ΕΛΛΗΝΙΚΗ ΔΗΜΟΚΡΑΤΙΑ
Εθνικόν και Καποδιστριακόν Πανεπιστήμιον Αθηνών
ΙΔΡΥΘΕΝ ΤΟ 1837

ΙΑΤΡΙΚΗ ΣΧΟΛΗ ΕΚΠΑ • NKUA MEDICAL SCHOOL • 1837 •

Α΄ Προπαιδευτική Παθολογική Κλινική • Ιατρικής Σχολής ΕΚΠΑ • 1918 •

ΕΛΛΗΝΙΚΗ ΕΤΑΙΡΕΙΑ ΑΘΗΡΟΣΚΛΗΡΩΣΗΣ 25.05.2002

EAS European Atherosclerosis Society

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

1ο ΒΗΜΑ: ΑΠΟΚΛΕΙΣΜΟΣ ΔΕΥΤΕΡΟΠΑΘΟΥΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑΣ

First steps: Exclude secondary causes

Secondary causes of very high LDL-C include:

- **Nephrotic syndrome**
- **Primary biliary cholangitis**
- **Untreated hypothyroidism**
- **Anorexia**
- **Some medications**

Hegele RA et al. Lancet Diabetes Endocrinol 2020;8:50-67

DIAGNOSTIC WORK-UP

- Εργαστηριακές εξετάσεις κ.φ.
- Μη καπνιστής
- BMI 25 Kg/m^2
- ΑΠ 120/80 mmHg

2ο ΒΗΜΑ: ΑΤΟΜΙΚΟ & ΟΙΚΟΓΕΝΕΙΑΚΟ ΙΣΤΟΡΙΚΟ

Διαγνωστικές ερωτήσεις

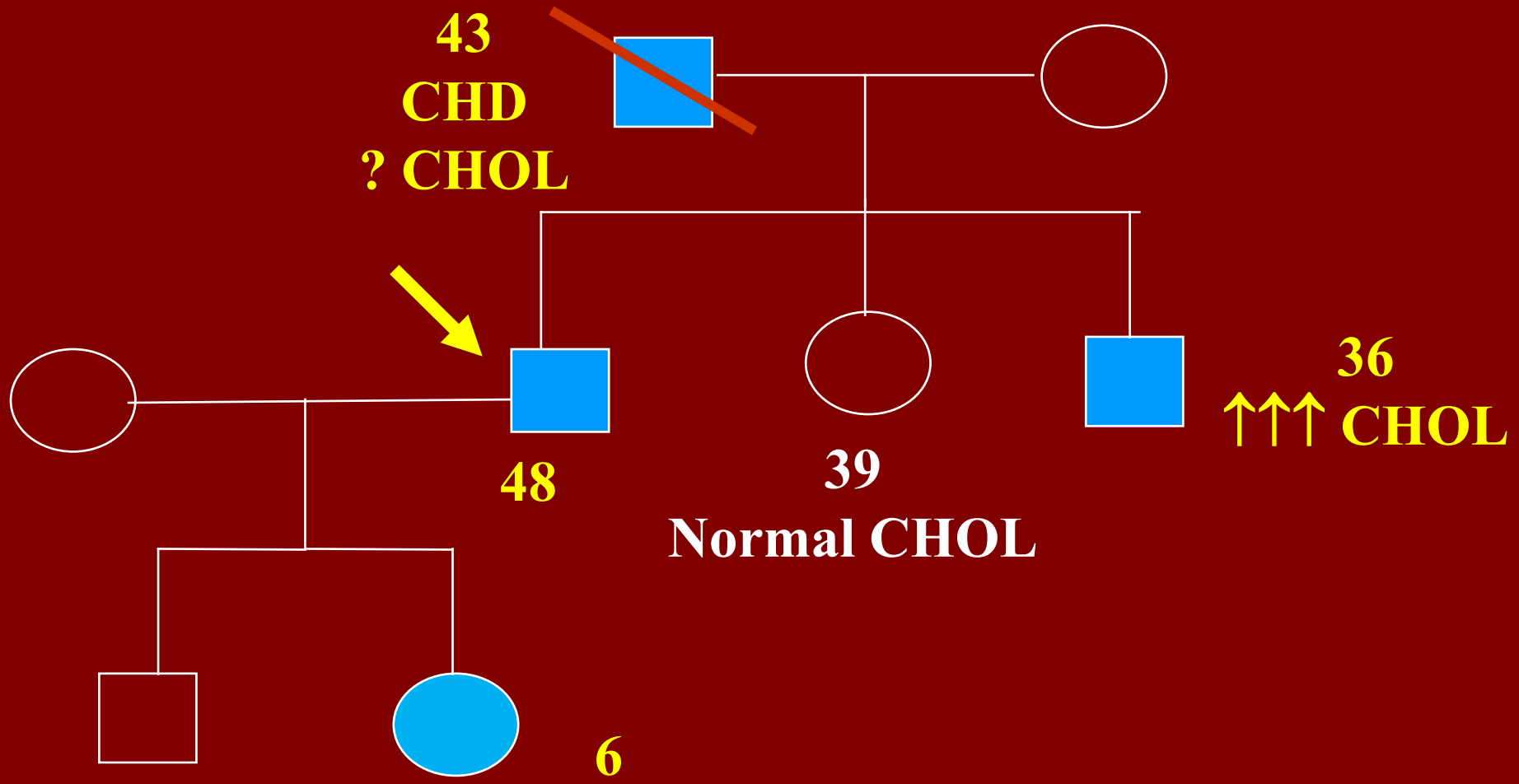
1) Έχει ο ασθενής ατομικό ιστορικό CVD;

2) Τι LDL χοληστερόλη και ιστορικό CVD έχουν οι γονείς;

2) Τι LDL χοληστερόλη και ιστορικό CVD έχουν τα αδέρφια του;

3) Τι LDL χοληστερόλη και ιστορικό CVD έχουν τα παιδιά του;

FAMILY TREE


43
CHD
? CHOL
48
39
Normal CHOL
36
↑↑↑ CHOL
8
Normal CHOL
6
LDL CHOL 160 mg/dL

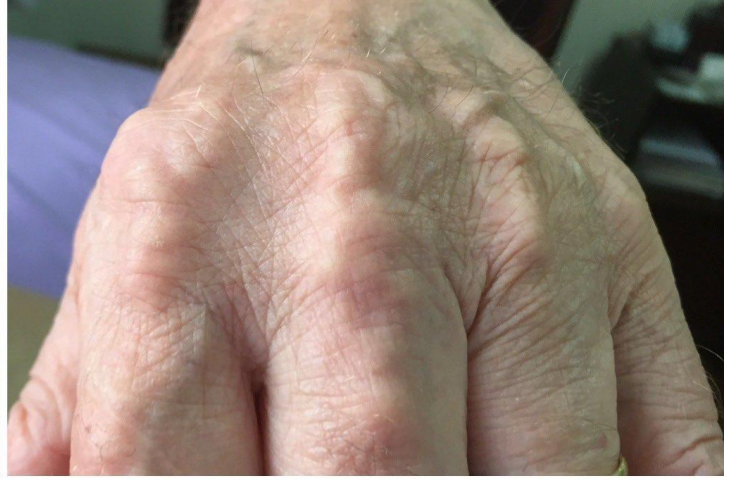
3ο ΒΗΜΑ: ΦΥΣΙΚΗ ΕΞΕΤΑΣΗ

Consider FH

Clinical evidence of:

- Corneal Arcus
- Xanthelasma
- Tendon xanthomas in the hands and Achilles tendons

EAS



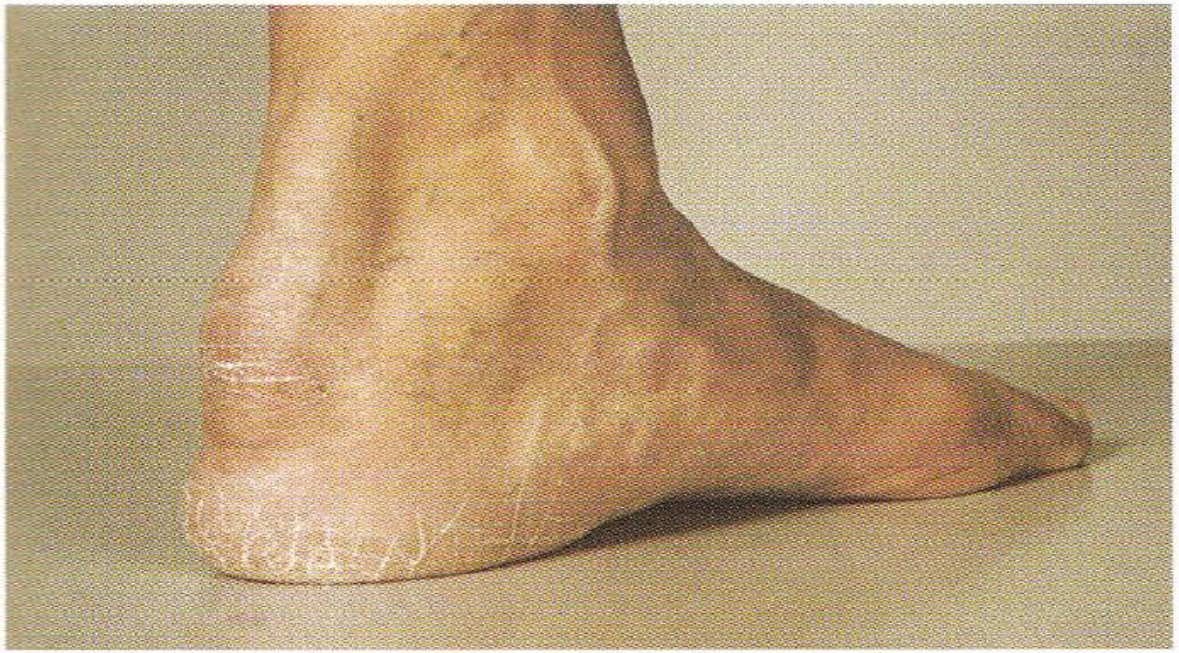


Plate 1 *Achilles tendon xanthoma (heterozygous familial hypercholesterolaemia)*

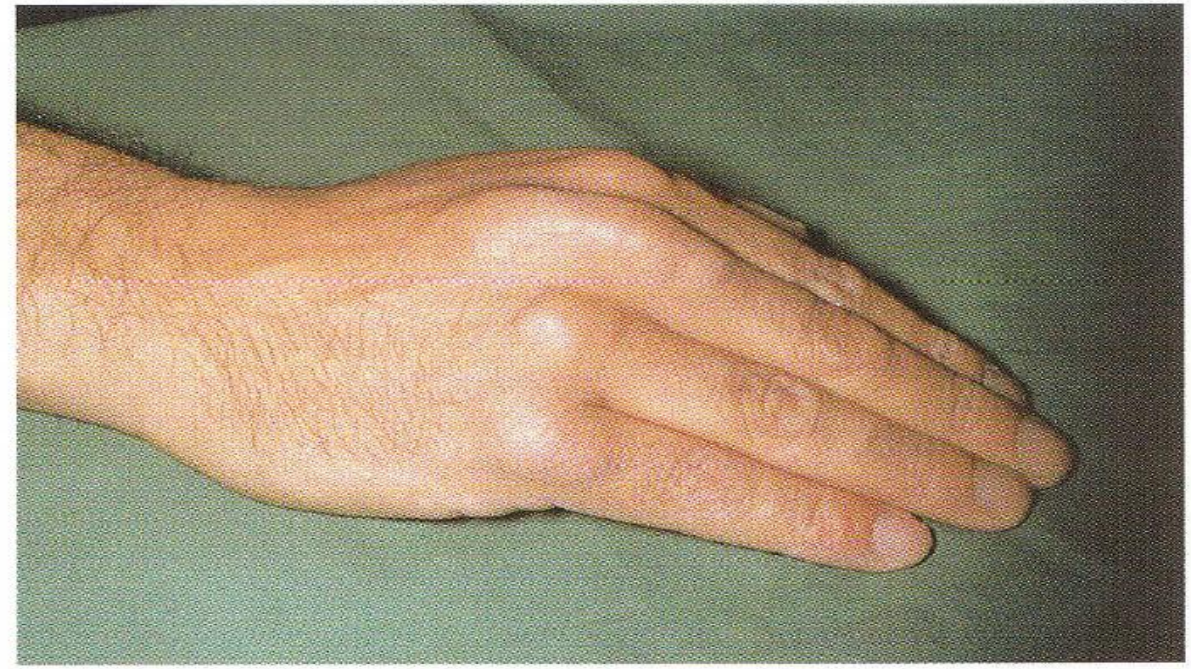


Plate 3 *Tendon xanthomata on dorsum of hand (heterozygous familial hypercholesterolaemia) (courtesy of Dr J. Barth)*

