ΤΙ ΣΗΜΑΙΝΕΙ ΝΑ ΕΧΕΙ ΚΑΠΟΙΟΣ ΟΙΚΟΓΕΝΗ
ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ;

Heterozygous FH

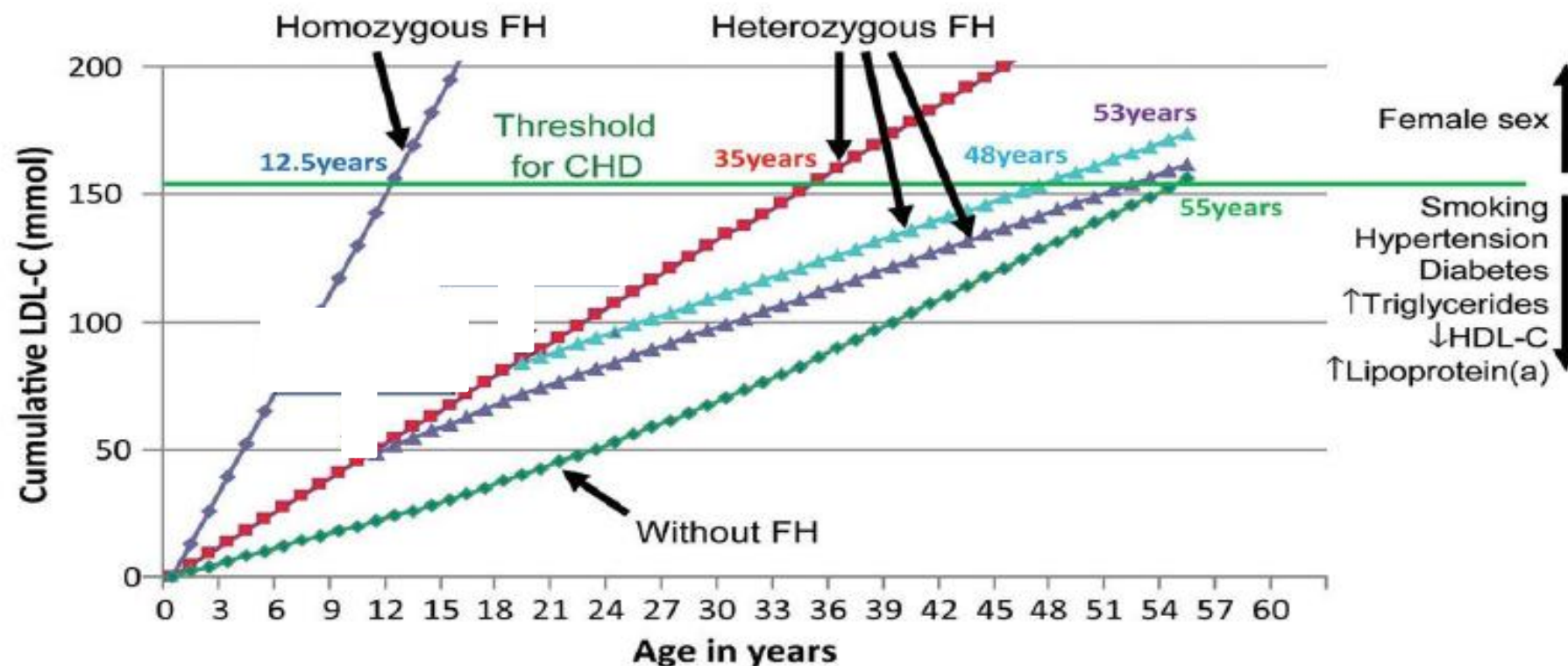
- 20-fold increased risk of CVD
- If untreated:
 - Men have 50% risk of CVD by age 50
 - Women have 30% risk of CVD by age 60
- Many HeFH patients present with established CVD
(angina, MI)

“About 5% of heart attacks under age 60 and as many as 20% under age 45 are due to FH”



Hopkins P, Toth P. Familial hypercholesterolemias: prevalence, genetics, diagnosis and screening recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Clin Lipidol. 2011 Jun;5(3 Suppl):S9–17.

LDL cholesterol burden in individuals with or without familial hypercholesterolaemia as a function of the age of initiation of statin therapy.



Adapted from Steve Humphries 2013

Nordestgaard et al. Eur Heart J 2013; 34: 3478-3490

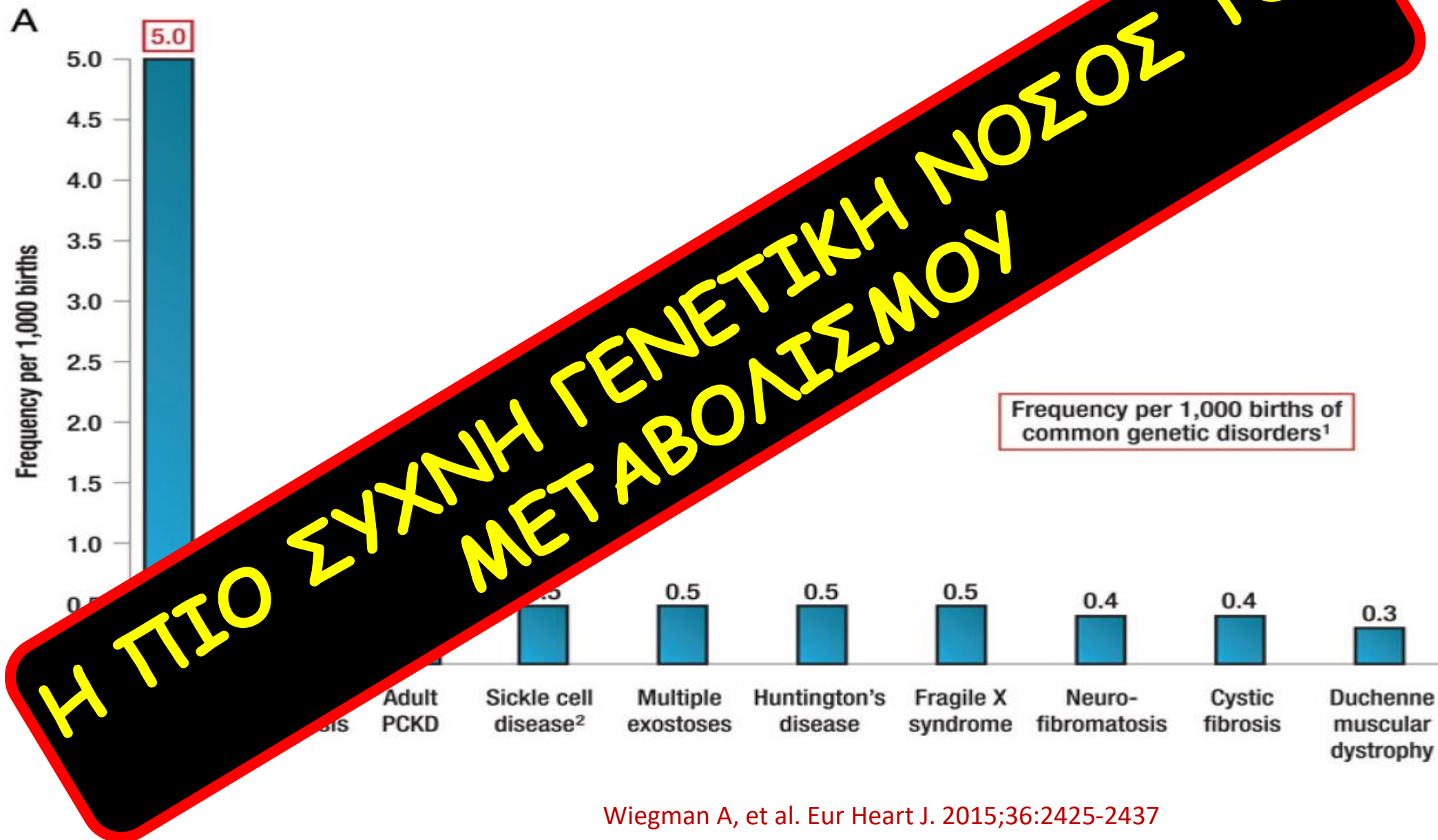
© The Author 2013. Published by Oxford University Press on behalf of the European Society of Cardiology

ASCVD RISK MODIFIERS IN FH

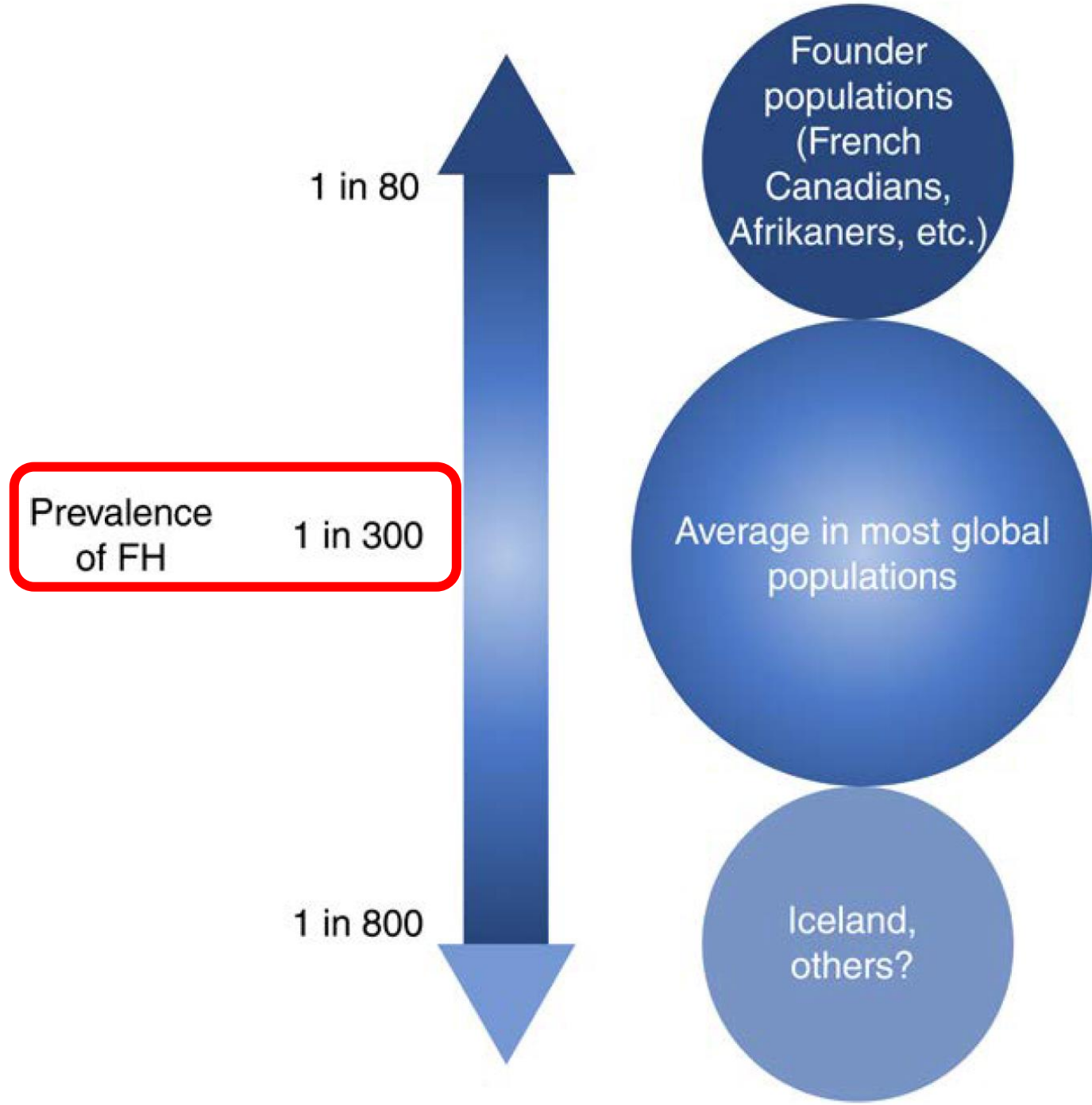
1. Severity of high LDL-C
2. High Lp(a)
3. Diabetes
4. Obesity
5. Strong family history of premature ASCVD
6. Smoking
7. Male sex
8. Hypertension
9. Late treatment onset
10. Low HDL-C
11. Imaging (CAC score)

**ΠΟΣΟ ΣΥΧΝΟ ΕΙΝΑΙ ΤΟ ΝΟΣΗΜΑ ΣΤΟΝ
ΠΛΗΘΥΣΜΟ;**

FH is more common than other genetic disorders



What Is the Prevalence of Familial Hypercholesterolemia?

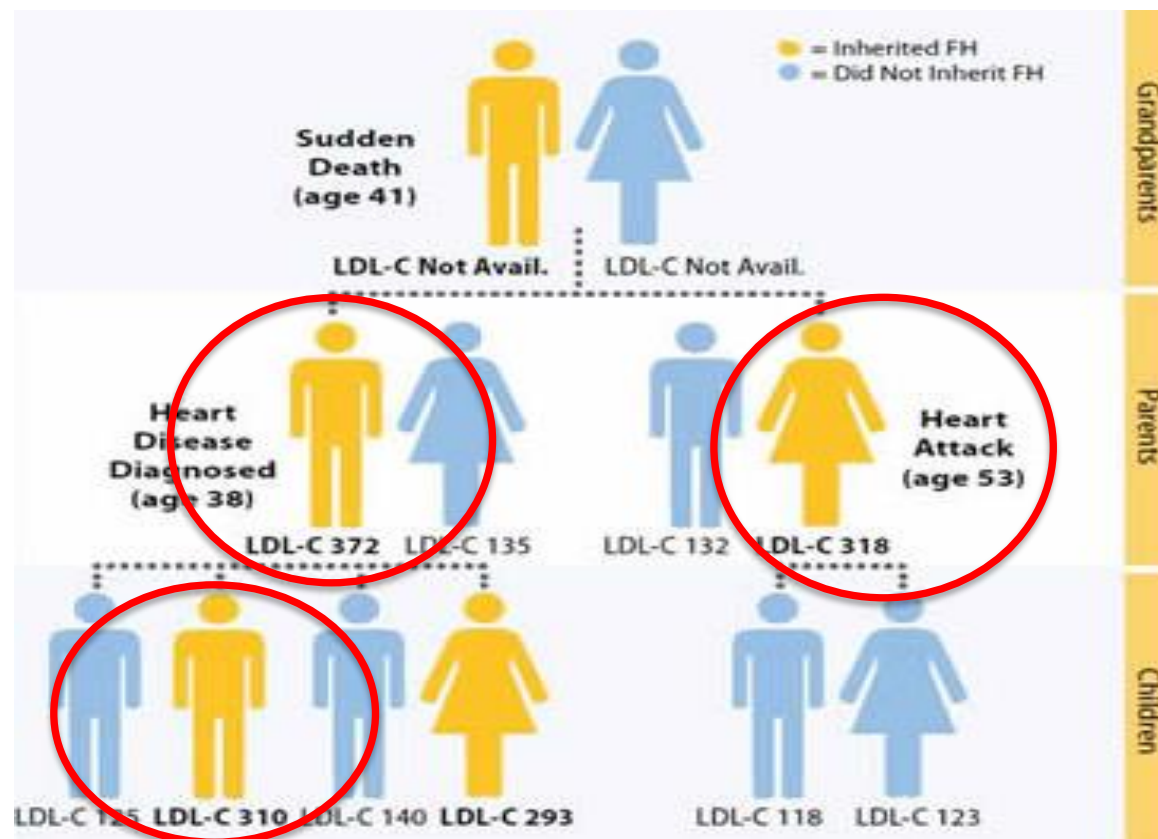


ΕΧΕΙ ΤΕΡΑΣΤΙΑ ΣΗΜΑΣΙΑ Η ΕΓΚΑΙΡΗ
ΑΝΙΧΝΕΥΣΗ ΤΩΝ ΑΤΟΜΩΝ ΤΟΥ
ΠΛΗΘΥΣΜΟΥ ΠΟΥ ΕΧΟΥΝ ΟΙΚΟΓΕΝΗ
ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ ΠΡΟΚΕΙΜΕΝΟΥ
ΝΑ ΕΦΑΡΜΟΣΘΟΥΝ ΚΑΤΑΛΛΗΛΑ
ΠΡΟΛΗΠΤΙΚΑ ΜΕΤΡΑ ΑΠΟ ΤΗΝ ΠΑΙΔΙΚΗ
ΗΛΙΚΙΑ

CASCADE SCREENING

Cardiologist/
Lipidologist

Pediatrician



Cardiologist

ORIGINAL ARTICLE

Child–Parent Familial Hypercholesterolemia Screening in Primary Care

We obtained capillary blood samples to measure cholesterol levels and to test for familial hypercholesterolemia mutations in 10,095 children 1 to 2 years of age during routine immunization visits. Children were considered to have positive

CONCLUSIONS

Child–parent screening was feasible in primary care practices at routine child immunization visits. For every 1000 children screened, 8 persons (4 children and 4 parents) were identified as having positive screening results for familial hypercholesterolemia and were consequently at high risk for cardiovascular disease. (Funded by the Medical Research Council.)