ΦΥΣΙΚΗ ΕΞΕΤΑΣΗ HoFH

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

Macchiaiolo M e.a. Lancet, 2012;379:1330

4ο ΒΗΜΑ: ΔΙΑΓΝΩΣΗ

ΟΙΚΟΓΕΝΗΣ (50% των 1ου βαθμού συγγενών)

+

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

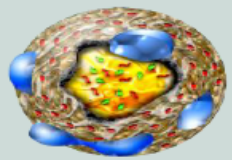
=

ΟΙΚΟΓΕΝΗΣ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ (FH)

European Heart Journal

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) – 5.5 or higher – 6.5 to 8.4 – 5.0 to 6.4 – 4.0 to 4.9	 8 5 3 1
DNA analysis: functional mutation in the *LDLR*, *APOB* or *PCSK9* 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).

*FH Foundation

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

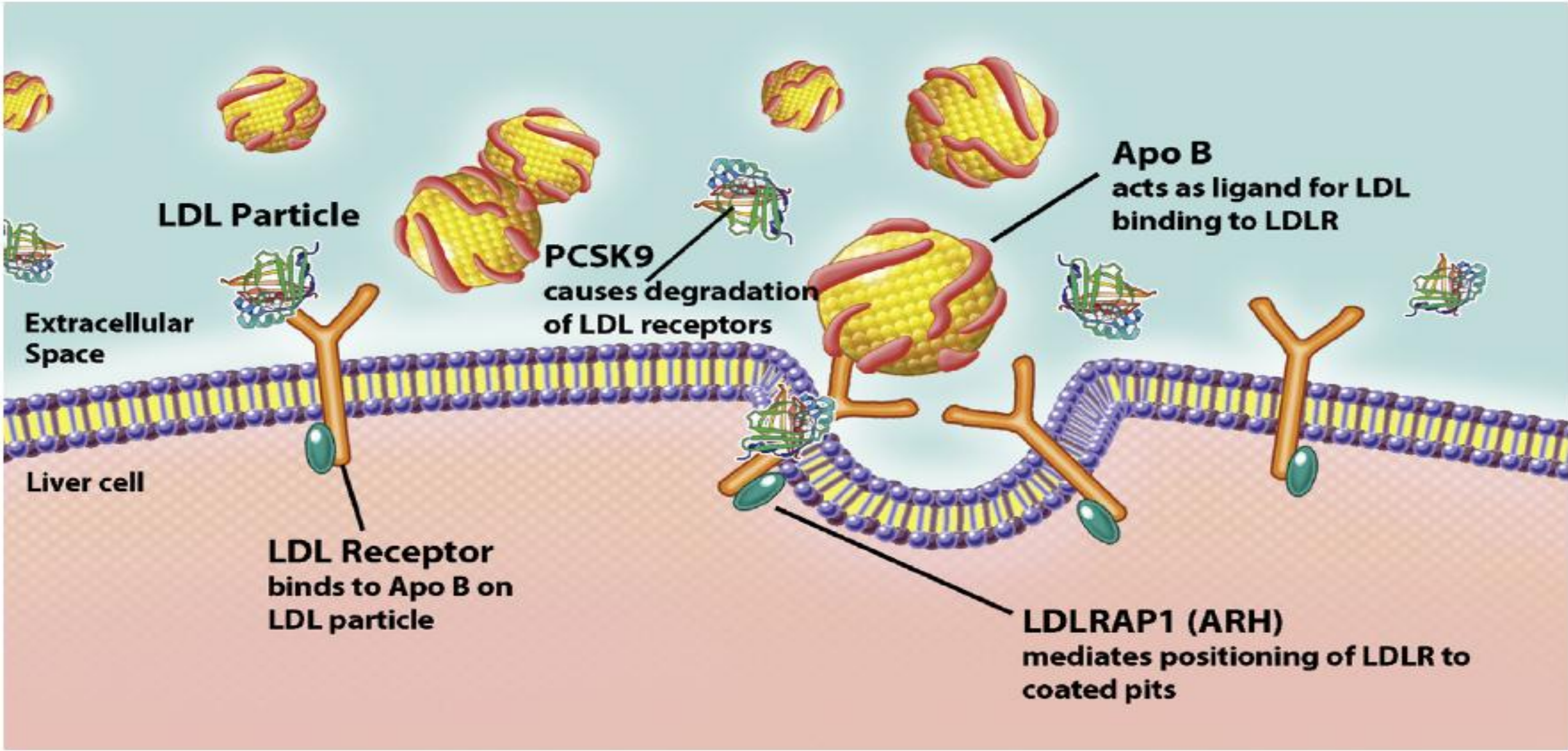
- Genetic confirmation of bi-allelic pathogenic/likely pathogenic variants on different chromosomes at the *LDLR*, *APOB*, *PCSK9*, or *LDLRAP1* genes or ≥2 such variants at different loci

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

EAS

5ο ΒΗΜΑ: ΓΕΝΕΤΙΚΗ ΔΙΑΓΝΩΣΗ [ΟΧΙ ΑΠΑΡΑΙΤΗΤΗ]

Figure 2 Major Molecular Causes of Familial Hypercholesterolemia



Molecular genetics

Numerous genes and variants

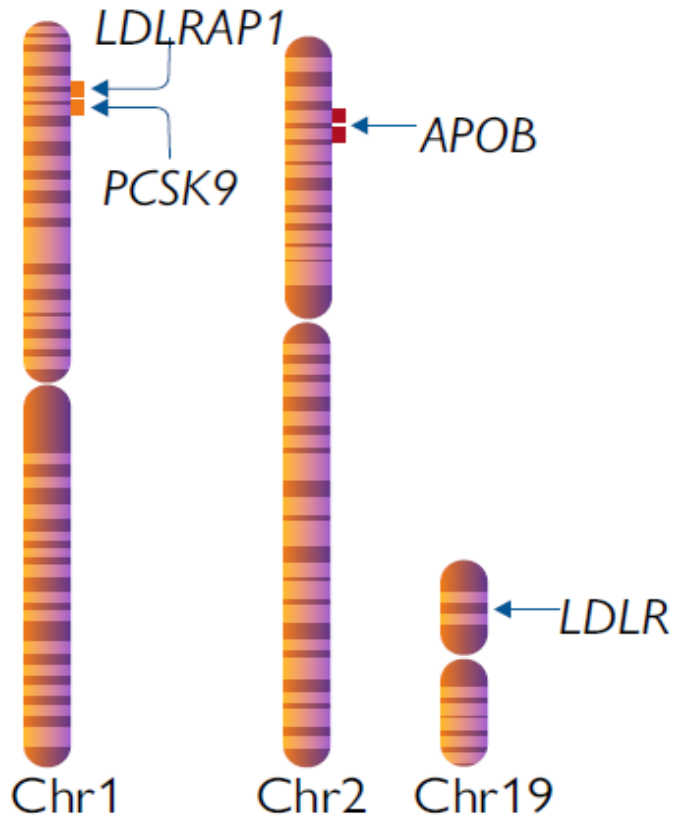
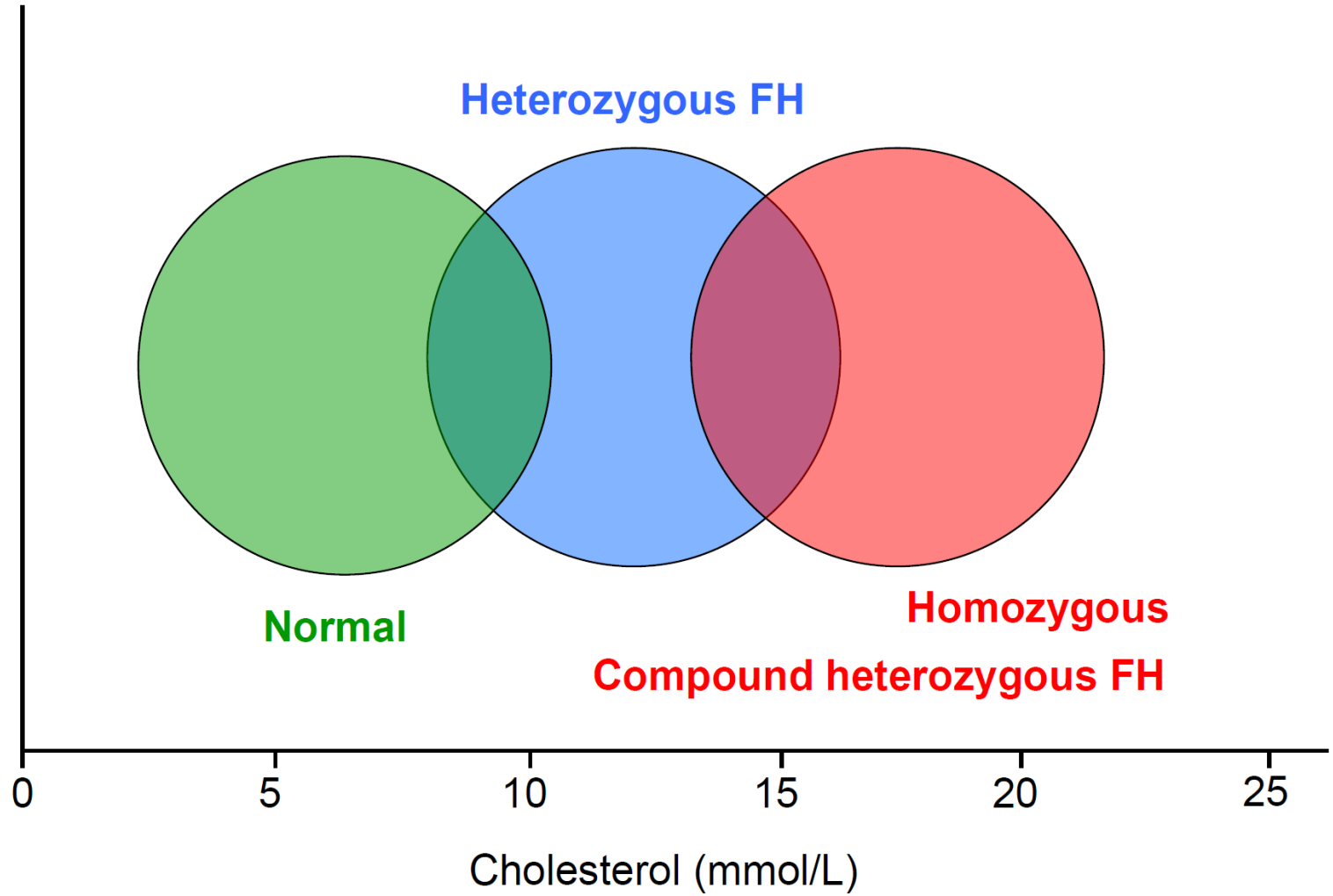