The overall mutation prevalence was 1 in 273 children

Types of Screening

Cholesterol Screening

<u>Age</u>	<u>Type</u>	<u>Criteria</u>
≥ 2 yrs of age	Selective	• 1 or both biologic parents known to have hypercholesterolemia or are receiving LLM; or • Family history of premature CVD (i.e. men < 55 yrs; women < 65 yrs); or • Whose family history is unknown (e.g. children who were adopted).
≥ 10 yrs of age*	Universal	• Regardless of general health or the presence/absence of CVD risk factors. • If normal, repeat every 5 yrs.

*Selective screening if clinically indicated.

LLM = lipid-lowering medications; CVD = cardiovascular disease

National Lipid Association Annual Summary of Clinical Lipidology 2017. J of Clinical Lipidology (2016) , S1-S50

FH Paediatric Screening

Moving Prevention From Evidence to Action:

Overcoming the Barriers to Implementation

Hybrid Event under the Auspices of the Czech EU Presidency
6th September 2022





EAS FHSC

[HOME](#)

[ABOUT](#)

[LOGIN](#)

[REGISTER](#)

[CONTACT](#)

EAS

FHSC



The EAS Familial Hypercholesterolaemia Studies Collaboration

FH Global Registry

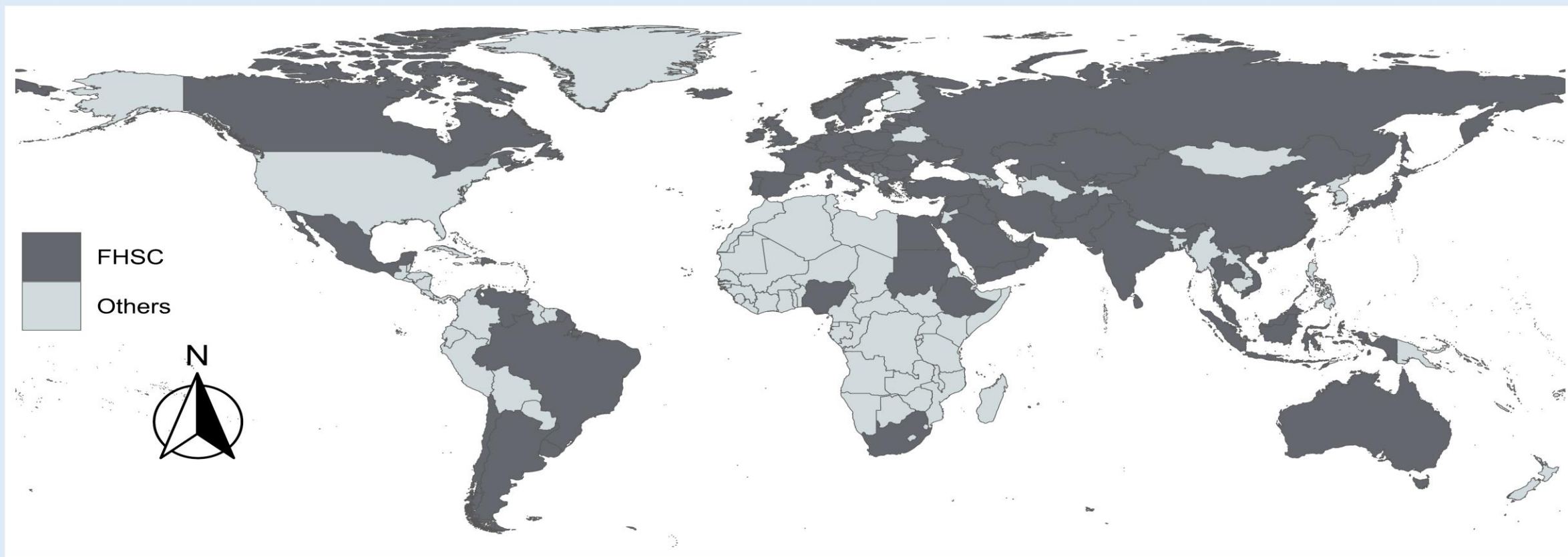




FHSC

EAS Familial
Hypercholesterolaemia
Studies Collaboration

GET INVOLVED



FHSC spans 76 countries and includes 92 [National Lead Investigators](#).
The FHSC Registry includes approx. **Approx. 80K cases across 68 countries.**

Global perspective of familial hypercholesterolaemia: a cross-sectional study from the EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC)

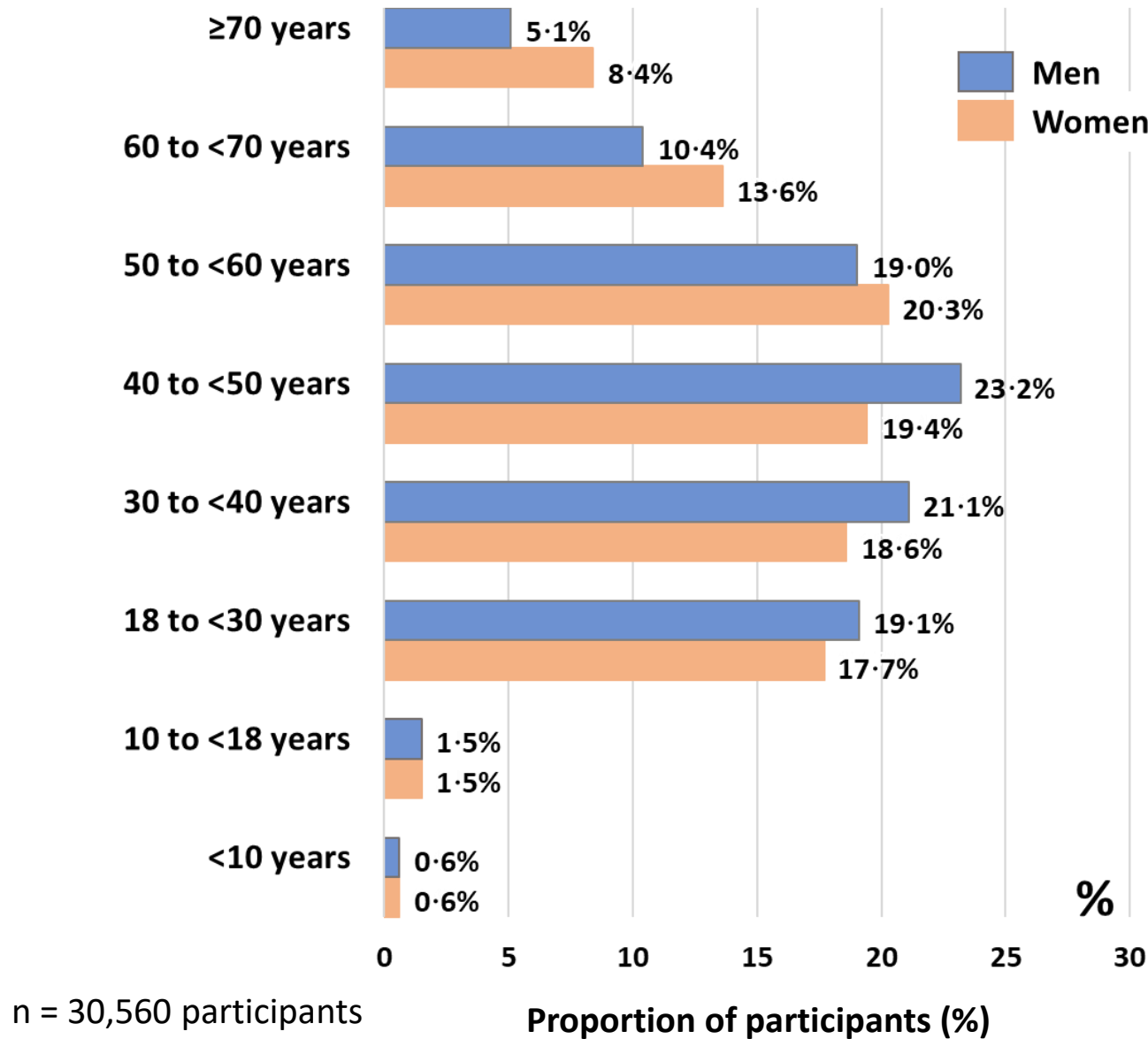


*EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC)**

Vallejo-Vaz AJ, Stevens CAT, Lyons ARM, Dharmayat KS, Freiburger T, Hovingh GK, Mata P, Raal FJ, Santos RD, Soran H, Watts GF, Abifadel M, Aguilar-Salinas CA, Alhabib KF, Alkhnifsawi M, Almahmeed W, Alnouri F, Alonso R, Al-Rasadi K, Al-Sarraf A, Al-Sayed N, Araujo F, Ashavaid TF, Banach M, Béliard S, Benn M, Binder CJ, Bogsrud MP, Bourbon M, Chlebus K, Corral P, Davletov K, Descamps OS, Durst R, Ezhov M, Gaita D, Genest J, Groselj U, Harada-Shiba M, Holven KB, Kayikcioglu M, Khovidhunkit W, Lalic K, Latkovskis G, Laufs U, **Liberopoulos E**, Lima-Martinez MM, Lin J, Maher V, Marais AD, März W, Mirrakhimov E, Miserez AR, Mitchenko O, Nawawi H, Nordestgaard BG, **Panayiotou AG**, Paragh G, Petrulioniene Z, Pojskic B, Postadzhiyan A, Raslova K, Reda A, Reiner Z, Sadiq F, Sadoh WE, Schunkert H, Shek AB, Stoll M, Stroes E, Su TC, Subramaniam T, Susekov AV, Tilney M, Tomlinson B, Truong TH, Tselepis AD, Tybjærg-Hansen A, Vázquez Cárdenas A, Viigimaa M, Wang L, Yamashita S, Tokgozoglu L, Catapano AL, Ray KK;

On behalf of the EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC) Investigators.

Age at FH diagnosis among Adults with HeFH



Age at FH diagnosis
Median 44.4 years (IQR 32.5 – 56.5)

Men	43.0 years (32.0 – 54.4)
Women	46.0 years (33.0 – 58.3)

Mean difference: –2.5 years (95%CI –2.8, –2.1)

40.2% diagnosed **age <40 years**
(Men: 42.3%; Women: 38.4%)

2.1% diagnosed **age <18 years**

HELLAS FH REGISTRY

EAS
FHSC



International collaboration
towards understanding the
contemporary burden of
Familial Hypercholesterolaemia



Ελληνική Εταιρεία Αθηροσκλήρωσης
Hellenic Atherosclerosis Society



Ελληνική Εταιρεία Αθηροσκλήρωσης

Τίτλος Μελέτης

**Εθνικό Μητρώο Καταγραφής Ασθενών με Οικογενή Υπερχοληστερολαιμία –
The Hellenic Familial Hypercholesterolemia Registry: “Hellas-FH”**