Fig. 2. Geographic distribution of the six most common *LDLR* mutations in Greece. The distribution of mutations is only shown for the index cases with determined exact origin. Four patients originating from Minor Asia carried the mutations c.1646G > A ($n = 2$), and c.81C > G ($n = 2$), and one patient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

FH



Adapted from Cuchel M, *Eur Heart J* 2014;35:2146-57

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)

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

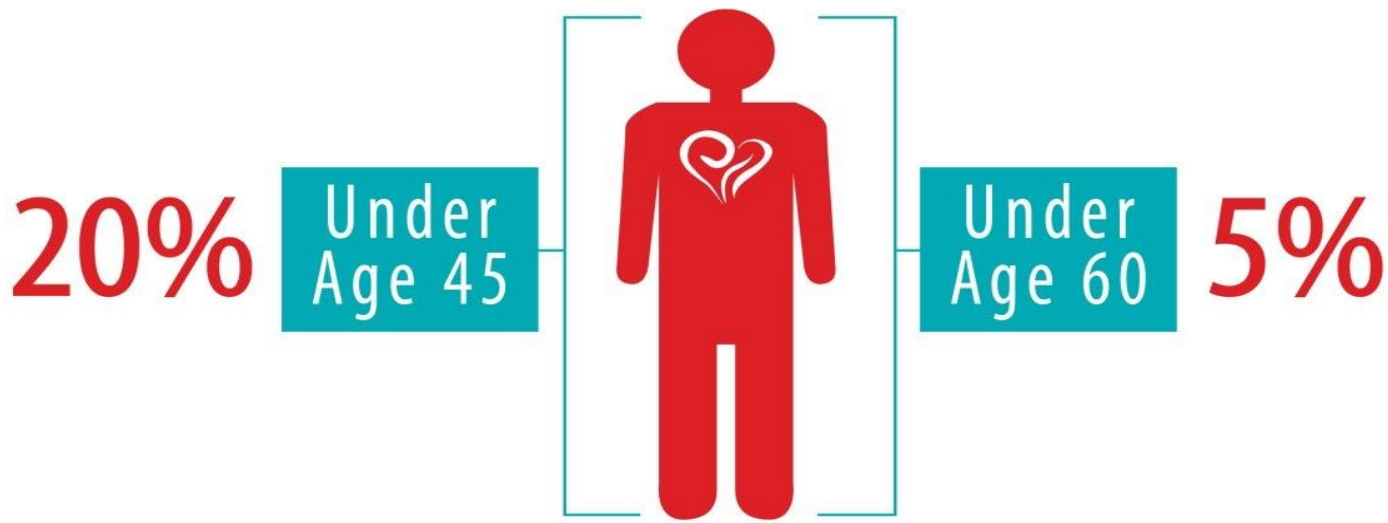
EAS

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

FH FOUNDATION

Heart Attacks due to

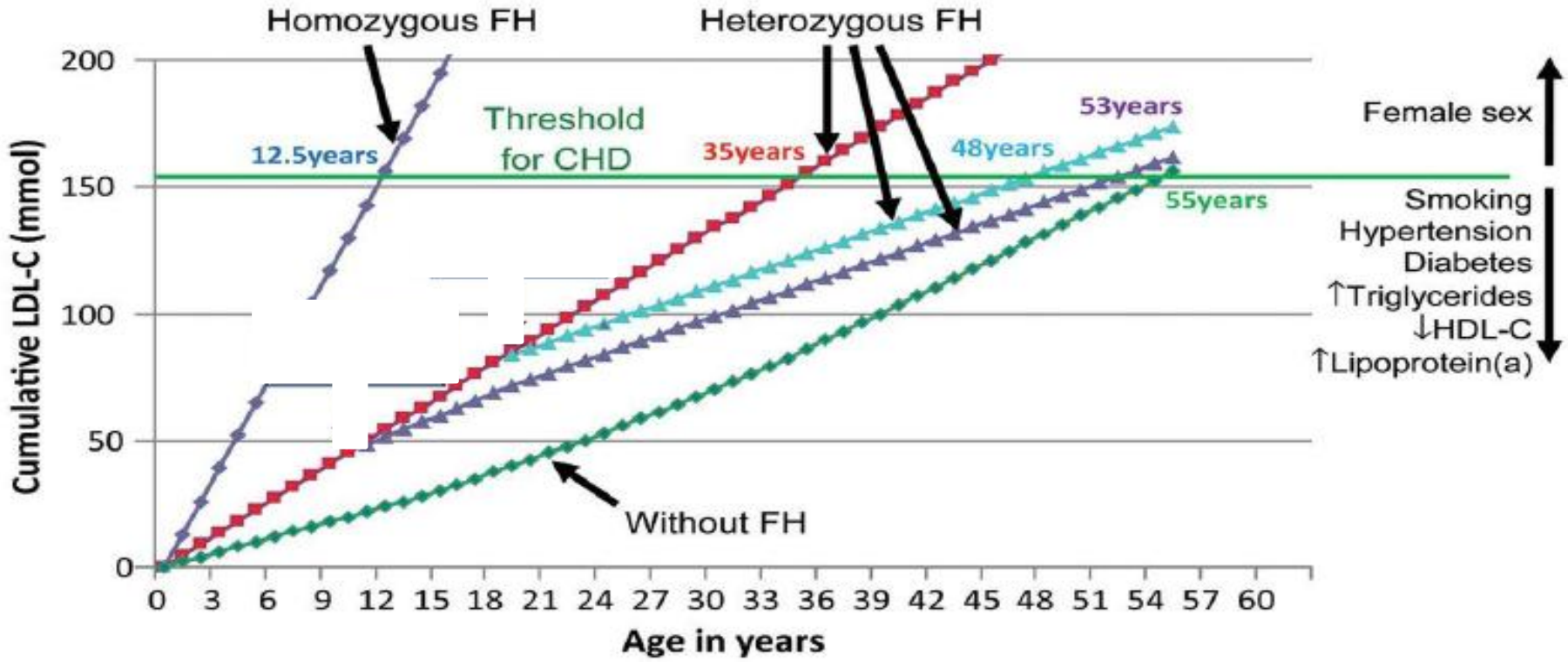
FAMILIAL HYPERCHOLESTEROLEMIA



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.

European Heart Journal



Adapted from Steve Humphries 2013

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

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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 disord

Η ΠΙΟ ΣΥΧΝΗ ΓΕΝΕΤΙΚΗ ΝΟΣΟΣ ΤΟΥ ΜΕΤΑΒΟΛΙΣΜΟΥ

Wiegman A, et al. Eur Heart J. 2015;36:2425-2437

What Is the Prevalence of Familial Hypercholesterolemia?

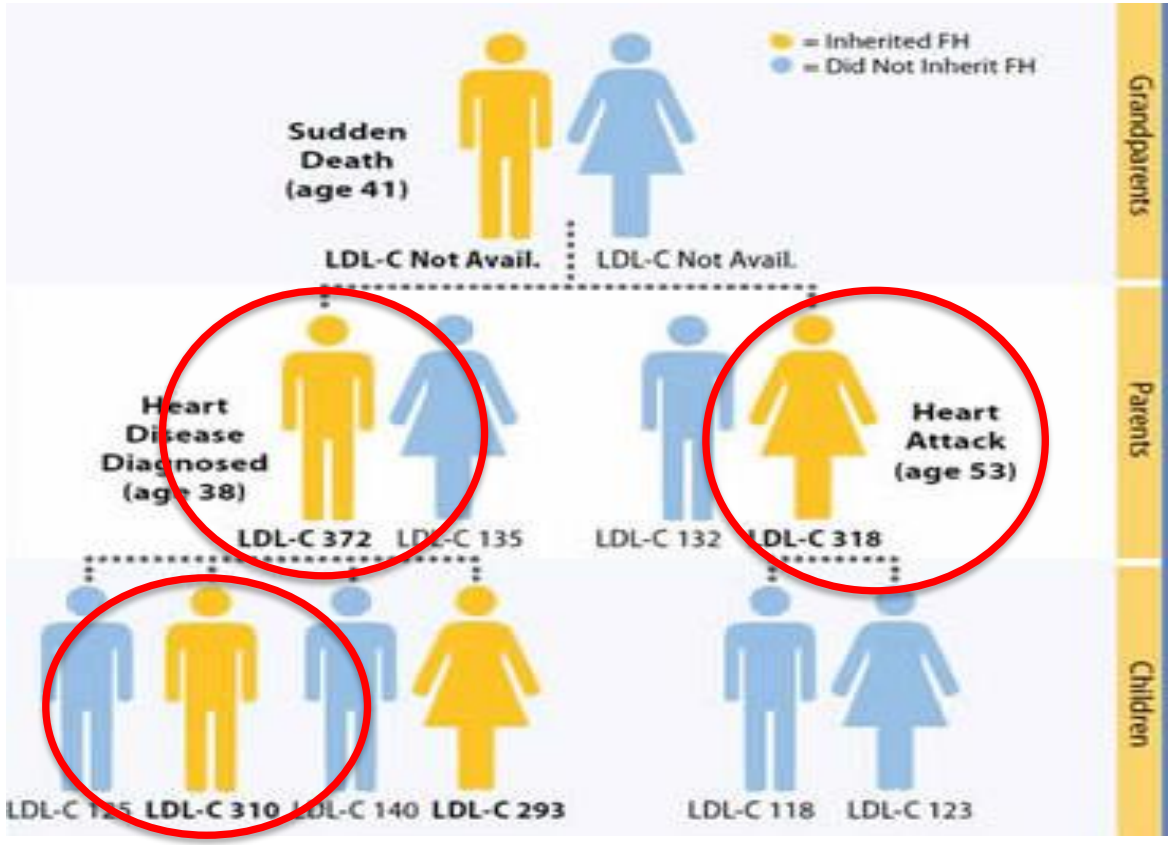
Arterioscler Thromb Vasc Biol. 2021;41:2629–2631. DOI: 10.1161/ATVBAHA.121.316862

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

Adapted from http://pcna.net/patients---preventive-cardiovascular-nurses-association/familial-hypercholesterolemia

The NEW ENGLAND JOURNAL of MEDICINE

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

FH Paediatric Screening
Moving Prevention From Evidence to Action:
Overcoming the Barriers to Implementation

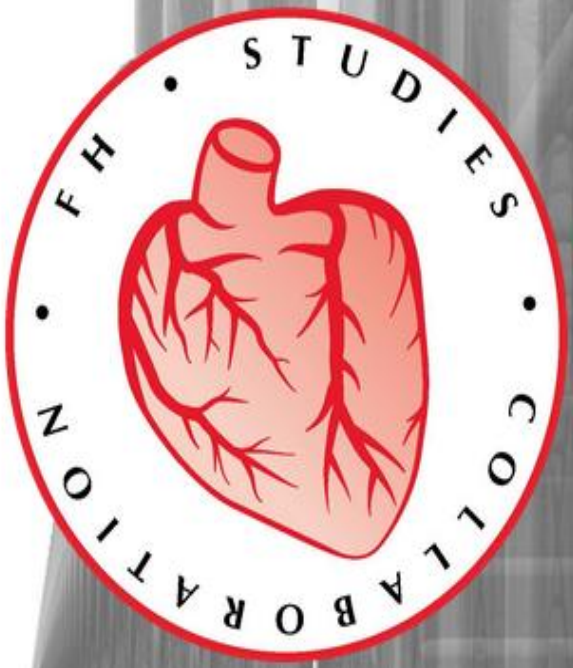
Hybrid Event under the **Auspices of the Czech EU Presidency**

6th September 2022

FH Europe
The European FH Patient Network

EU2022.CZ

EAS FHSC

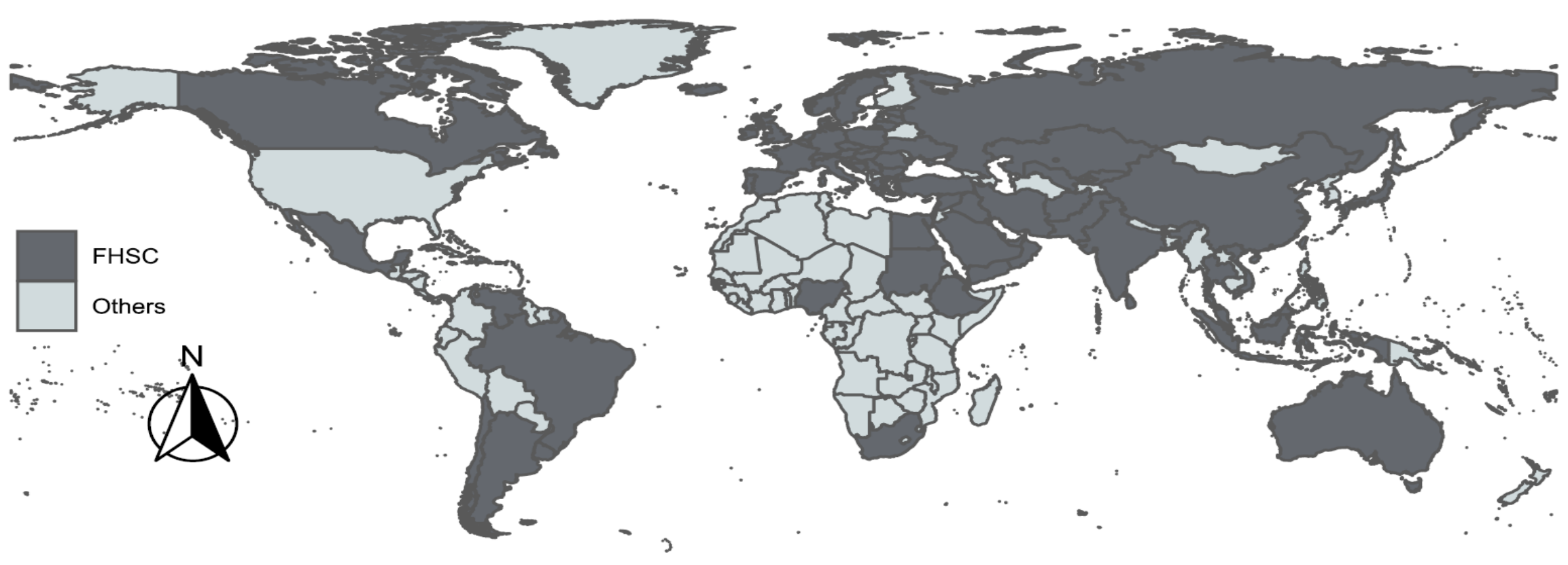


The EAS Familial Hypercholesterolaemia Studies Collaboration

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. 85K cases across 69 countries

THE LANCET

Articles

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

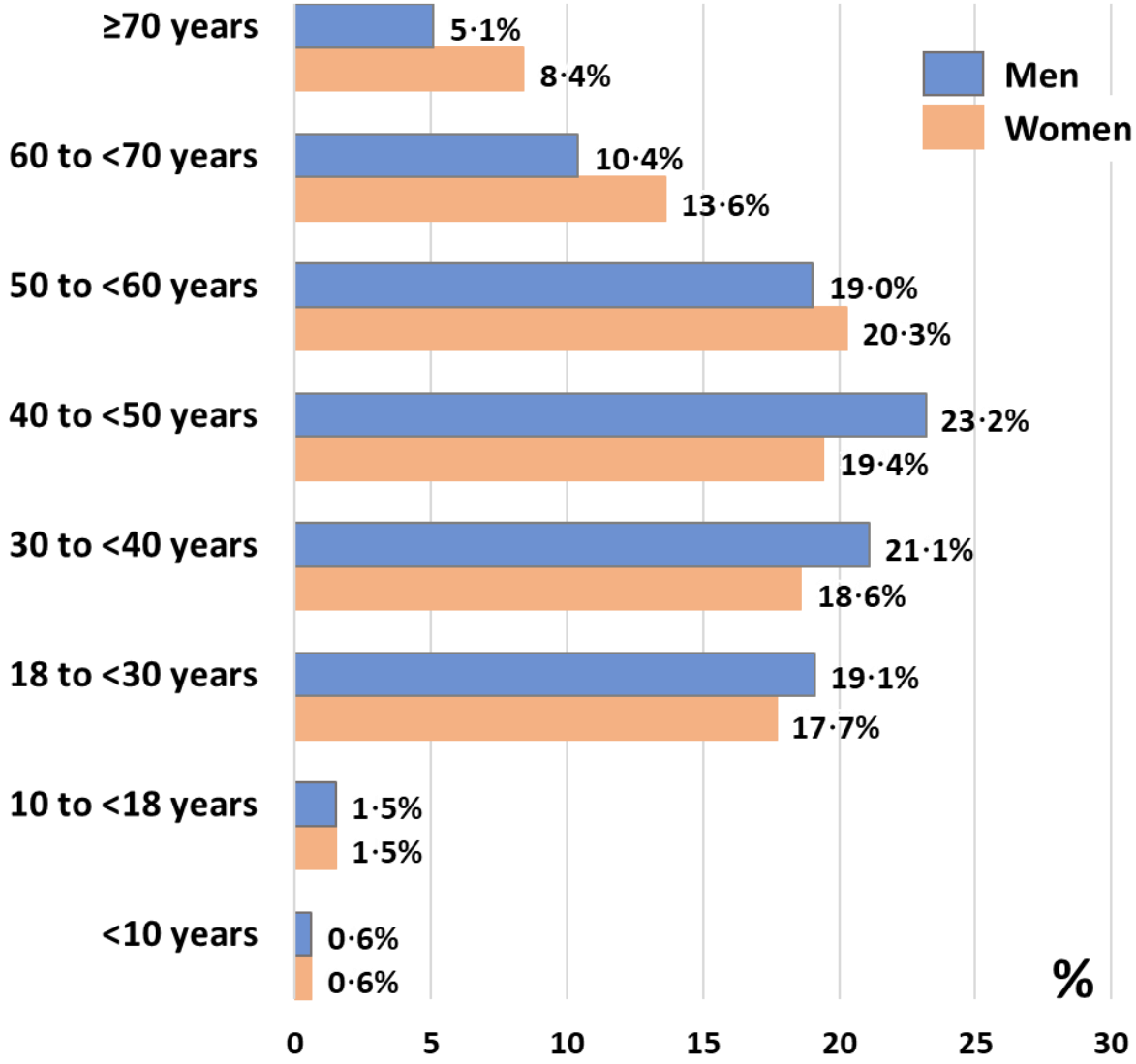
*EAS Familial Hypercholesterolaemia Studies Collaboration (FHSC)**

Vallejo-Vaz AJ, Stevens CAT, Lyons ARM, Dharmayat KS, Freiberger 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.

EAS FHSC Investigators. *Lancet* 2021; 398(10312):1713-1725. doi: 10.1016/S0140-6736(21)01122-3.

Age at FH diagnosis among Adults with HeFH



n = 30,560 participants

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**

EAS FHSC Investigators. *Lancet* 2021;398(10312):1713-1725.

HELLAS FH REGISTRY

EAS FHSC
International collaboration towards understanding the contemporary burden of Familial Hypercolesterolaemia