ΠΡΩΤΟΚΟΛΛΟ ΜΗΤΡΩΟΥ ΚΑΤΑΓΡΑΦΗΣ ΑΣΘΕΝΩΝ



HELLAS FH REGISTRY

HELLAS-FH Progress Report

February 2025

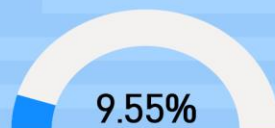
EAS
FHSC



3818

Total patients

Estimated percentage of Greek FH patients recorded

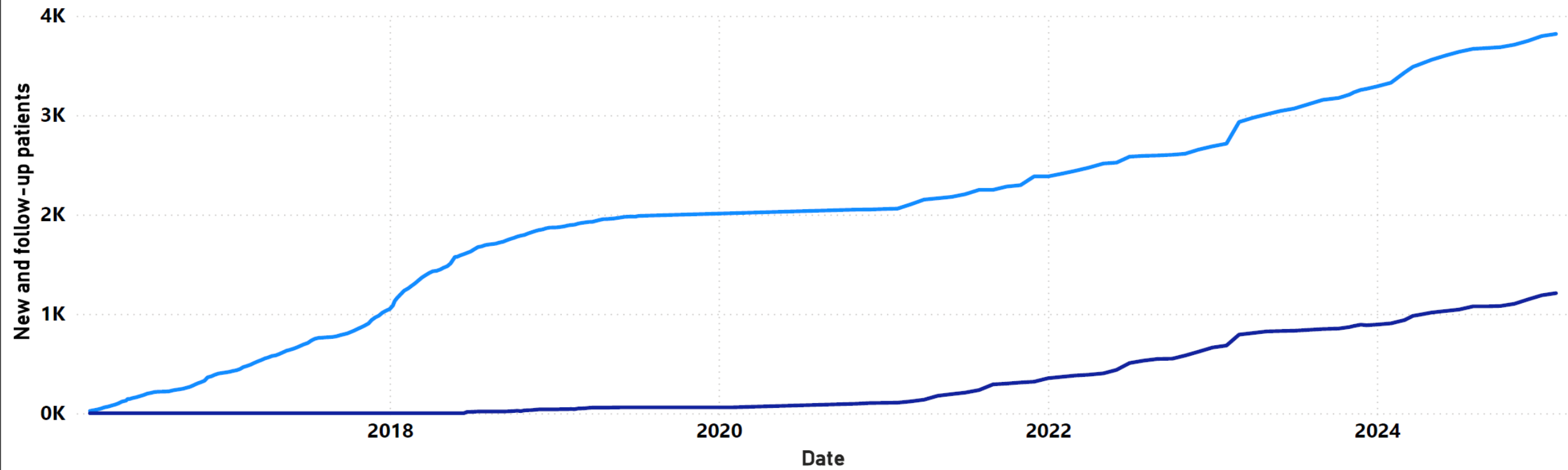


1209

Total follow-ups

HELLAS-FH progress

● New patients ● Follow up



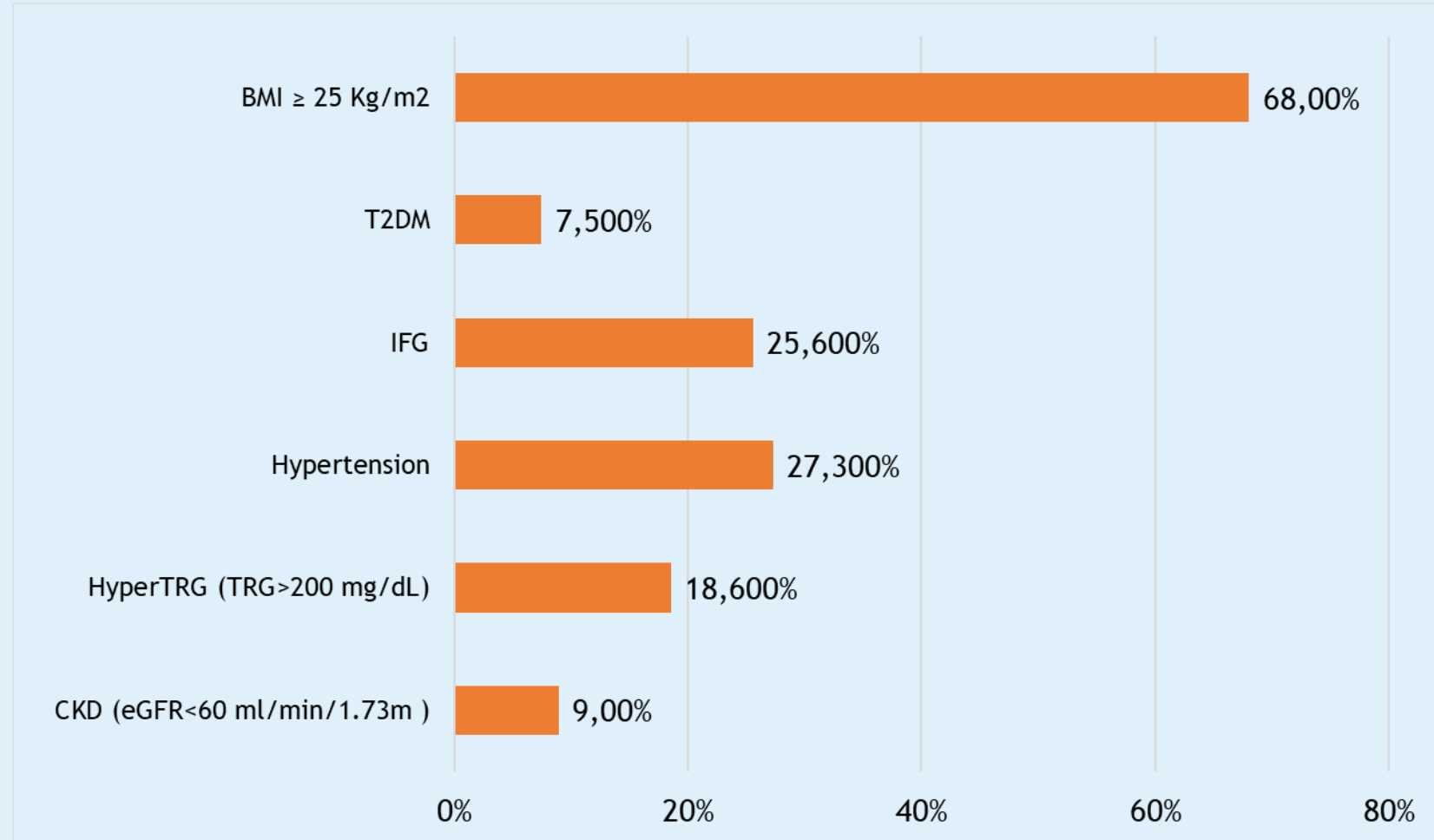
HELLAS-FH: Results

- Οι ασθενείς με FH καθυστερούν να διαγνωσθούν



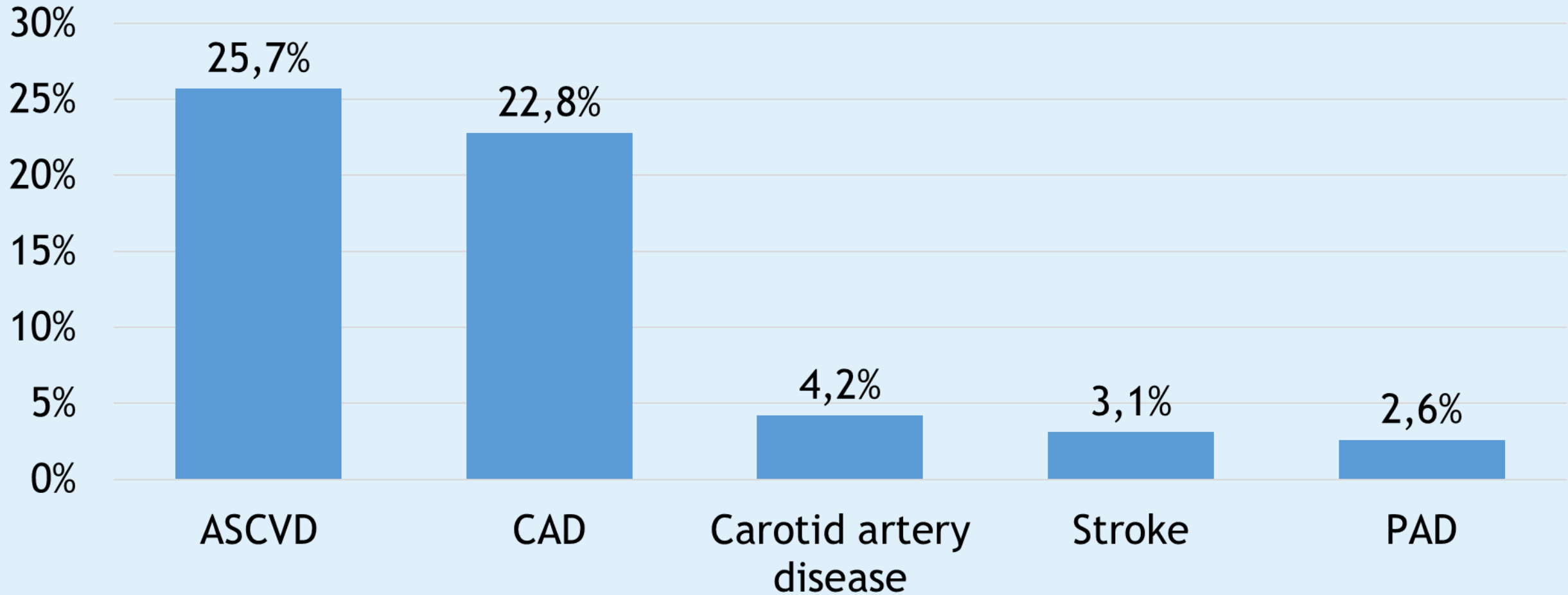
44 έτη

- Οι ασθενείς με FH έχουν συχνά συνοσηρότητες



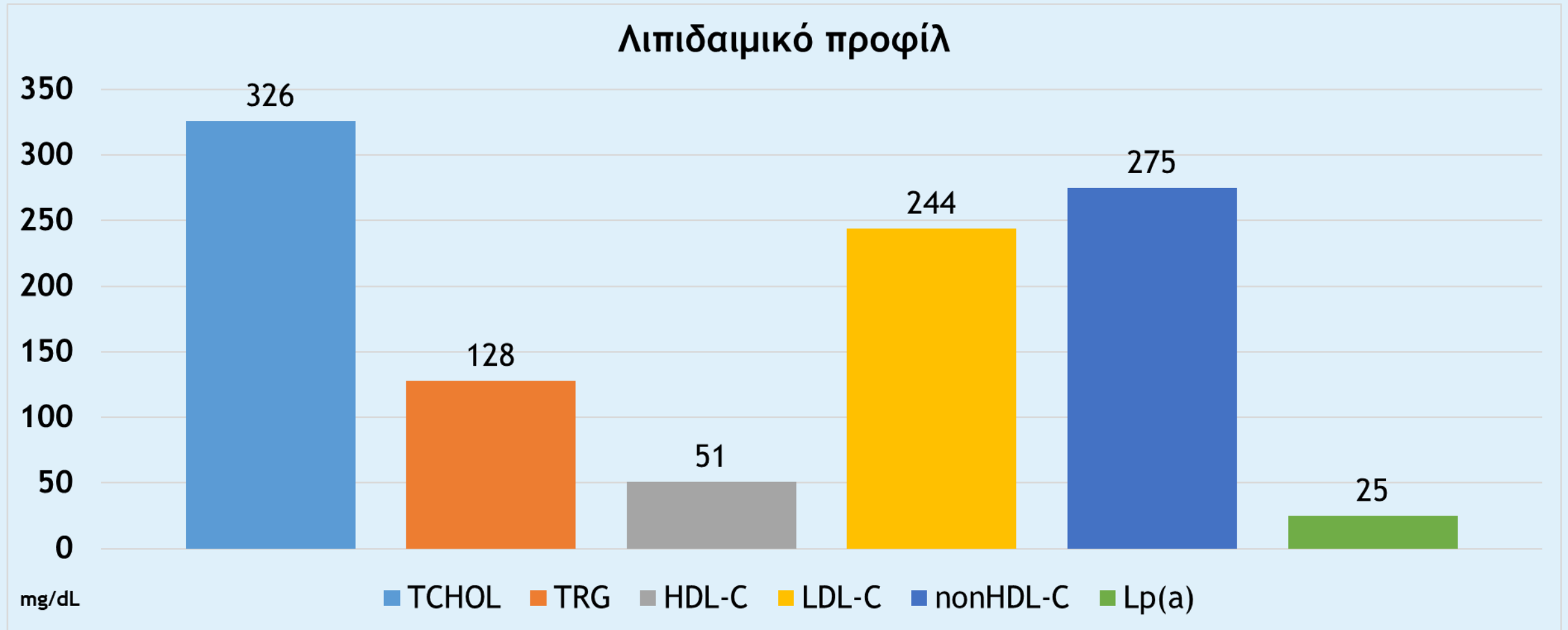
HELLAS-FH: Results

- Οι ασθενείς με FH έχουν αυξημένο επιπολασμό ASCVD



HELLAS-FH: Results

- Οι ασθενείς με FH έχουν πολύ αυξημένα επίπεδα χοληστερόλης





Οικογενής Υπερχοληστερολαιμία

Familial Hypercholesterolemia (FH)

Μάθε τι σημαίνει. Μπορεί να σε αφορά!

ΠΑΓΚΟΣΜΙΑ ΗΜΕΡΑ ΟΙΚΟΓΕΝΟΥΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑΣ

Familial Hypercholesterolemia (FH)

24 ΣΕΠΤΕΜΒΡΙΟΥ

Μάθε τι σημαίνει, μπορεί να σε αφορά!

www.hellasfh.gr

Τι είναι η ΟΙΚΟΓΕΝΗΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ (FH);

Είναι η πιο συχνή **κληρονομική** νόσος του μεταβολισμού (1:250 άτομα). Οι άνθρωποι με οικογενή υπερχοληστερολαιμία έχουν γεννηθεί με πολύ αυξημένα επίπεδα LDL (“κακής”) χοληστερόλης.

Πρώιμα Καρδιακά Επεισόδια



Ανδρες με FH χωρίς θεραπεία έχουν 50% πιθανότητα να εμφανίσουν καρδιακό επεισόδιο έως την ηλικία των 50 ετών.

Γυναίκες με FH χωρίς θεραπεία έχουν 30% πιθανότητα να εμφανίσουν καρδιακό επεισόδιο έως την ηλικία των 60 ετών.

Αυξημένος Κίνδυνος



Καρδιακού
Επεισοδίου



Εγκεφαλικού
Επεισοδίου

Πρόωρος θάνατος



ΓΝΩΡΙΣΤΕ ΤΑ ΣΗΜΑΔΙΑ



Πολύ υψηλή LDL (“κακή”) χοληστερόλη σε μικρή ηλικία.
>160 mg/dL στα παιδιά
>190 mg/dL στους ενήλικες



Οξίδια
‘στο δέρμα
‘στους τένοντες
‘στα βλέφαρα



Γεροντότοξο:
Εμφάνιση λευκού
δακτυλίου στον
βολβό των ματιών.



ΘΕΡΑΠΕΙΑ

Φαρμακευτική αγωγή (στατίνες, δέσμευση χολικών οξέων, αναστολείς απορρόφησης της χοληστερόλης, αναστολείς PCSK9)



Διατροφή
& άσκηση

Θεραπεία αφαίρεσης της LDL από την κυκλοφορία του αίματος σε πολύ σοβαρές περιπτώσεις



Συνεχής
παρακολούθηση



Αν ένας από τους δύο γονείς πάσχει από Οικογενή Υπερχοληστερολαιμία, υπάρχει 50% πιθανότητα το κάθε παιδί να την κληρονομήσει. Σκεφτείτε τον έγκαιρο έλεγχο των παιδιών, αν πάσχετε από την ασθένεια.



HoFH

Ομόζυγη Οικογενής Υπερχοληστερολαιμία

μια σπάνια θανατηφόρα μορφή Οικογενούς
Υπερχοληστερολαιμίας



ΕΙΝΑΙ ΠΑΓΚΟΣΜΙΑ

Η HoFH είναι μια σπάνια πάθηση που επηρεάζει περίπου 1 στους 300.000 ανθρώπους παγκοσμίως.



ΕΙΝΑΙ ΚΛΗΡΟΝΟΜΙΚΗ

Η HoFH είναι κληρονομική. Αν κληρονομήσεις την μετάλλαξη και από τους δύο γονείς τότε πάσχεις από Ομόζυγο Οικογενή Υπερχοληστερολαιμία



ΜΠΟΡΕΙ ΝΑ ΔΙΑΓΝΩΣΘΕΙ

Για την διάγνωση της HoFH χρειάζεται μια απλή εξέταση αίματος, μια κλινική εξέταση από τον γιατρό και ένα οικογενειακό ιστορικό. Η HoFH μπορεί να επιβεβαιωθεί με γενετικό έλεγχο. Τα κλινικά σημεία και τα συμπτώματα της HoFH, ακόμα και οι τιμές της LDL χοληστερόλης, διαφέρουν σε κάθε άνθρωπο.



ΠΡΟΚΑΛΕΙ ΠΡΩΙΜΗ ΝΟΣΟ



Εάν αφεθεί χωρίς θεραπεία, είναι πιθανό να εμφανισθεί καρδιακή προσβολή ή αιφνίδιος θάνατος ή στένωση της αορτικής βαλβίδας ακόμα και στην εφηβεία.



ΕΞΑΙΡΕΤΙΚΑ ΥΨΗΛΗ ΧΟΛΗΣΤΕΡΟΛΗ

Η HoFH οδηγεί σε επιθετική αθηροσκλήρωση (βλάβη των αρτηριών από την εναπόθεση λιπιδίων στο τοίχωμά τους).

Η HoFH ΘΕΡΑΠΕΥΕΤΑΙ

Η αλλαγές στον τρόπο ζωής δεν αρκούν για να θεραπεύσουν μια τόσο σοβαρή πάθηση. Απαιτείται ένας σωστός συνδυασμός φαρμακευτικής αγωγής και σε ορισμένες περιπτώσεις LDL αφαίρεσης από το αίμα. Πάντα να συμβουλευέστε το γιατρό σας.



ΘΕΡΑΠΕΙΕΣ

Η χορήγηση υπολιπιδαιμικής θεραπείας είναι πολύ αποτελεσματική.

Περιλαμβάνει την χορήγηση στατινών, εζετιμίμης, κολεσεβαλάνης, αναστολέων της PCSK9 και λομιταπίδης.



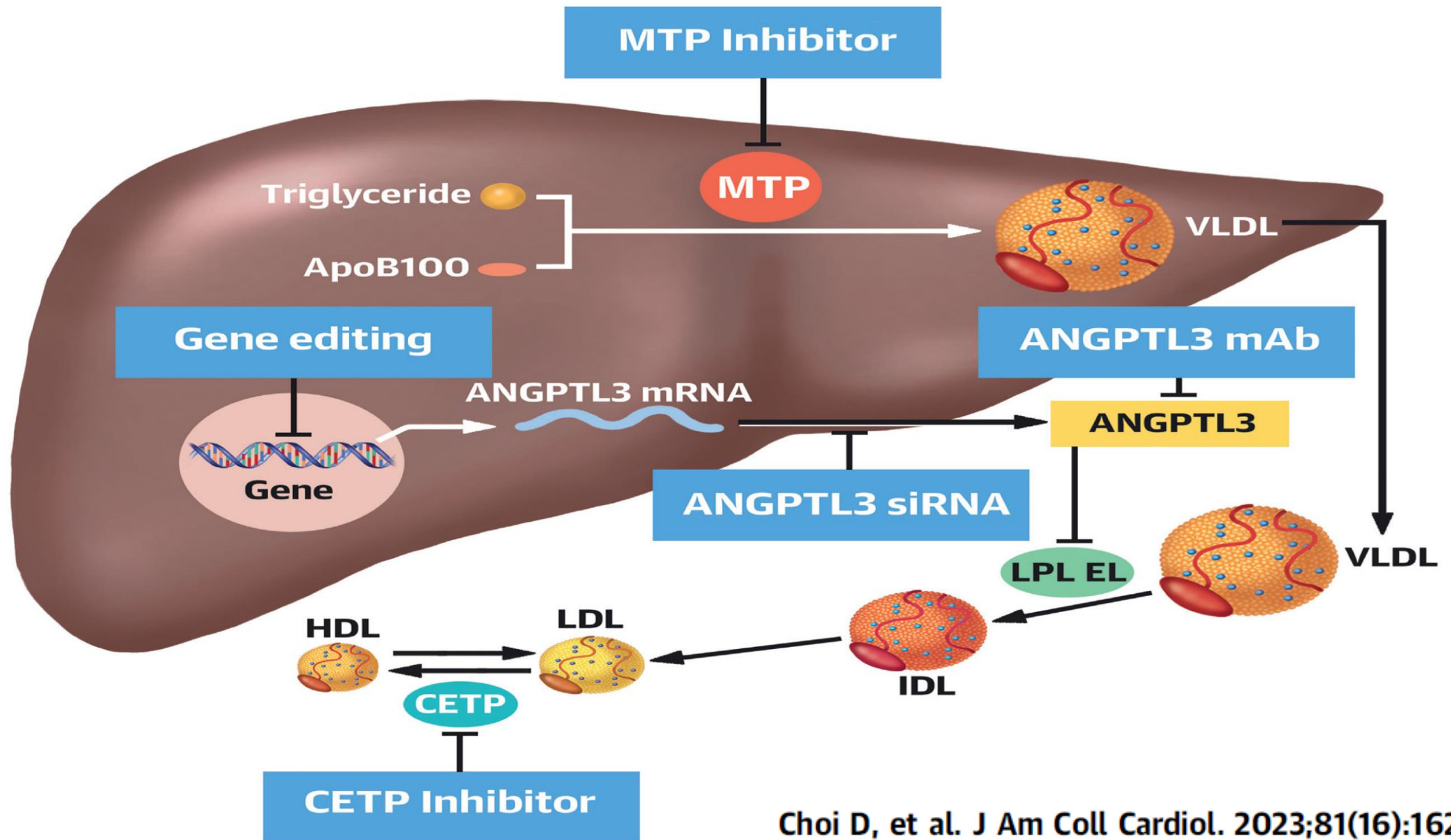
Με αυτή τη διαδικασία αφαιρείται η LDL από το αίμα.

ΠΩΣ ΘΑ ΘΕΡΑΠΕΥΣΟΥΜΕ ΤΟΝ ΑΣΘΕΝΗ;

LDL-R DEPENDENT TREATMENTS

1. High-intensity statins
2. Ezetimibe
3. Bempedoic acid
4. Resins
5. PCSK9i

LDL-R INDEPENDENT TREATMENTS

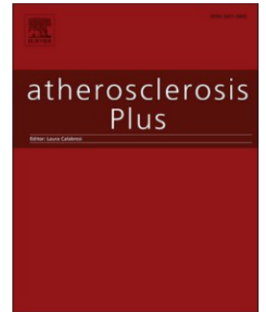




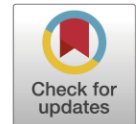
Contents lists available at [ScienceDirect](#)

Atherosclerosis Plus

journal homepage: www.elsevier.com/locate/atherosclerosis



Executive summary of the Hellenic Atherosclerosis Society guidelines for the diagnosis and treatment of dyslipidemias - 2023



Katsiki N^{a,b,1}, Filippatos Td^{c,1}, Vlachopoulos C^d, Panagiotakos D^e, Milionis H^f, Tselepis A^g, Garoufi A^h, Rallidis Lⁱ, Richter D^j, Nomikos T^e, Kolovou G^k, Kypreos K^{b,1}, Chrysohoou C^m, Tziomalos Kⁿ, Skoumas I^o, Koutagiar I^p, Attilakos A^q, Papagianni M^r, Boutari C^s, Kotsis V^t, Pitsavos C^u, Elisaf M^{v,2}, Tsioufis K^w, Liberopoulos E^{x,*}

LDL-C TARGETS 2023

CVD RISK

VERY HIGH RISK

- ESTABLISHED ASCVD
- DIABETES WITH TARGET ORGAN DAMAGE or ≥ 3 MAJOR RISK FACTORS
- FAMILIAL HYPERCHOLESTEROLEMIA PLUS ≥ 1 MAJOR RISK FACTOR
- CKD 4-5
- HELLENIC SCORE II $\geq 10\%$

↓ LDL-C <55 mg/dL
PLUS
LDL-C >50%

HIGH RISK

- SEVERE RISK FACTOR
- FH WITHOUT ANY MAJOR RISK FACTOR
- DIABETES ≥ 10 YEARS PLUS ≥ 1 MAJOR RISK FACTOR
- CKD 3
- AUTOIMMUNE RHEUMATIC DISEASE/HIV INFECTION
- HELLENIC SCORE II ≥ 5 -<10%

↓ LDL-C <70 mg/dL
PLUS
LDL-C ~50%

MODERATE RISK

- DIABETES <10 YEARS IN PATIENTS <50 YEARS
- HELLENIC SCORE II ≥ 1 -<5%

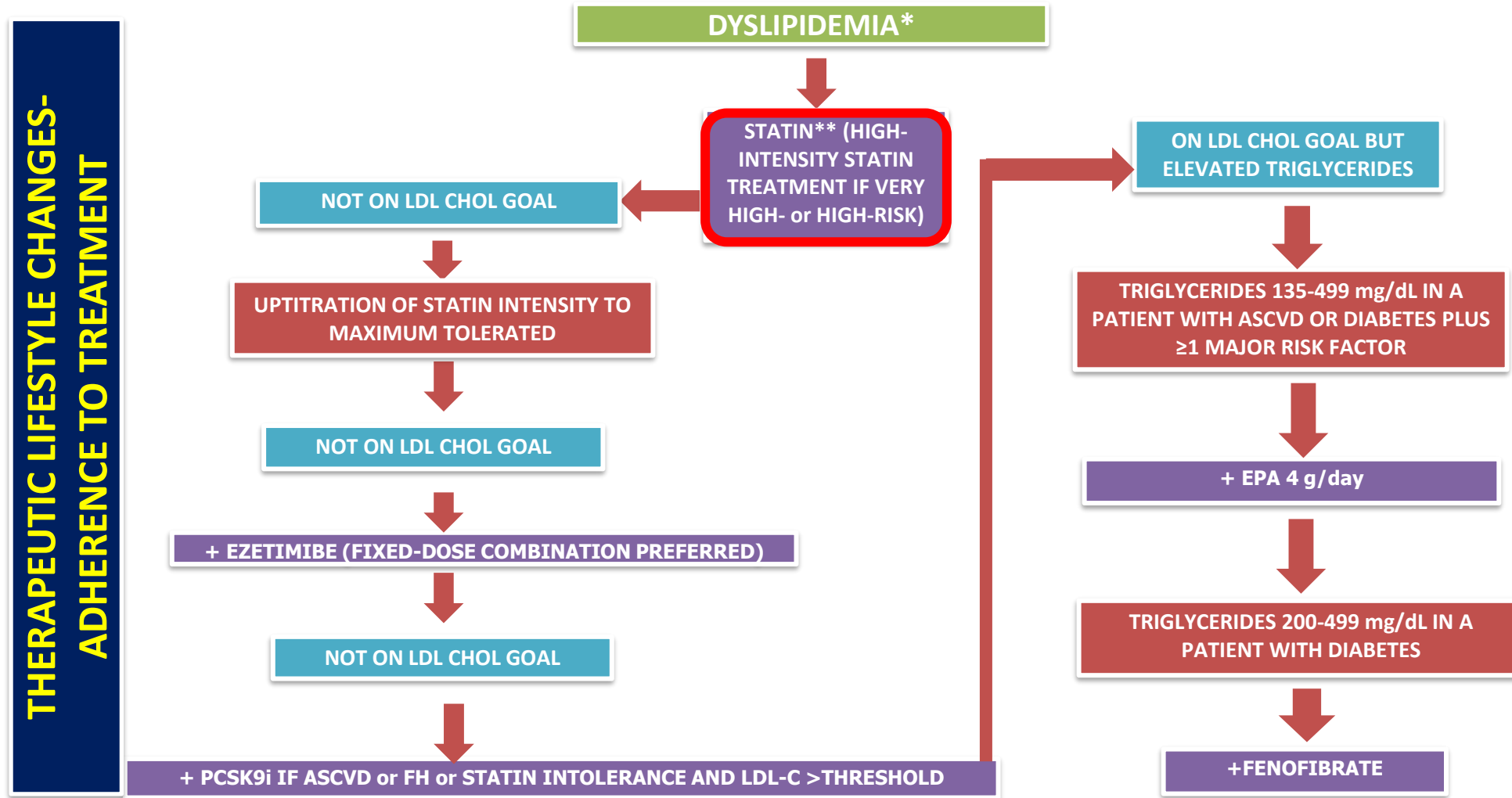
LDL-C <100
mg/dL

LOW RISK

- HELLENIC SCORE II <1%

LDL-C <116
mg/dL

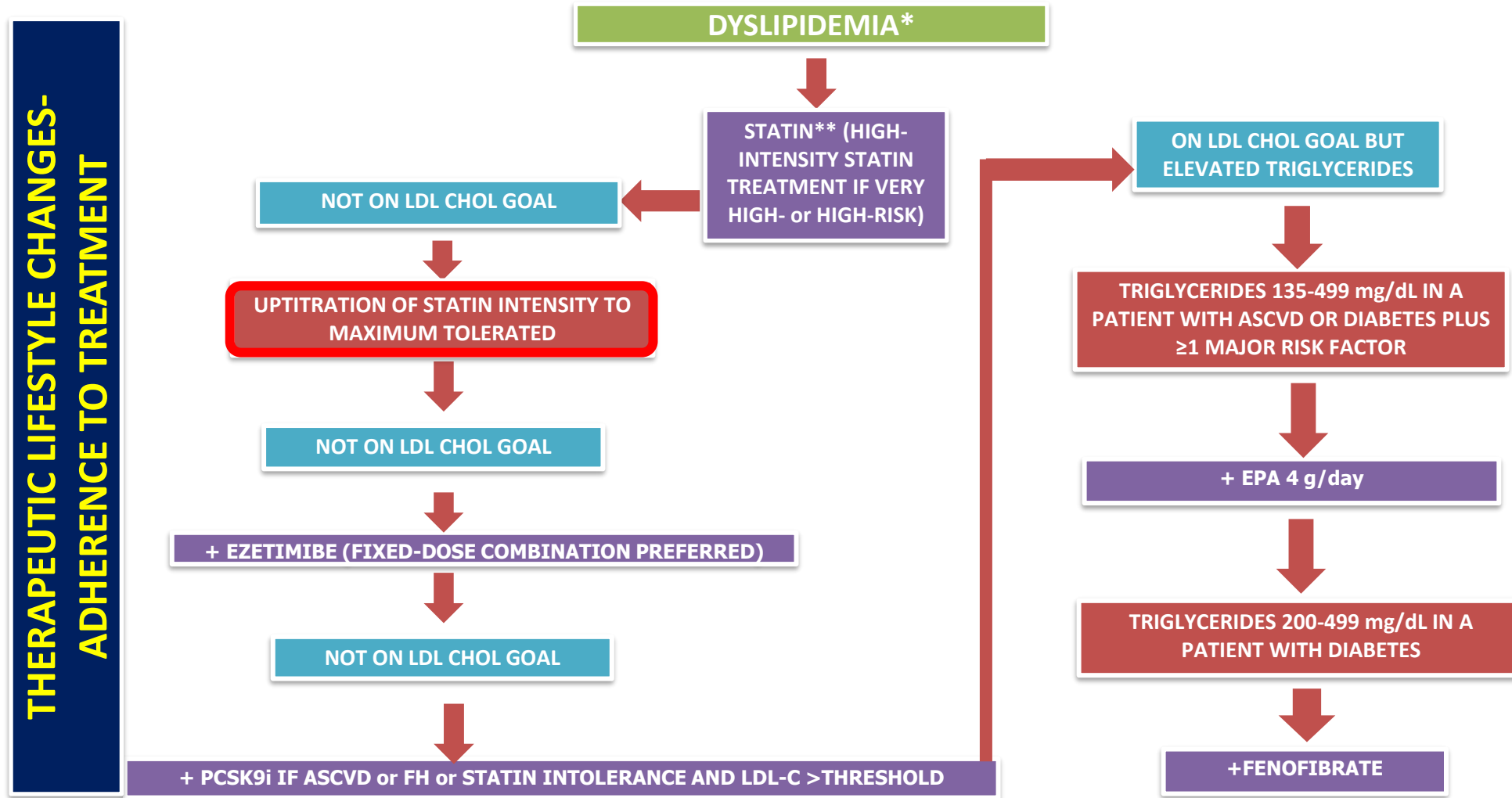
ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023