Ελληνική Εταιρεία Αθηροσκλήρωσης
Hellenic Atherosclerosis Society

Ελληνική Εταιρία 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 2026

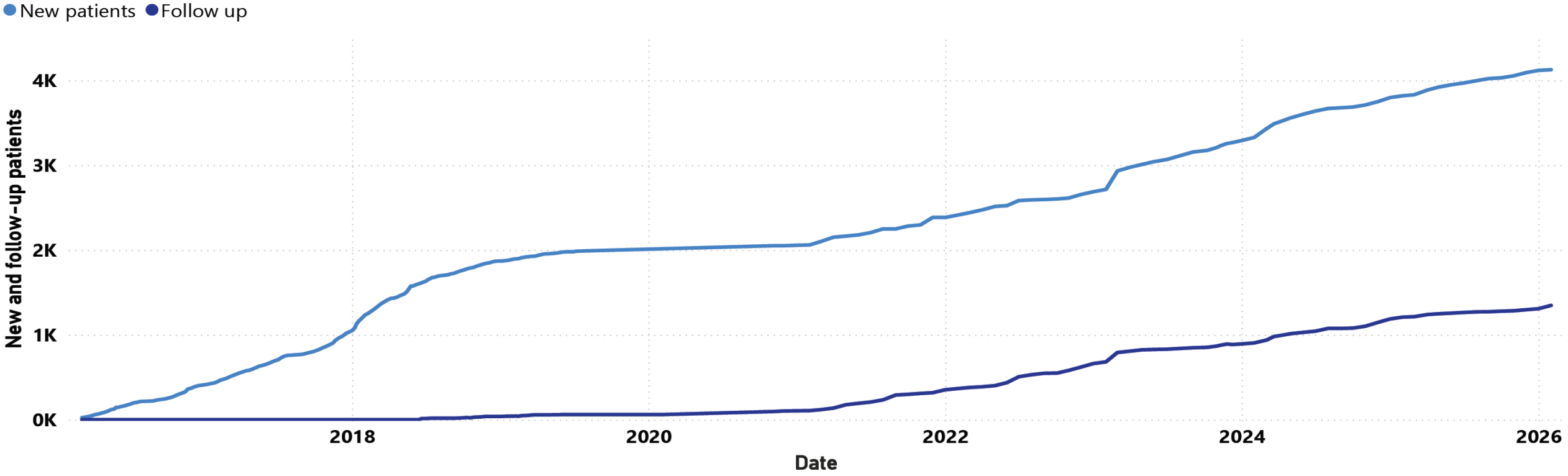
EAS FHSC

4125
Total patients

Estimated percentage of Greek FH patients recorded

1347
Total follow-ups

HELLAS-FH progress

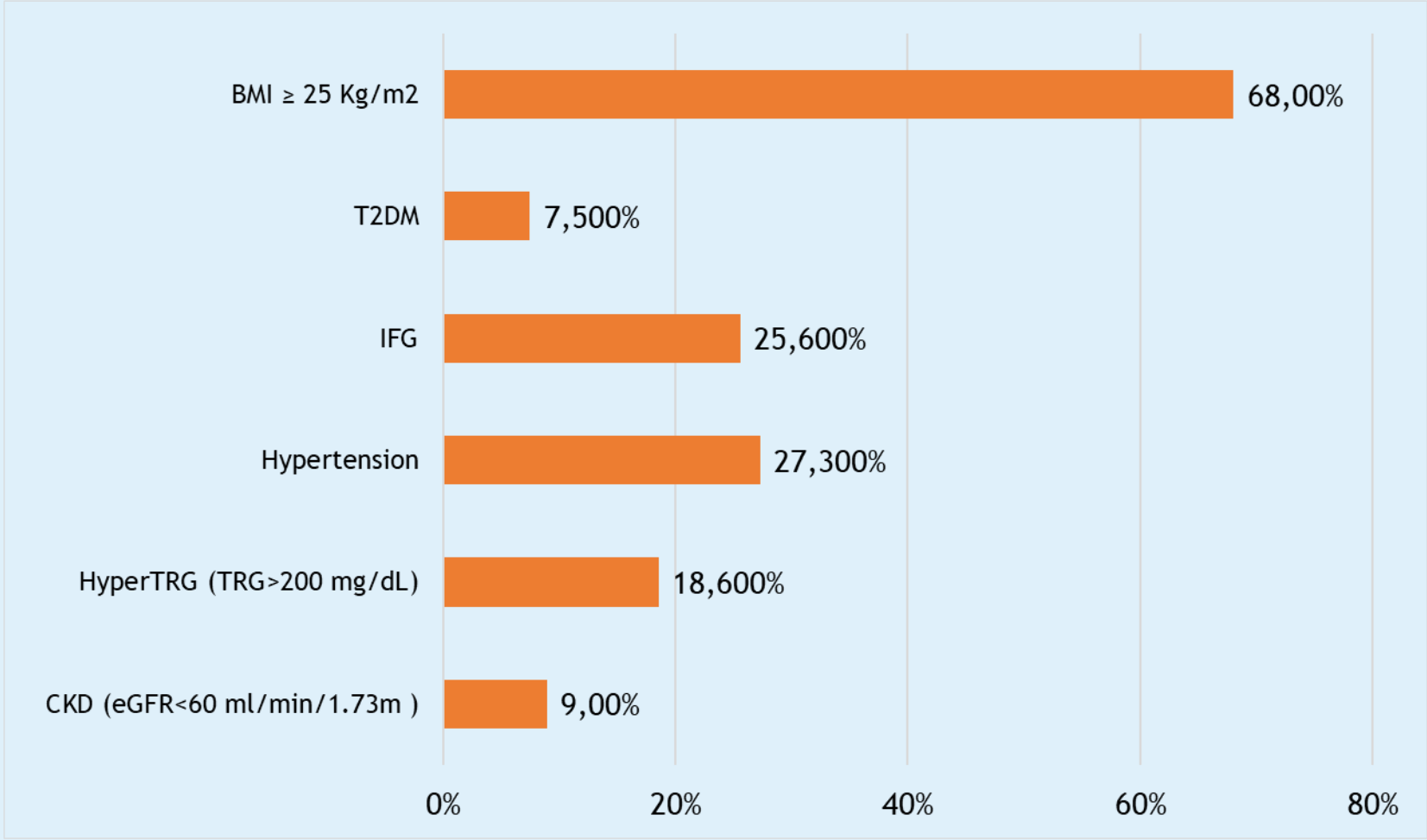


HELLAS-FH: Results

- Οι ασθενείς με FH καθυστερούν να διαγνωσθούν

44 έτη

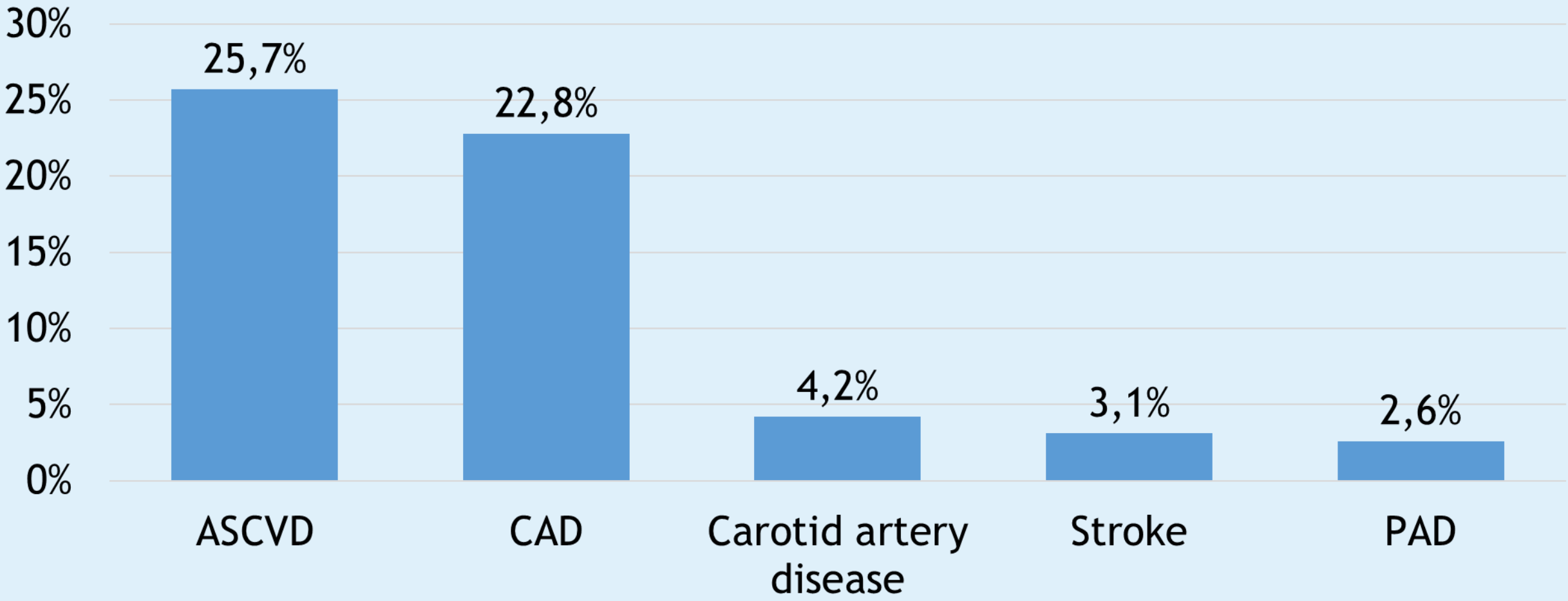
- Οι ασθενείς με FH έχουν συχνά συνοσηρότητες



Rizos CV et al. Achieving low-density lipoprotein cholesterol targets as assessed by different methods in patients with familial hypercholesterolemia: an analysis from the HELLAS-FH registry. Lipids Health Dis. 2020 May 28;19(1):114.

HELLAS-FH: Results

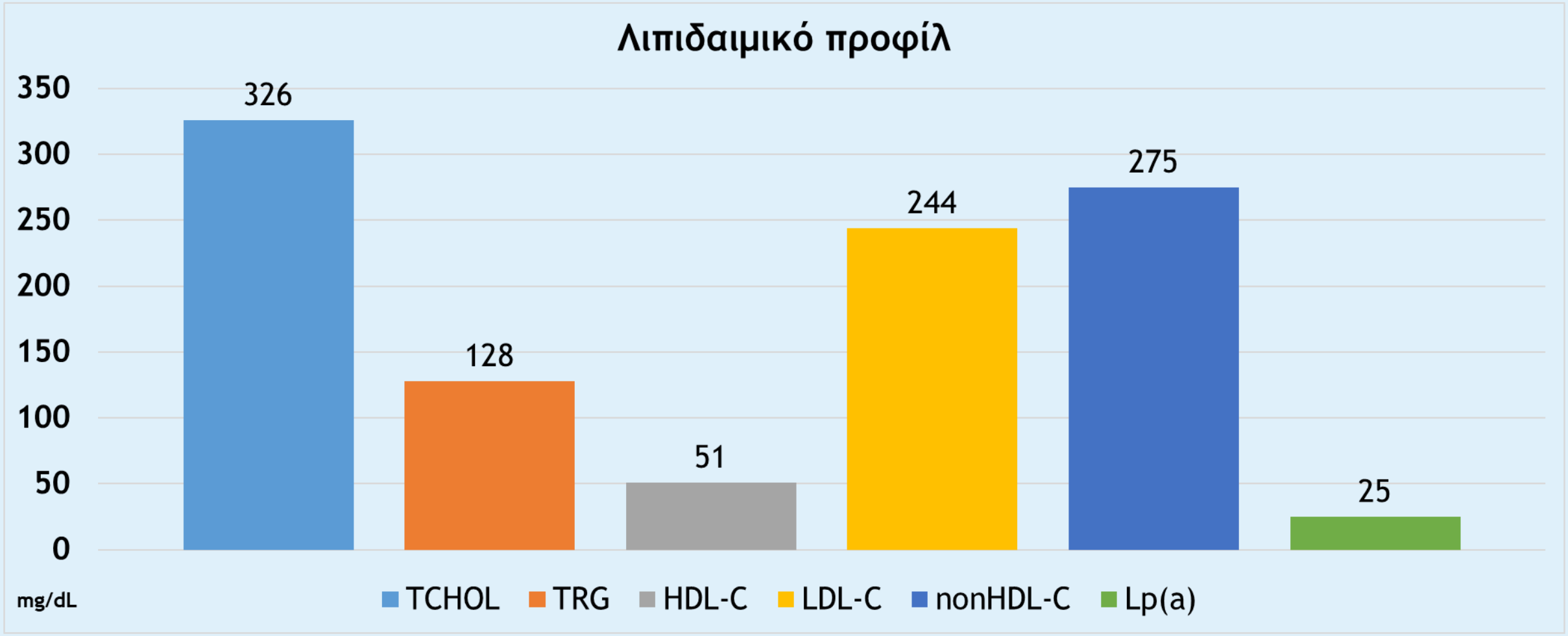
- **Οι ασθενείς με FH έχουν αυξημένο επιπολασμό ASCVD**



Rizos CV et al. Achieving low-density lipoprotein cholesterol targets as assessed by different methods in patients with familial hypercholesterolemia: an analysis from the HELLAS-FH registry. Lipids Health Dis. 2020 May 28;19(1):114.
Anagnostis P et al. Prevalence of Non-coronary Heart Disease in Patients with Familial Hypercholesterolemia: An Analysis from the HELLAS-FH. Curr Pharm Des. 2021;27(21):2537-2544.