*IF TRIGLYCERIDES > 500 mg/dL → START IMMEDIATELY WITH FENOFIBRATE + STATIN ± HIGHLY PURIFIED OMEGA-3 FATTY ACIDS

**IF LDL-C > 110 mg/dL IN A PATIENT WITH ASCVD → START IMMEDIATELY WITH HIGH INTENSITY STATIN PLUS EZETIMIBE (FIXED-DOSE COMBINATION PREFERRED)

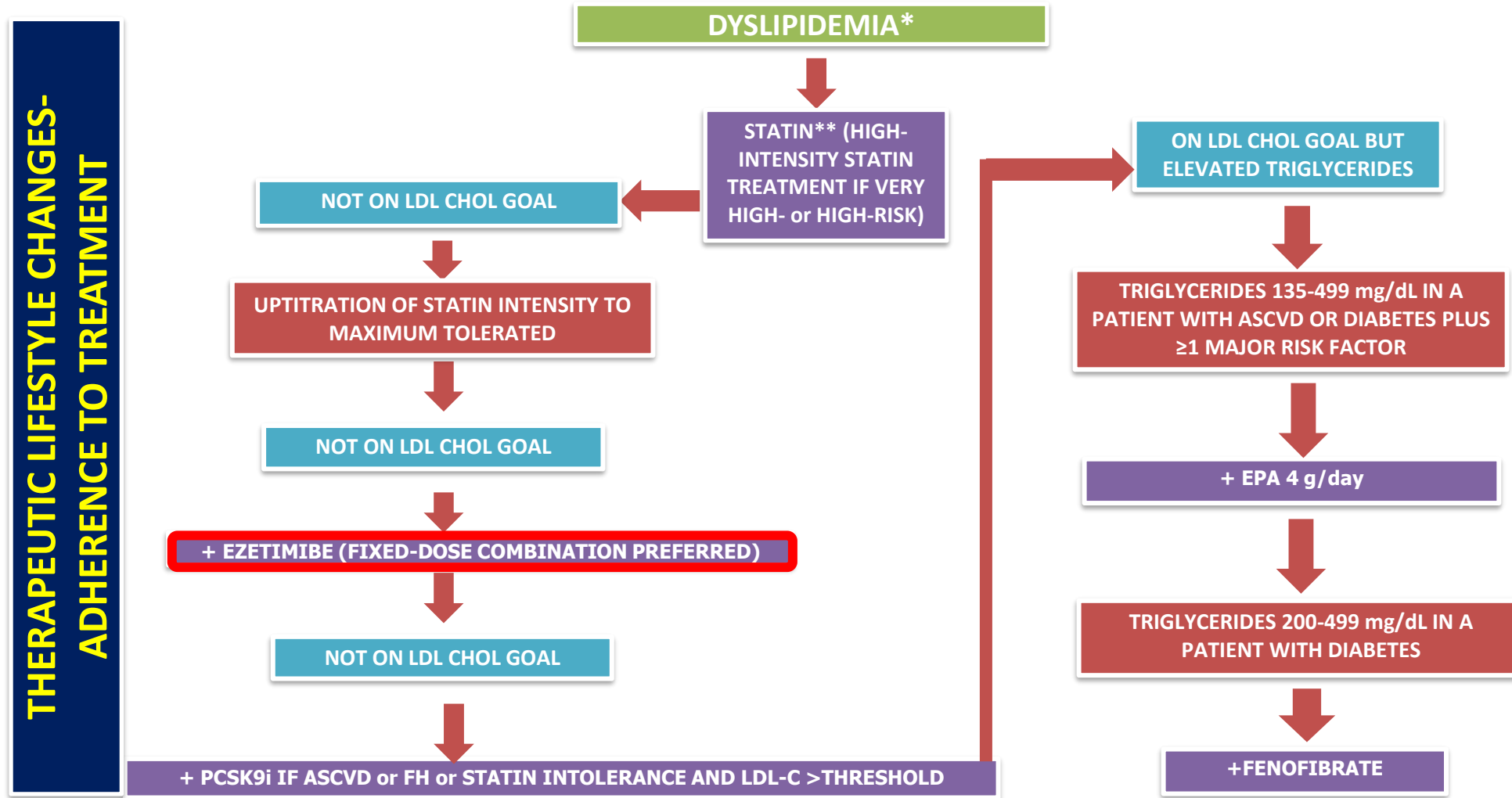
ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023



*IF TRIGLYCERIDES > 500 mg/dL → START IMMEDIATELY WITH FENOFIBRATE + STATIN ± HIGHLY PURIFIED OMEGA-3 FATTY ACIDS

**IF LDL-C > 110 mg/dL IN A PATIENT WITH ASCVD → START IMMEDIATELY WITH HIGH INTENSITY STATIN PLUS EZETIMIBE (FIXED-DOSE COMBINATION PREFERRED)

ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023



*IF TRIGLYCERIDES>500 mg/dL → START IMMEDIATELY WITH FENOFIBRATE + STATIN ± HIGHLY PURIFIED OMEGA-3 FATTY ACIDS

**IF LDL-C>110 mg/dL IN A PATIENT WITH ASCVD → START IMMEDIATELY WITH HIGH INTENSITY STATIN PLUS EZETIMIBE (FIXED-DOSE COMBINATION PREFERRED)

ΑΝΤΙΜΕΤΩΠΙΖΟΝΤΑΣ ΤΟΝ ΑΣΘΕΝΗ ΜΕ ΟΙΚΟΓΕΝΗ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ

ROSUVASTATIN 40 mg X 1



LDL CHOL κατά ~55% → LDL CHOL 126 mg/dL

ΑΜΕΣΗ ΕΝΑΡΞΗ!

ΕΠΙΤΥΓΧΑΝΟΝΤΑΣ ΤΟΥΣ ΣΤΟΧΟΥΣ ΤΗΣ ΘΕΡΑΠΕΙΑΣ

ΠΡΟΣΘΗΚΗ ΕΖΕΤΙΜΙΒΕ 10 mg X 1

↓ LDL CHOL κατά 20% → LDL CHOL 101 mg/dL

**ΠΡΟΣΟΧΗ! ΣΥΜΒΟΥΛΗ ΓΙΑ ΔΙΑΚΟΠΗ
ΣΤΑΤΙΝΗΣ + ΕΖΕΤΙΜΙΠΤΗΣ ~3 ΜΗΝΕΣ
ΠΡΙΝ ΠΡΟΓΡΑΜΜΑΤΙΣΜΟ ΕΠΟΜΕΝΗΣ
ΚΥΗΣΗΣ**

**ΣΤΗ ΔΙΑΡΚΕΙΑ ΤΗΣ ΚΥΗΣΗΣ ΚΑΙ ΤΗΣ
ΓΑΛΟΥΧΙΑΣ ΕΠΙΤΡΕΠΕΤΑΙ ΜΟΝΟ Η
ΚΟΛΕΣΕΒΕΛΑΜΗ-LDL ΑΦΑΙΡΕΣΗ ΣΕ ΒΑΡΙΕΣ
ΠΕΡΙΠΤΩΣΕΙΣ**

ΣΤΗ ΔΙΑΡΚΕΙΑ ΤΗΣ ΚΥΗΣΗΣ ΚΑΙ ΤΗΣ
ΓΑΛΟΥΧΙΑΣ ΕΠΙΤΡΕΠΕΤΑΙ ΜΟΝΟ Η
ΚΟΛΕΣΕΒΕΛΑΜΗ-LDL ΑΦΑΙΡΕΣΗ ΣΕ ΒΑΡΙΕΣ
ΠΕΡΙΠΤΩΣΕΙΣ



U.S. FOOD & DRUG
ADMINISTRATION

Statins: Drug Safety Communication - FDA Requests Removal of Strongest Warning Against Using Cholesterol-lowering Statins During Pregnancy

[Subscribe to Email Updates](#)

[f Share](#)

[t Tweet](#)

[in LinkedIn](#)

[✉ Email](#)

[🖨 Print](#)

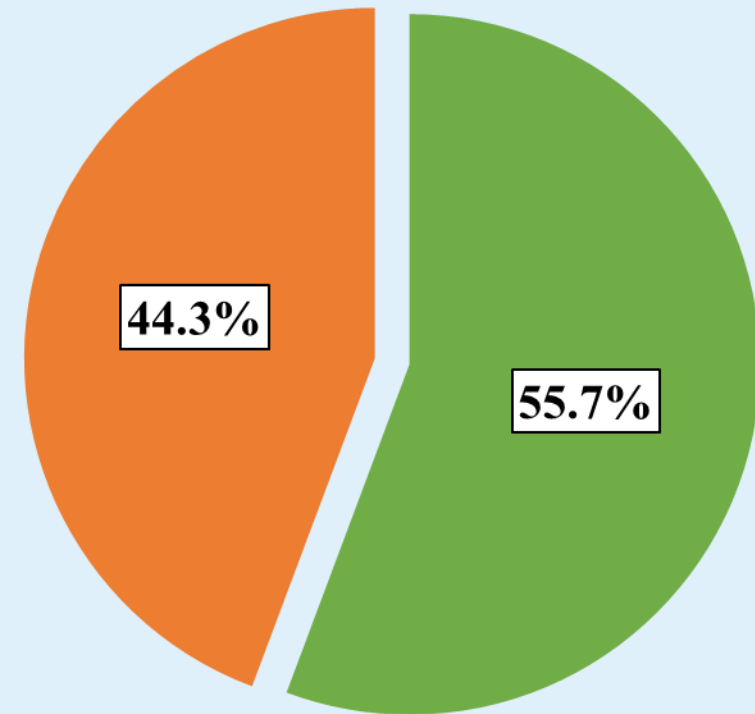
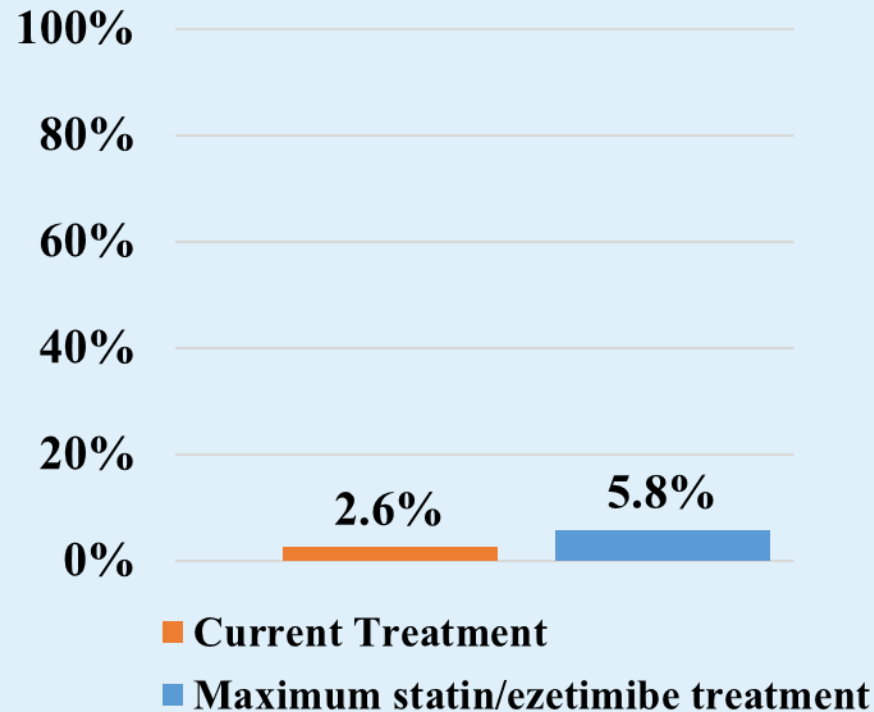
[Posted 07/20/2021]

FDA expects removing the contraindication will enable health care professionals and patients to make individual decisions about benefit and risk, especially for those at very high risk of heart attack or stroke. This includes patients with homozygous familial hypercholesterolemia and those who have previously had a heart attack or stroke.