HELLAS-FH: Results

- Οι ασθενείς με FH έχουν πολύ αυξημένα επίπεδα χοληστερόλης



Rizos CV et al. Achieving low-density lipoprotein cholesterol targets as assessed by different methods in patients with familial hypercholesterolemia: an analysis from the HELLAS-FH registry. Lipids Health Dis. 2020 May 28;19(1):114.

www.hellasfh.gr

HellasFH

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

Άνδρες 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

Οζίδια
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)

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

Διατροφή & άσκηση

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 συμβουλεύεστε το γιατρό σας.

ΘΕΡΑΠΕΙΕΣ

Η χορήγηση υπολιπιδαιμικής θεραπείας είναι πολύ αποτελεσματική. Περιλαμβάνει την χορήγηση στατινών, εζετιμίμπης, κολεσεβαλάμης, αναστολέων της PCSK9 και λομιταπίδης.

LDL ΑΦΑΙΡΕΣΗ

Με αυτή τη διαδικασία αφαιρείται η LDL από το αίμα.

Ελληνική Εταιρεία Αθηροσκλήρωσης, Ίωνος Δραγούμη 3, Αθήνα, ΤΚ. 11528, Τηλ. 2017210055, E-mail: info@atherosclerosis.gr

ΠΩΣ ΘΑ ΘΕΡΑΠΕΥΣΟΥΜΕ ΤΟΝ ΑΣΘΕΝΗ;

LDL-R DEPENDENT TREATMENTS

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

https://atherosclerosis.gr/slide-set-anatheorimenon-kateythyntirion-odigion/

Atherosclerosis Plus 55 (2024) 74–92

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 L[i], Richter D[j], Nomikos T[e], Kolovou G[k], Kypreos K[b,l], Chrysohoou C[m], Tziomalos K[n], 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 ≥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%

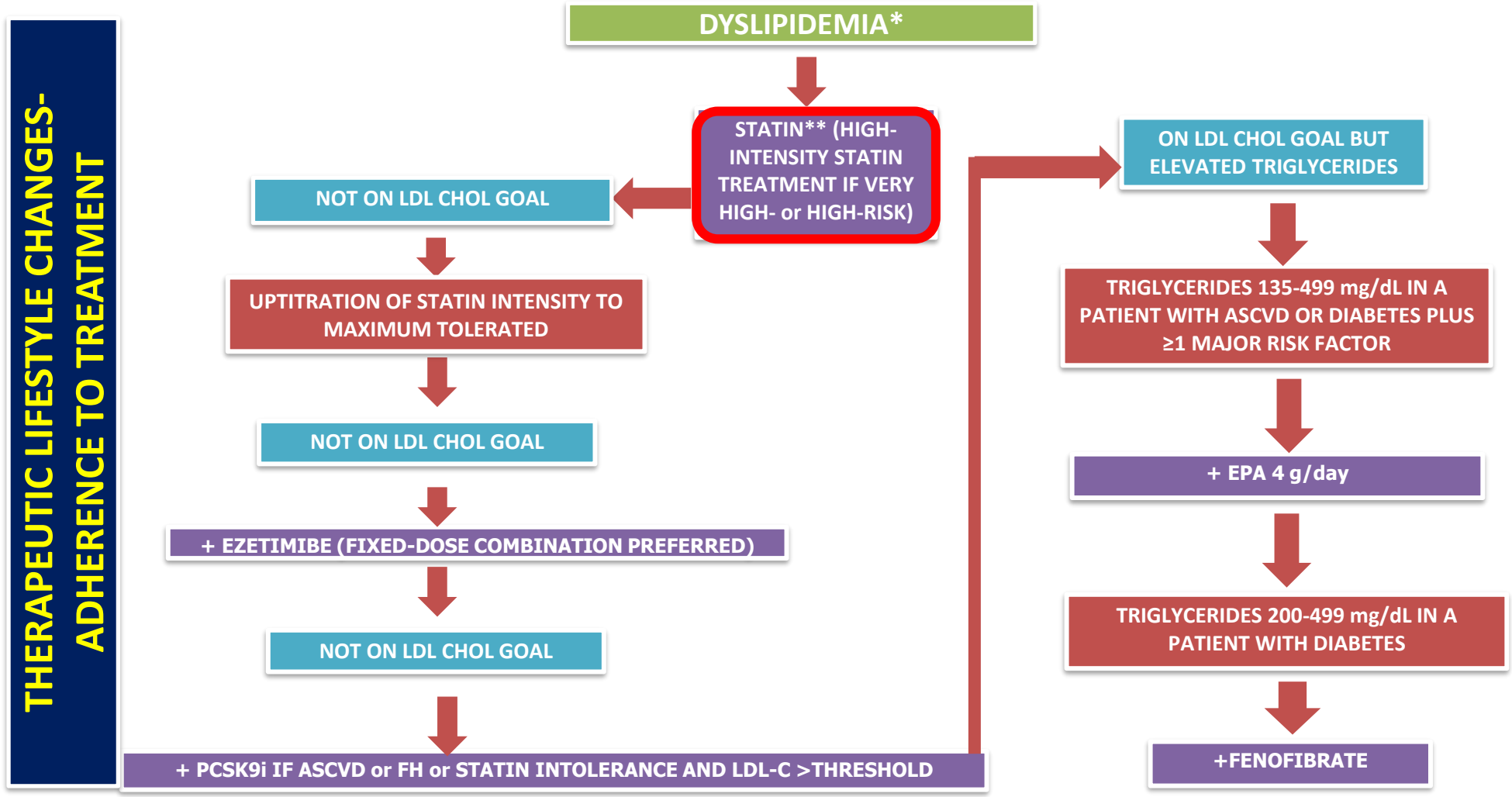
LDL-C <100 mg/dL

LOW RISK

HELLENIC SCORE II <1%

LDL-C <116 mg/dL

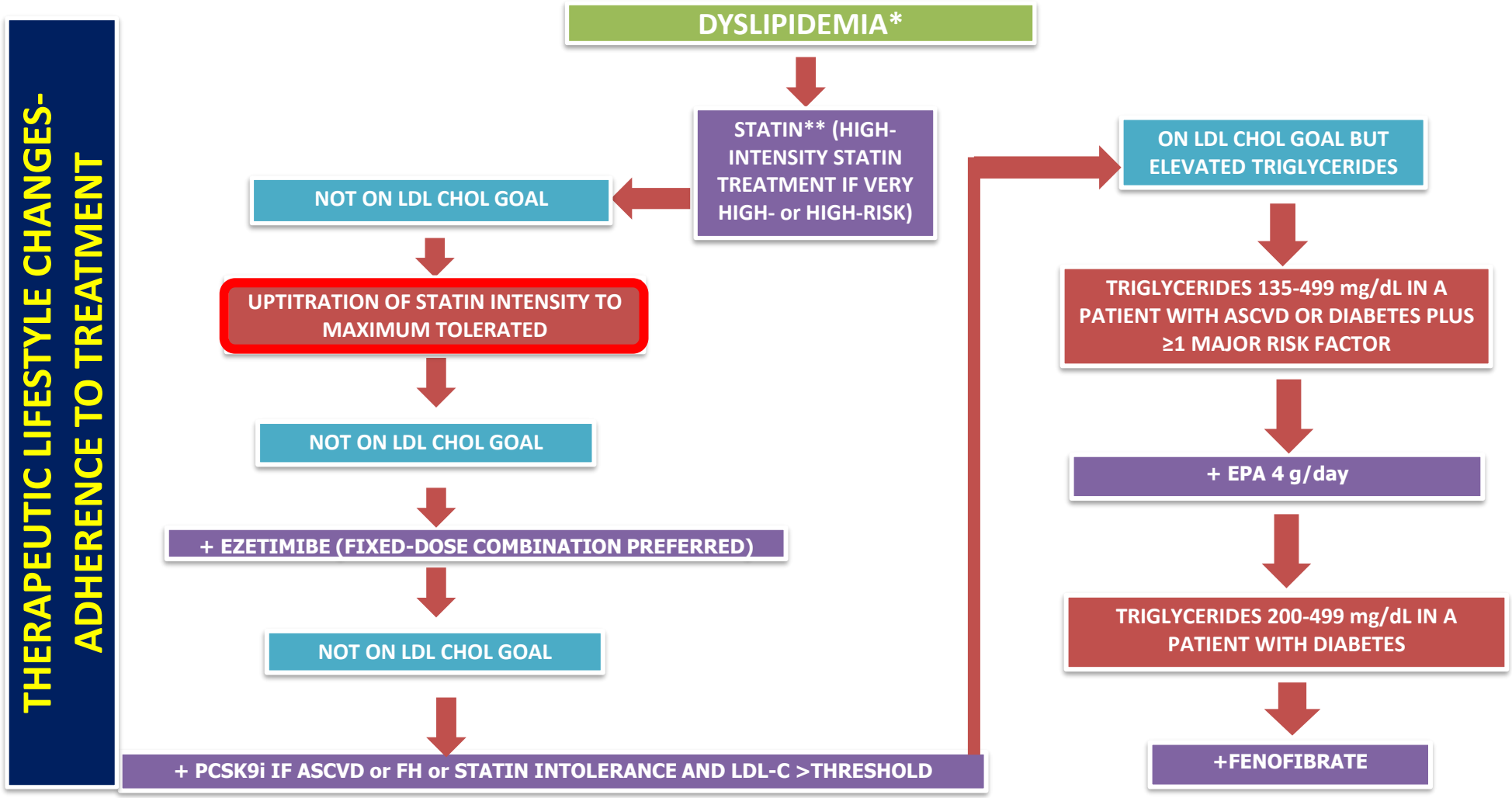
ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023