HELLAS-FH: Results

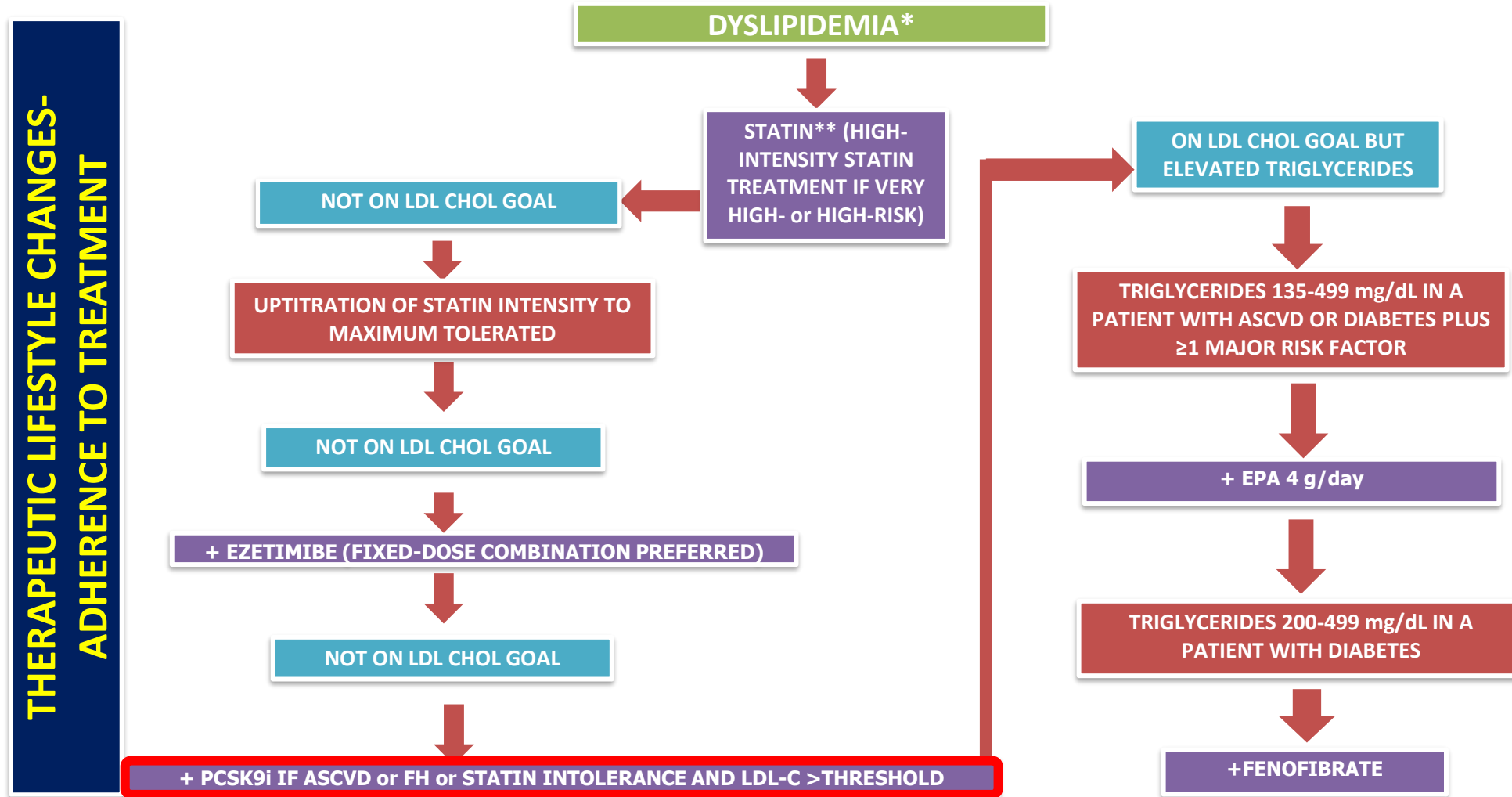
- Οι ασθενείς με FH χρήζουν επιπρόσθετης υπολιπιδαιμικής θεραπείας
- Οι ασθενείς με FH συχνά χρήζουν θεραπείας με PCSK9i

LDL-C target achievement



■ Eligible ■ Non Eligible

ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023



*IF TRIGLYCERIDES > 500 mg/dL → START IMMEDIATELY WITH FENOFIBRATE + STATIN ± HIGHLY PURIFIED OMEGA-3 FATTY ACIDS

**IF LDL-C > 110 mg/dL IN A PATIENT WITH ASCVD → START IMMEDIATELY WITH HIGH INTENSITY STATIN PLUS EZETIMIBE (FIXED-DOSE COMBINATION PREFERRED)

ELIGIBLE PATIENTS FOR PCSK9 INHIBITORS

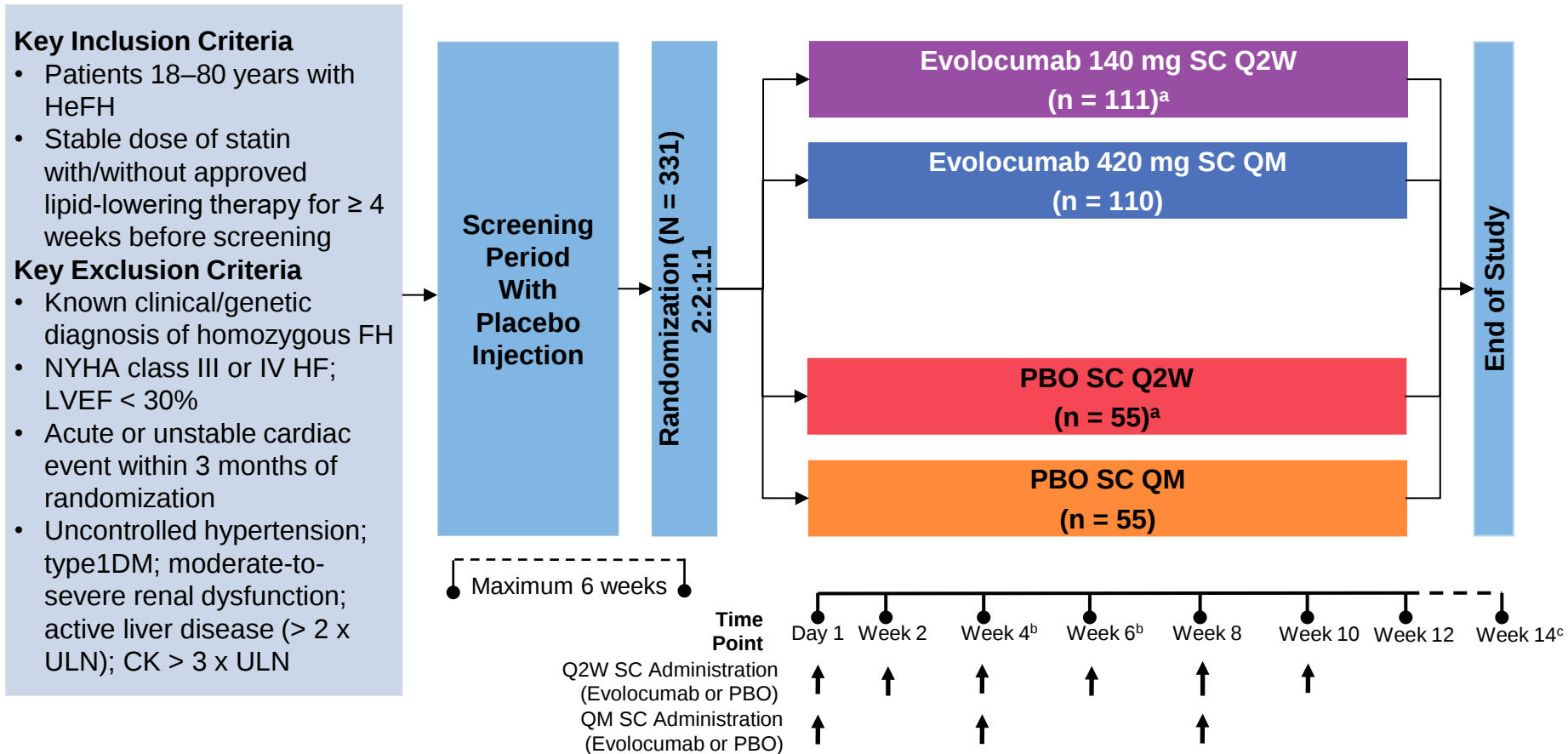
1. ASCVD PLUS FH OR RECURRENT/PROGRESSIVE DISEASE DURING THE LAST 2 YEARS OR PREMATURE ASCVD (MEN <45/WOMEN <55 YEARS) WITH LDL-C $\geq$ 70 mg/dL

2. OTHER ASCVD AND LDL-C $\geq$ 100 mg/dL

3. FAMILIAL HYPERCHOLESTEROLEMIA AND LDL-C $\geq$ 100 mg/dL

ON HIGH-INTENSITY STATIN
TREATMENT
(ATORVASTATIN 40/80 mg,
ROSUVASTATIN 20/40 mg)
PLUS EZETIMIBE 10 mg OR
MAXIMUM TOLERATED
STATIN PLUS EZETIMIBE
WHEN STATIN INTOLERANT

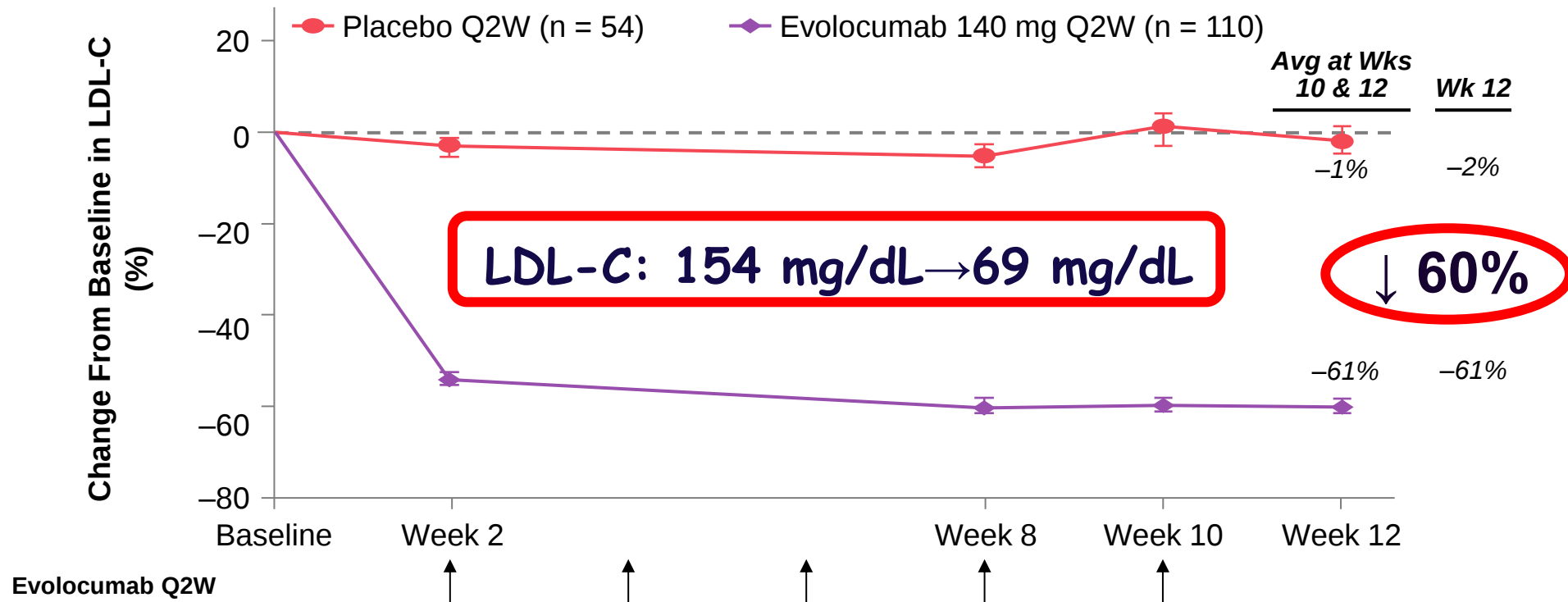
RedUction of LDL-C With PCSK9 InhibiTion in HETeRozygous FAmilial HyperchOlesteRolemia DIsorder Study-2 (RUTHERFORD-2)



^aOne patient in each of the Q2W dosing groups withdrew consent before treatment and did not receive study drug; the remaining 329 patients received ≥ 1 dose of study drug. ^bInjections were self-administered at home. ^cFinal AE data were collected by telephone for patients who received the study drug Q2W.

AE = adverse event; CK = creatine kinase; FH = familial hypercholesterolemia; HeFH = heterozygous familial hypercholesterolemia; HF = heart failure; LDL-C = low-density lipoprotein cholesterol; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PBO = placebo; Q2W = once every 2 weeks; QM = once monthly; SC = subcutaneous; type 1 DM = type 1 diabetes mellitus; ULN = upper limit of normal.

Evolocumab Q2W Significantly Reduces LDL-C by 61% in Patients With HeFH



The treatment difference of evolocumab compared with placebo at the mean of weeks 10 and 12 and at week 12 was –60% and –59%, respectively ($P < 0.0001$)

The arrows below the graph represent time points of evolocumab administration. Error bars are standard errors. The percentage change in LDL-C was ascertained by the Friedewald formula, with reflexive testing through preparative ultracentrifugation when the calculated LDL-C was ≤ 40 mg/dL (1.0 mmol/L) or triglyceride concentration was ≥ 400 mg/dL (4.5 mmol/L).

Avg = average; HeFH = heterozygous familial hypercholesterolemia; LDL-C = low-density lipoprotein cholesterol; Q2W = once every 2 weeks; Wk = week.

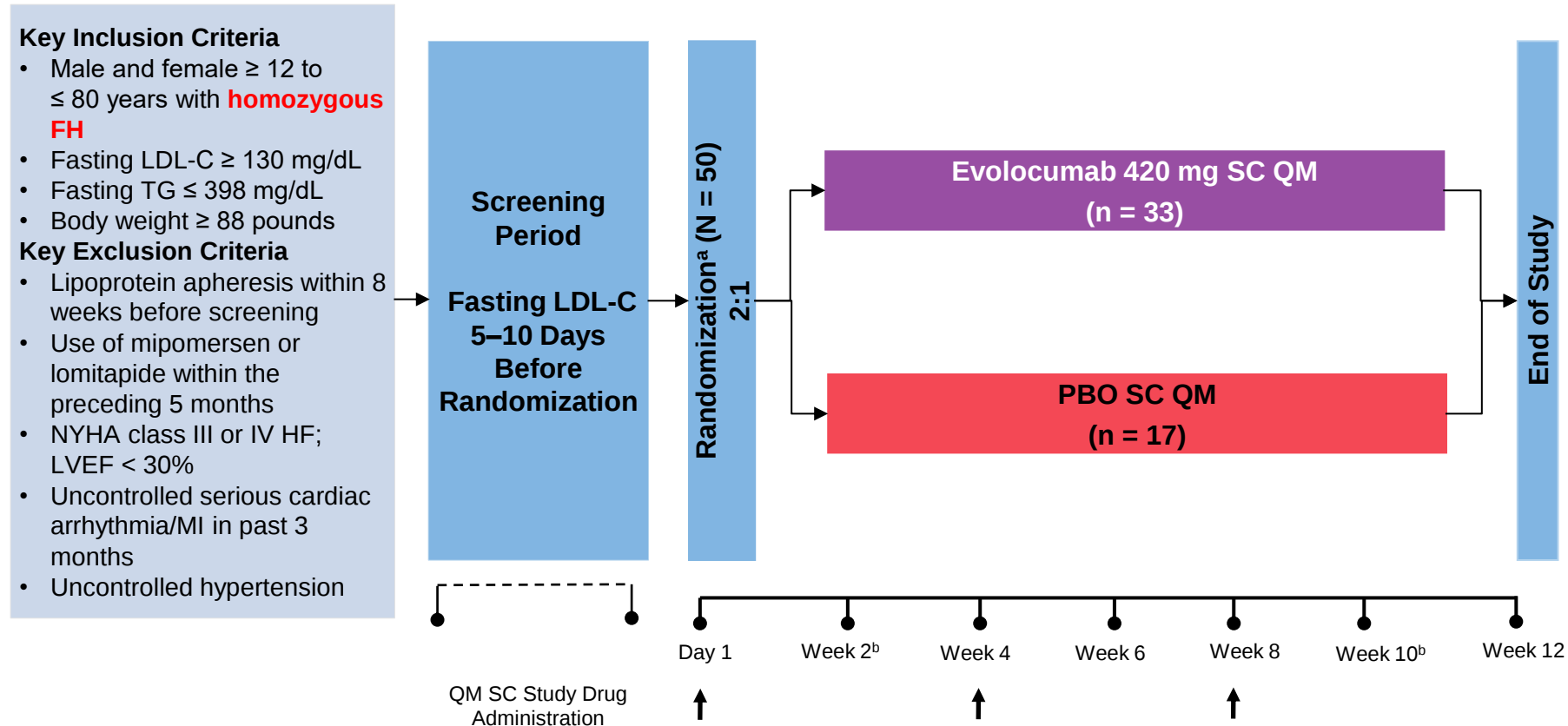
Adapted from Raal FJ, et al. *Lancet*. 2015;385:331-340.