*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



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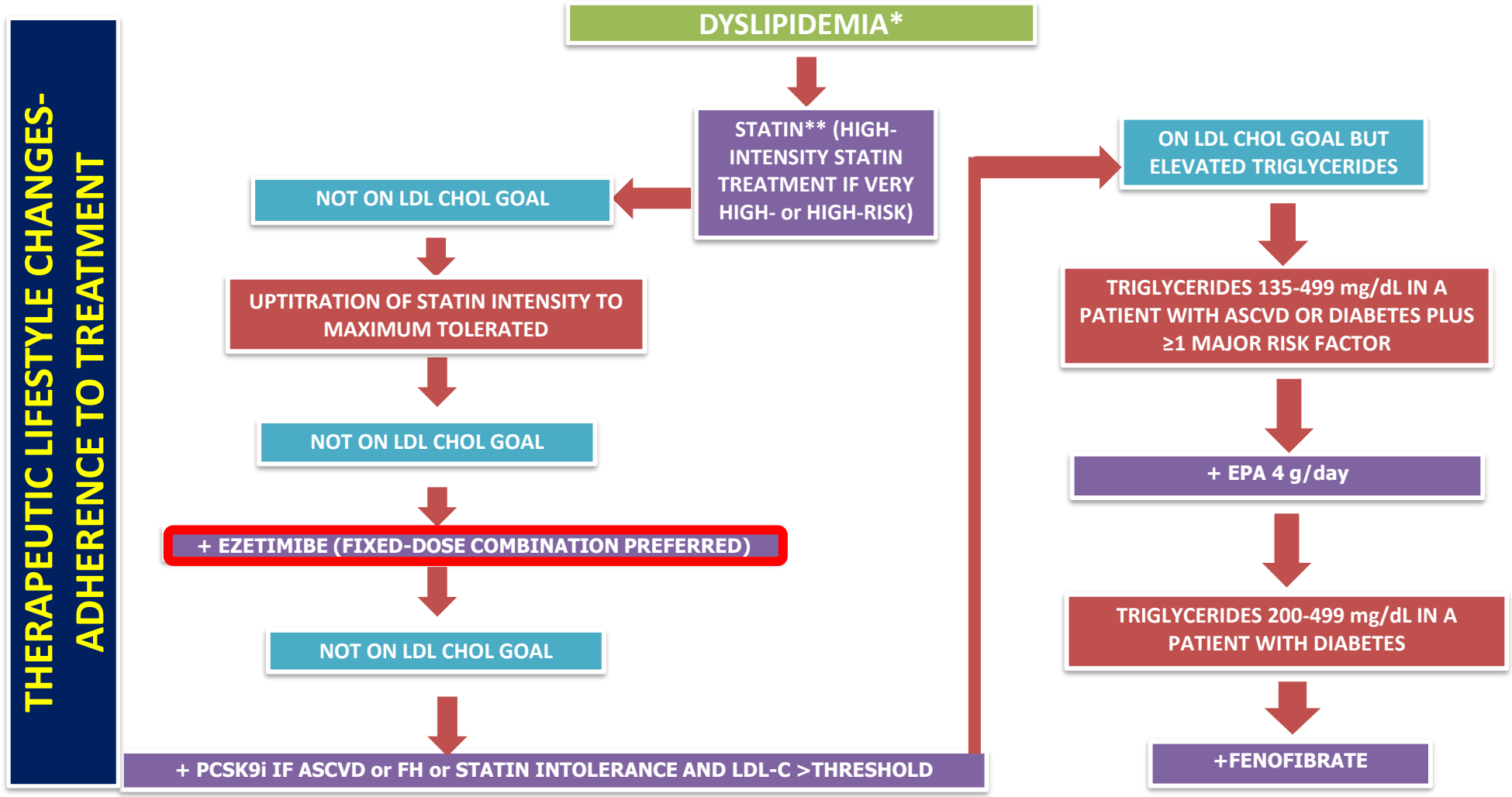

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ΑΝΤΙΜΕΤΩΠΙΖΟΝΤΑΣ ΤΟΝ ΑΣΘΕΝΗ ΜΕ ΟΙΚΟΓΕΝΗ ΥΠΕΡΧΟΛΗΣΤΕΡΟΛΑΙΜΙΑ

ROSUVASTATIN 40 mg X 1

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

ΑΜΕΣΗ ΕΝΑΡΞΗ!

ΕΠΙΤΥΓΧΑΝΟΝΤΑΣ ΤΟΥΣ ΣΤΟΧΟΥΣ ΤΗΣ ΘΕΡΑΠΕΙΑΣ

ΠΡΟΣΘΗΚΗ EZETIMIBE 10 mg X 1

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

ΠΡΟΣΟΧΗ! ΣΥΜΒΟΥΛΗ ΓΙΑ ΔΙΑΚΟΠΗ ΣΤΑΤΙΝΗΣ + ΕΖΕΤΙΜΙΜΠΗΣ ~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

FDA U.S. FOOD & DRUG ADMINISTRATION

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

[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.

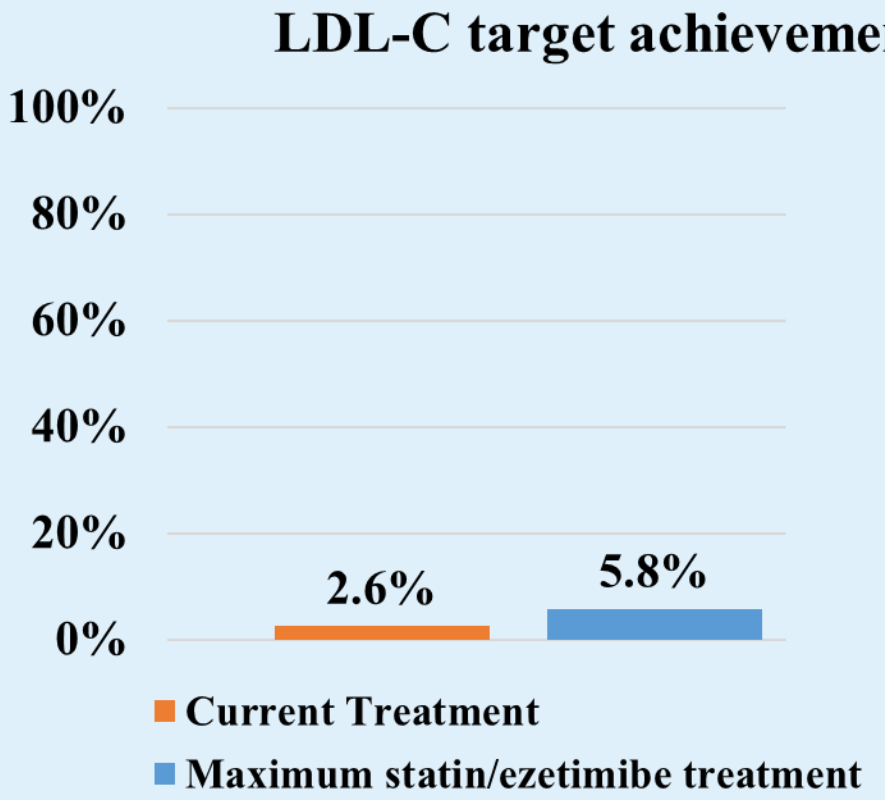
Recommendations for coronary artery disease and pregnancy

Recommendations	Class	Level
In pregnant women with chest pain, it is recommended to exclude life-threatening cardiovascular conditions, including PE, ACS (including SCAD), and acute aortic syndrome.	I	C
It is recommended to manage pregnant women with ACS in the same way as non-pregnant women, including diagnostic investigations and interventions.	I	C
Low-dose ASA is recommended as the antiplatelet treatment of choice during pregnancy and lactation when single antiplatelet treatment is indicated.	I	B
If DAPT is required, clopidogrel is recommended as the P2Y12 inhibitor of choice during pregnancy.	I	C
The duration of DAPT (aspirin and clopidogrel) in pregnant women undergoing coronary stent implantation is recommended to be the same as in non-pregnant women, with an individual approach considering ischaemic risk and delivery-related bleeding risks.	I	C
A vaginal delivery should be considered in most pregnant women with ACS, depending on LV function and clinical symptoms.	IIa	C
Continuation of statins may be considered during pregnancy in women with established ASCVD.	IIb	C

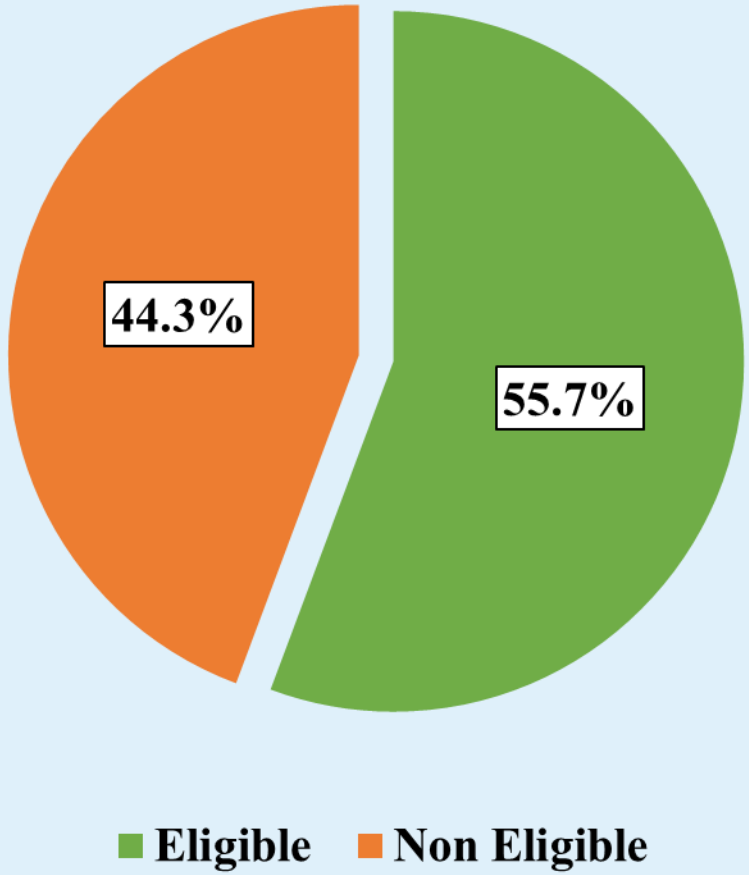
2025 ESC Guidelines for the management of cardiovascular disease and pregnancy
(European Heart Journal; 2025 – doi: 10.1093/eurheartj/ehaf193)