ΕΠΙΤΥΓΧΑΝΟΝΤΑΣ ΤΟΥΣ ΣΤΟΧΟΥΣ ΤΗΣ ΘΕΡΑΠΕΙΑΣ

ΠΡΟΣΘΗΚΗ EVOLOCUMAB 140 mg Q2W

↓ LDL CHOL κατά 60% → LDL CHOL 41 mg/dL

Trial Evaluating PCSK9 Antibody in Subjects With LDL Receptor Abnormalities Part B (TESLA)



^aRandomization stratified by screening LDL-C (< 425 mg/dL or ≥ 425 mg/dL)

^bWeek 2 and week 10 study visits were optional. 1 mmol/L LDL-C = 38.6 mg/dL; 1 mmol/L TG = 88.5 mg/dL.

AE = adverse event; FH = familial hypercholesterolemia; HF = heart failure; LDL-C = low-density lipoprotein cholesterol; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PBO = placebo; QM = once monthly; SC = subcutaneous.

Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial

Frederick J Raal, Narimon Honarpour, Dirk J Blom, G Kees Hovingh, Feng Xu, Rob Scott, Scott M Wasserman, Evan A Stein, for the TESLA Investigators*

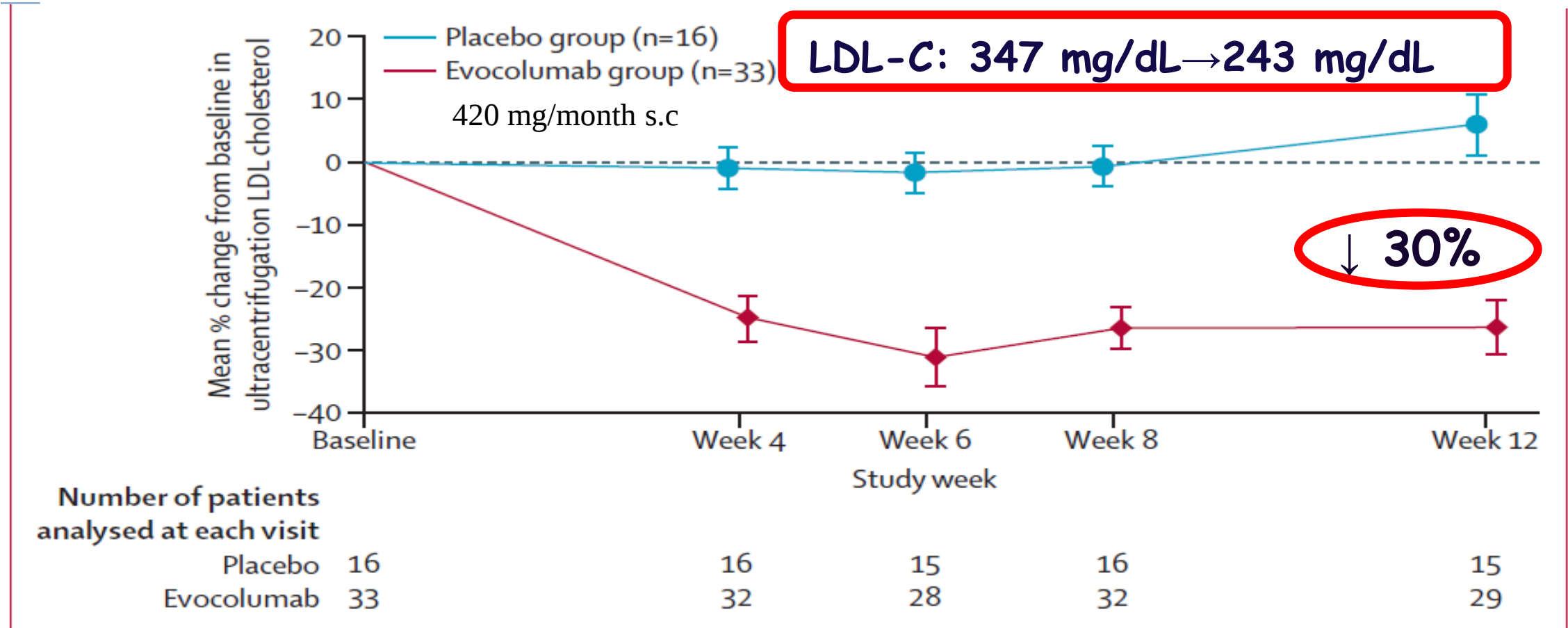
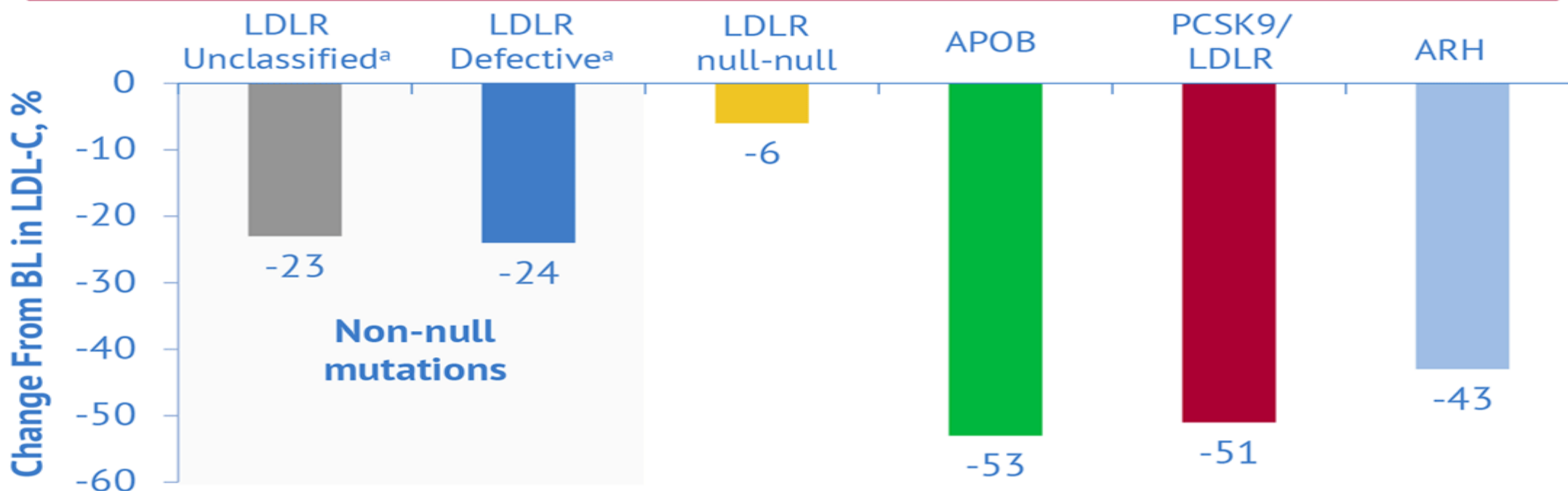


Figure 2: Mean percentage change in ultracentrifugation LDL cholesterol concentration from baseline to week 12

Impact of Mutation Status on Therapeutic Efficacy of PCSK9 Inhibitors



TAUSSIG: Evolocumab in Patients With HoFH (N = 54)⁶

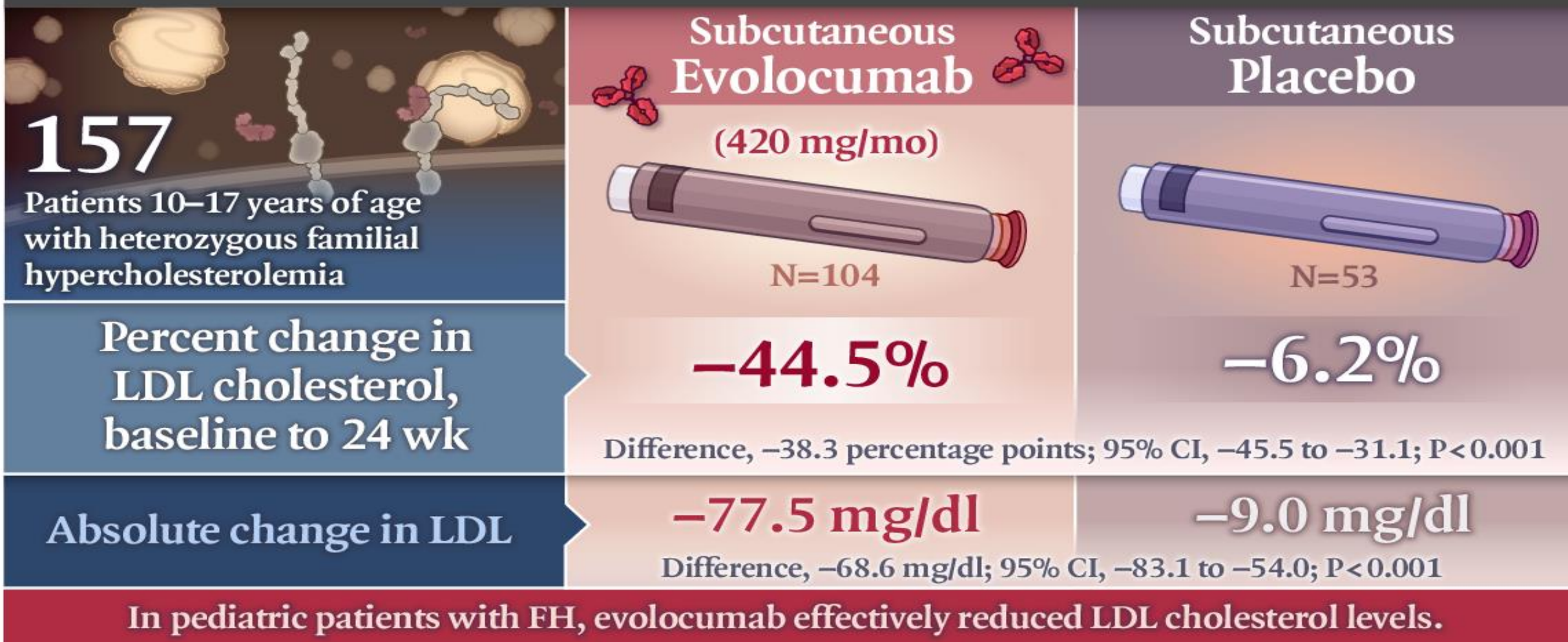


Patients with LDLR null-null mutations experienced lower reduction in LDL-C levels

^a One or both alleles.

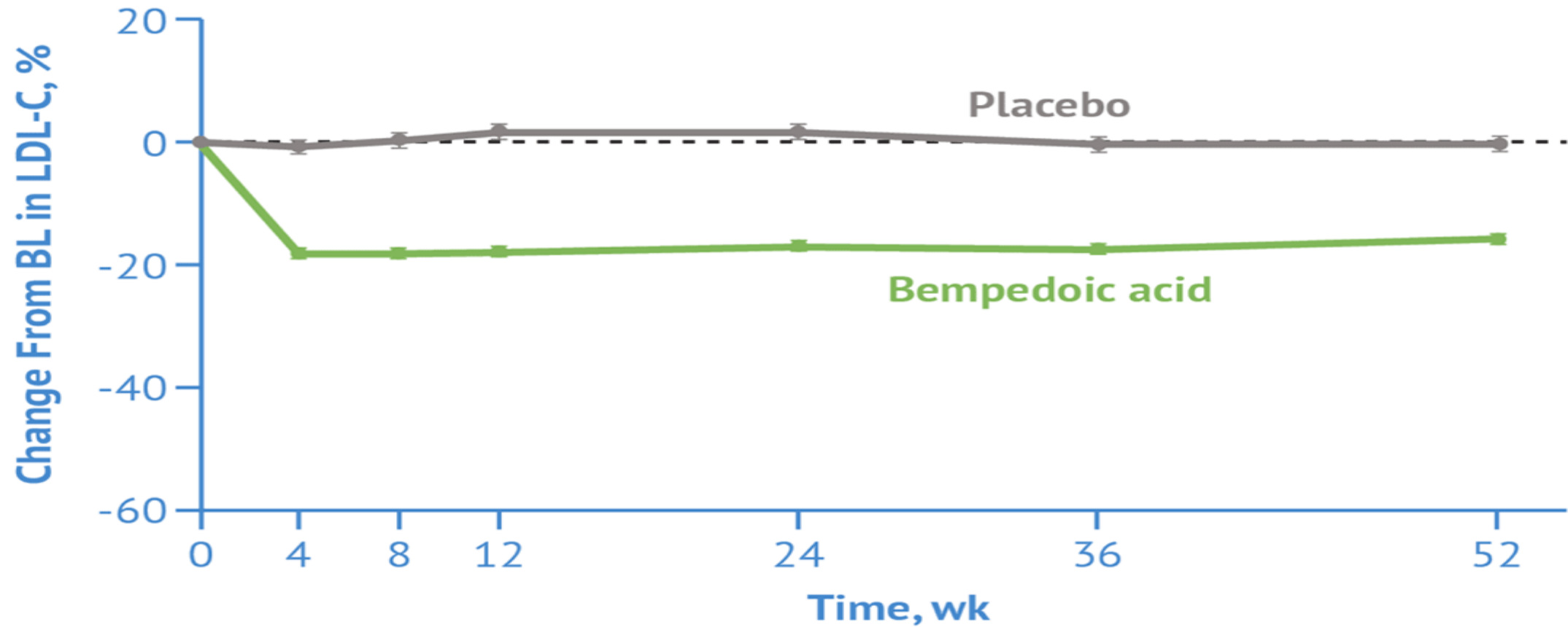
Evolocumab in Pediatric Heterozygous FH

DOUBLE-BLIND, RANDOMIZED, CONTROLLED TRIAL

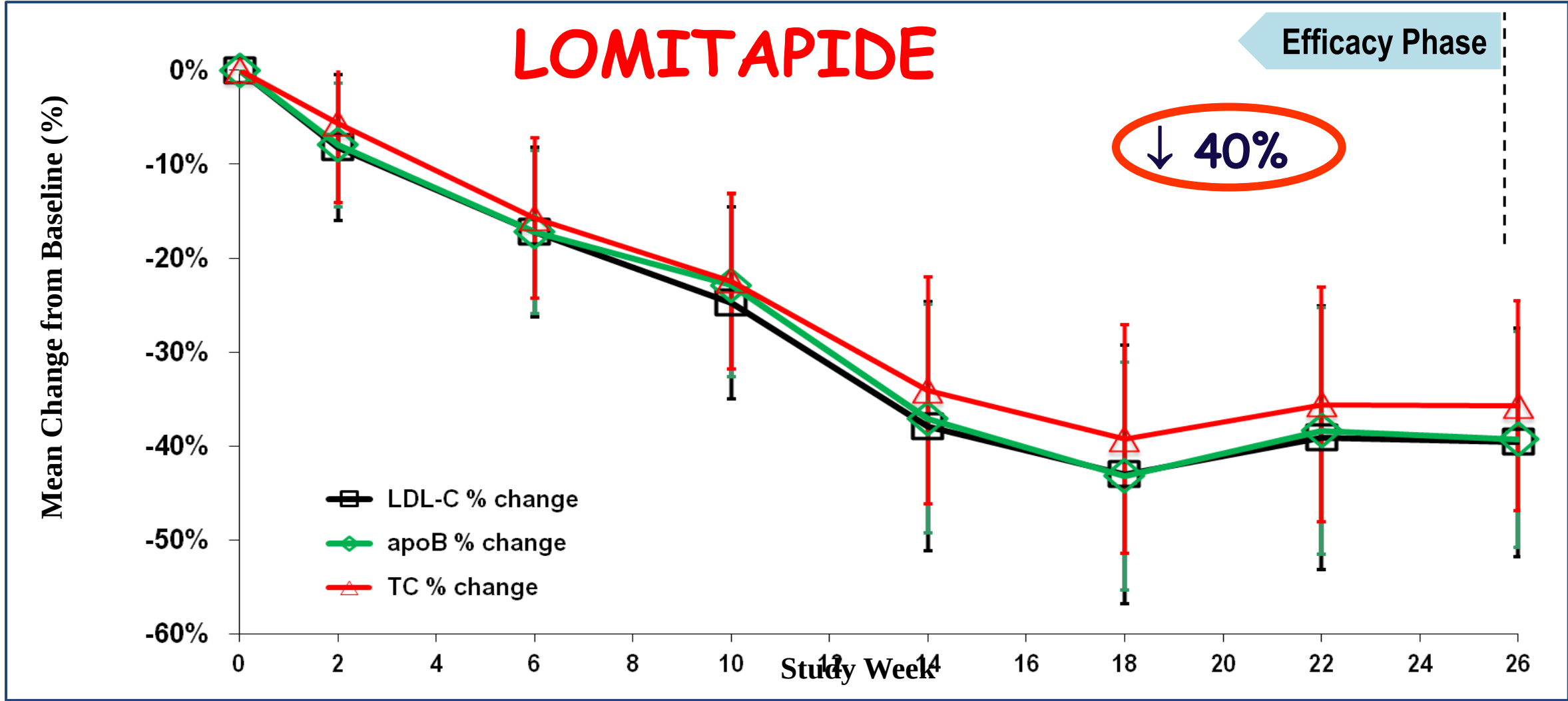


**ΑΛΛΑ ΦΑΡΜΑΚΑ ΓΙΑ ΤΗΝ ΟΙΚΟΓΕΝΗ
ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ**

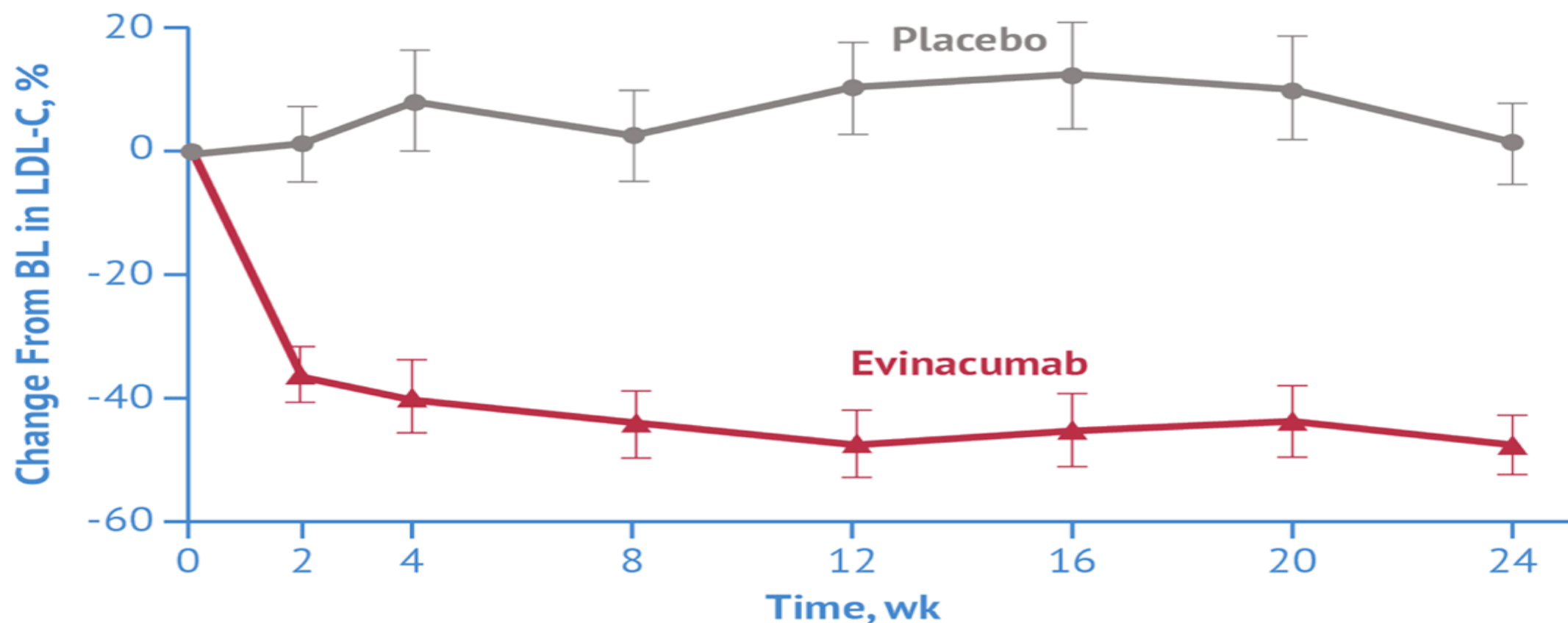
Bempedoic Acid and Reduction in LDL-C in HeFH¹⁶



Mean % Change in TC, LDL-C, and Apo B Through the Efficacy Phase (ITT, LOCF)



Evinacumab and Reduction in LDL-C in HoFH¹³



LDL-C was lower in the evinacumab group vs placebo for both null-null and non-null variants

LDL apheresis is current standard of care for HoFH

When LDL-C > 300 mg/dL on maximum therapy
(or >200 mg/dL if CVD present)

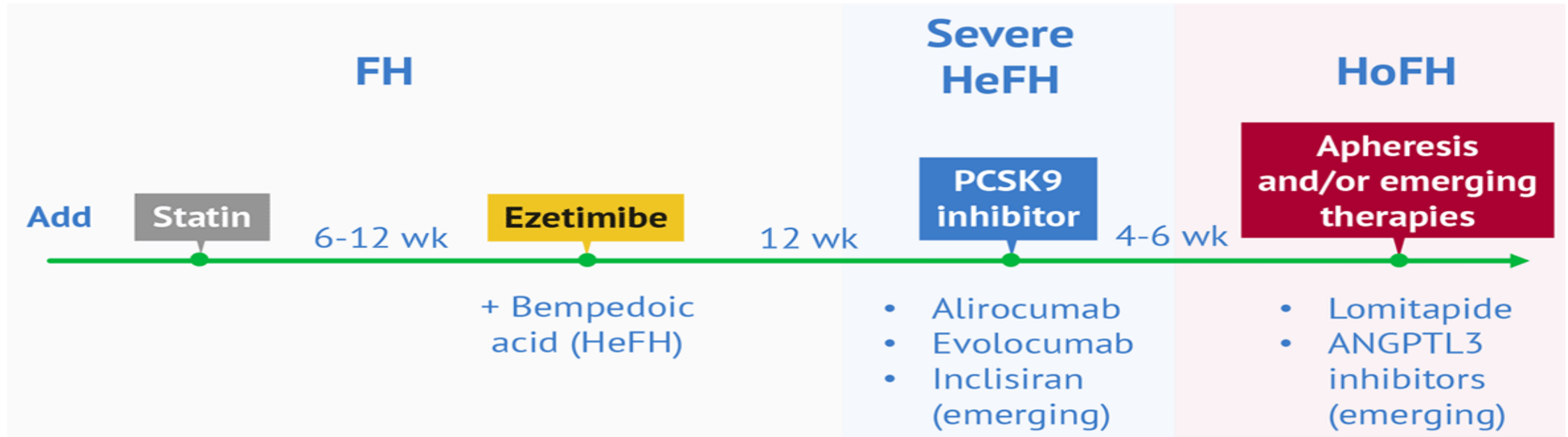


Treatment Algorithm for Severe FH



TARGET

70 mg/dL (ACC/AHA)³
or 55 mg/dL (ESC/EAS)⁴



The Future

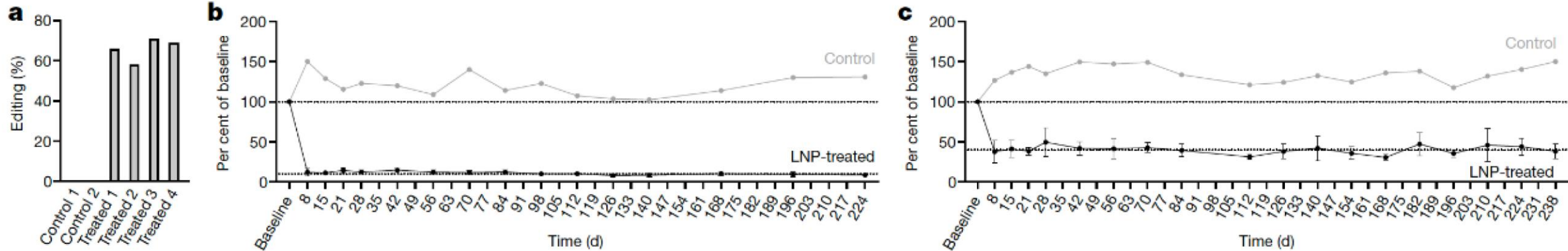
CrisprCas9 gene editing (in primates)



PCSK9 gene editing

% PCSK9 reduction

% LCL-C reduction



knockdown of *PCSK9* in the liver after a single infusion of lipid nanoparticles, with concomitant reductions in blood levels of PCSK9 and low-density lipoprotein cholesterol of approximately 90% and about 60%, respectively; all of these changes remained stable for at least 8 months after a single-dose treatment. In addition to

ΟΙΚΟΓΕΝΗΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ

1. Το πιο συχνό γενετικό νόσημα του μεταβολισμού
2. Πρώιμη καρδιαγγειακή νόσος
3. Οι περισσότεροι ασθενείς δεν έχουν διαγνωσθεί και δεν λαμβάνουν θεραπεία
4. Οι περισσότεροι ασθενείς που λαμβάνουν θεραπεία έχουν τιμές LDL-C εκτός στόχου

2025

Hellenic Atherosclerosis Society

WEBINAR SERIES

Emerging Therapies in Atherosclerosis and Cardiometabolic Diseases

Join Leading Scientists Worldwide: Sharing Cutting-Edge Knowledge
in Atherosclerosis & Cardiometabolic Diseases

DON'T MISS THIS UNIQUE OPPORTUNITY!

February 19, 2025 at 18.00 EET



For More Details
www.atherosclerosis.gr



Therapies for pediatric
familial hypercholesterolemia

Raul Santos

Associate Professor and Director
of the Lipid Clinic, Heart Institute,
University of São Paulo Medical School Hospital



ΕΑΡΙΝΗ ΣΥΝΑΝΤΗΣΗ
35^η ΔΙΗΜΕΡΙΔΑ
ΤΗΣ ΕΛΛΗΝΙΚΗΣ ΕΤΑΙΡΕΙΑΣ
ΑΘΗΡΟΣΚΛΗΡΩΣΗΣ

14-15 ΞΕΝΟΔΟΧΕΙΟ
ΜΑΡΤΙΟΥ ΑΜΑΛΙΑ
2025 ΝΑΥΠΛΙΟ



Web: atherosclerosis.gr
#HASEdu2025

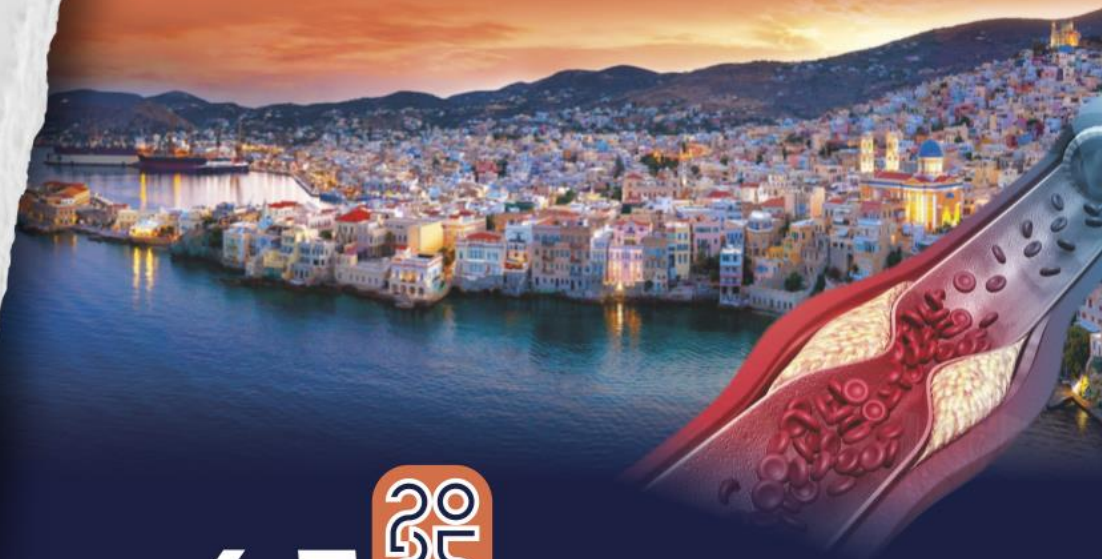


2025

ΕΛΛΗΝΙΚΗ ΕΤΑΙΡΕΙΑ
ΑΘΗΡΟΣΚΛΗΡΩΣΗΣ



18^ο ΘΕΡΙΝΟ
ΣΧΟΛΕΙΟ
ΕΛΛΗΝΙΚΗΣ ΕΤΑΙΡΕΙΑΣ
ΑΘΗΡΟΣΚΛΗΡΩΣΗΣ



6&7 **2025**
ΙΟΥΝΙΟΥ
Hermes Hotel
ΣΥΡΟΣ



Web: atherosclerosis.gr
#HASEdu2025