HELLAS-FH: Results

- Οι ασθενείς με FH χρήζουν επιπρόσθετης υπολιπιδαιμικής θεραπείας

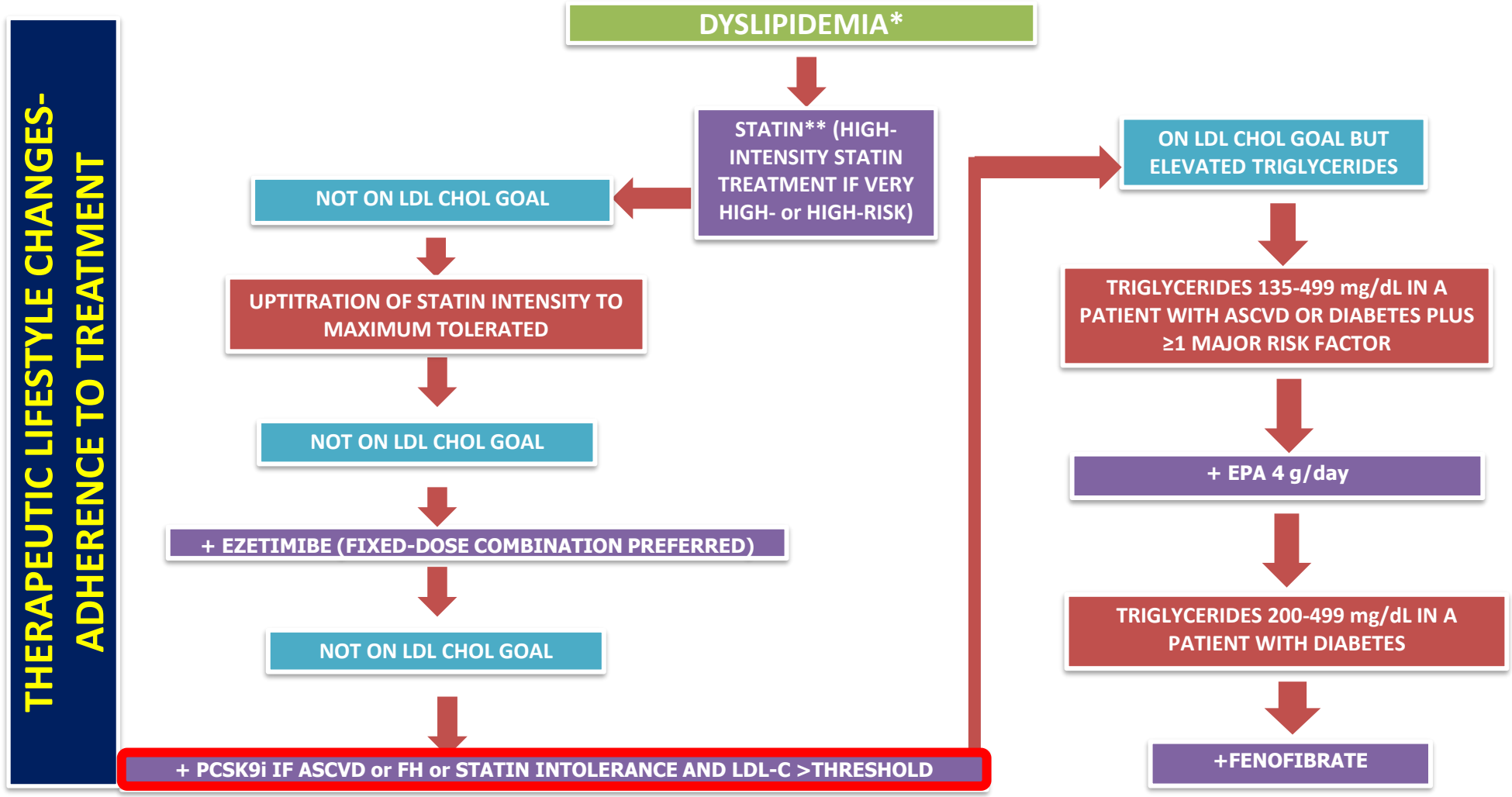


- Οι ασθενείς με FH συχνά χρήζουν θεραπείας με PCSK9i



Rizos CV et al. LDL cholesterol target achievement in heterozygous familial hypercholesterolemia patients according to 2019 ESC/EAS lipid guidelines: Implications for newer lipid-lowering treatments. Int J Cardiol. 2021 Oct 21:S0167-5273(21)01578-3. doi: 10.1016/j.ijcard.2021.10.024

ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023



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**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

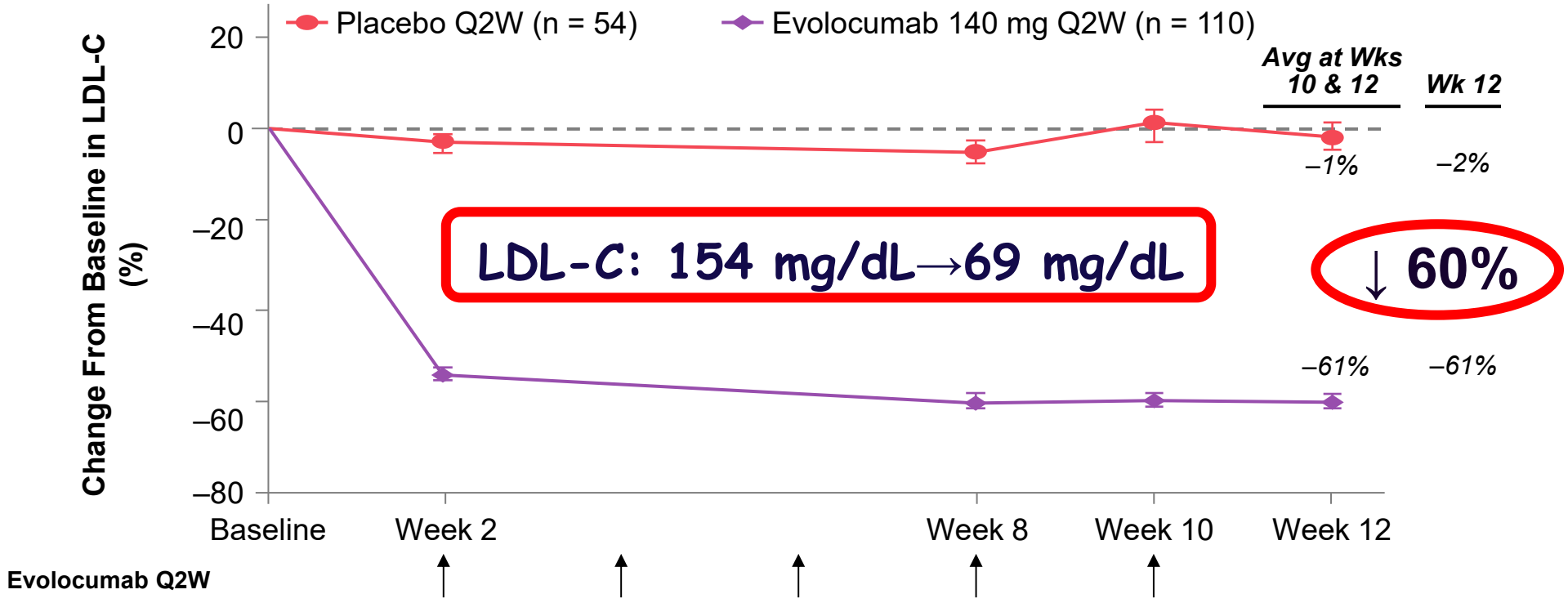
1. ASCVD PLUS FH OR RECURRENT/PROGRESSIVE DISEASE DURING THE LAST 2 YEARS OR PREMATURE ASCVD (MEN <45/WOMEN <55 YEARS) WITH LDL-C ≥70 mg/dL

2. OTHER ASCVD AND LDL-C ≥100 mg/dL

3. FAMILIAL HYPERCHOLESTEROLEMIA AND LDL-C ≥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

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

News Alert

U.S. Food and Drug Administration Approves LIB Therapeutics' LEROCHOL™ (lerodalcibep-liga) for Adults with Elevated LDL Cholesterol

FDA Approves LIB Therapeutics' LEROCHOL™ (lerodalcibep-liga) for Adults with High LDL Cholesterol

The U.S. Food and Drug Administration (FDA) has approved LEROCHOL™ (lerodalcibep-liga), a novel, third-generation PCSK9 inhibitor, for adults with high LDL lipoprotein cholesterol (LDL-C), including individuals with familial hypercholesterolemia (FH).

LEROCHOL is expected to be available in the United States in spring 2026.

Research

JAMA | Original Investigation

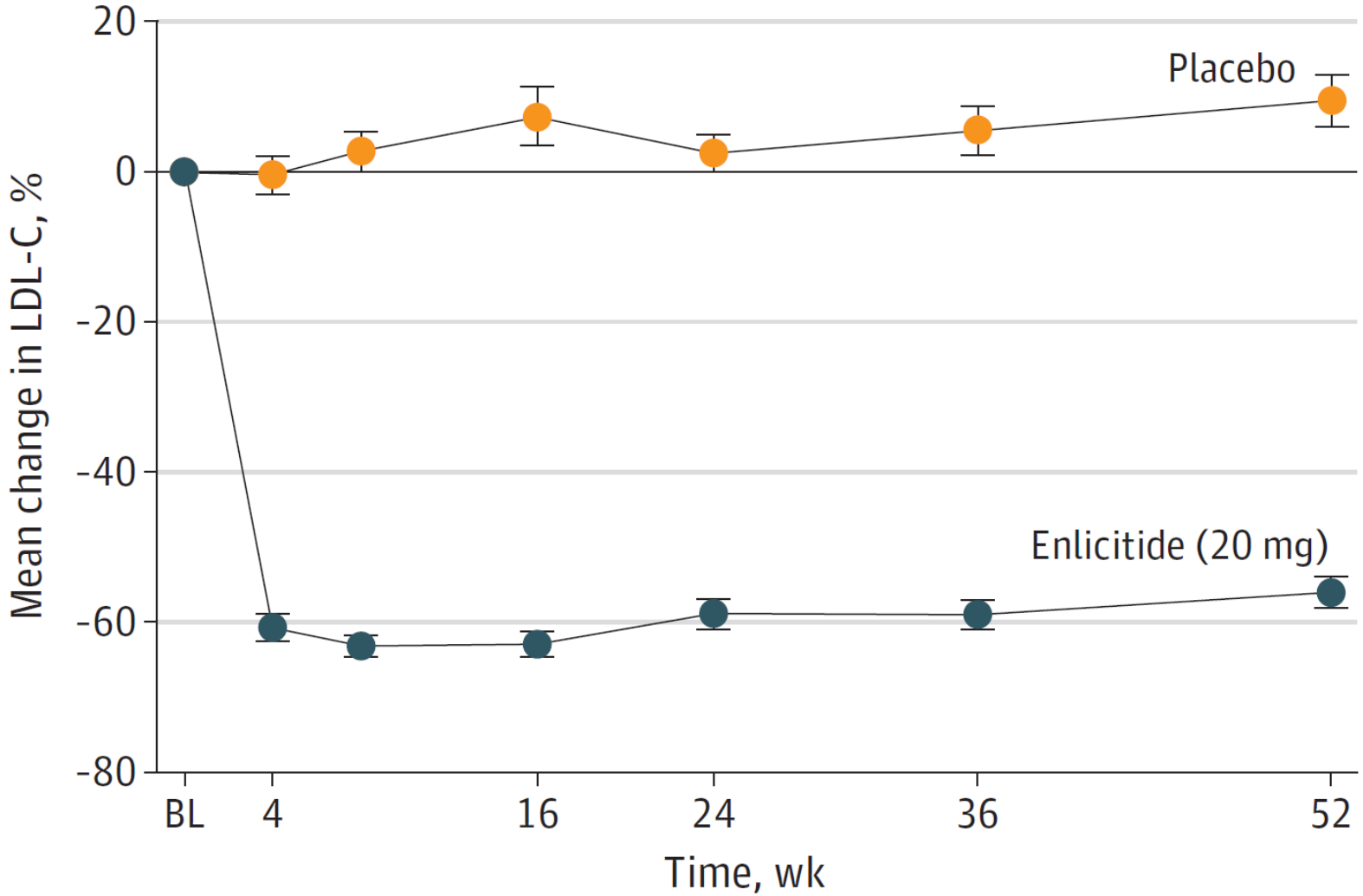
Efficacy and Safety of Oral PCSK9 Inhibitor Enlicitide in Adults With Heterozygous Familial Hypercholesterolemia

A Randomized Clinical Trial

Christie M. Ballantyne, MD; Laura Gellis, MD, MPH; Jean-Claude Tardif, MD; Puja Banka, MD; Ann Marie Navar, MD, PhD; Emil Andreas Asprusten, MD; Russell Scott, MD; Erik S. G. Stroes, MD; Samar Froman, BS; Geraldine Mendizabal, MD; Fan Wang, PhD; Alberico L. Catapano, MDHc, PhD

JAMA. doi:10.1001/jama.2025.20620
Published online November 9, 2025.

B Percentage change in LDL-C from baseline to 52 wk (secondary outcome)



No. of participants							
Placebo	101	96	95	94	96	94	94
Enlicitide (20 mg)	202	197	196	195	198	195	193

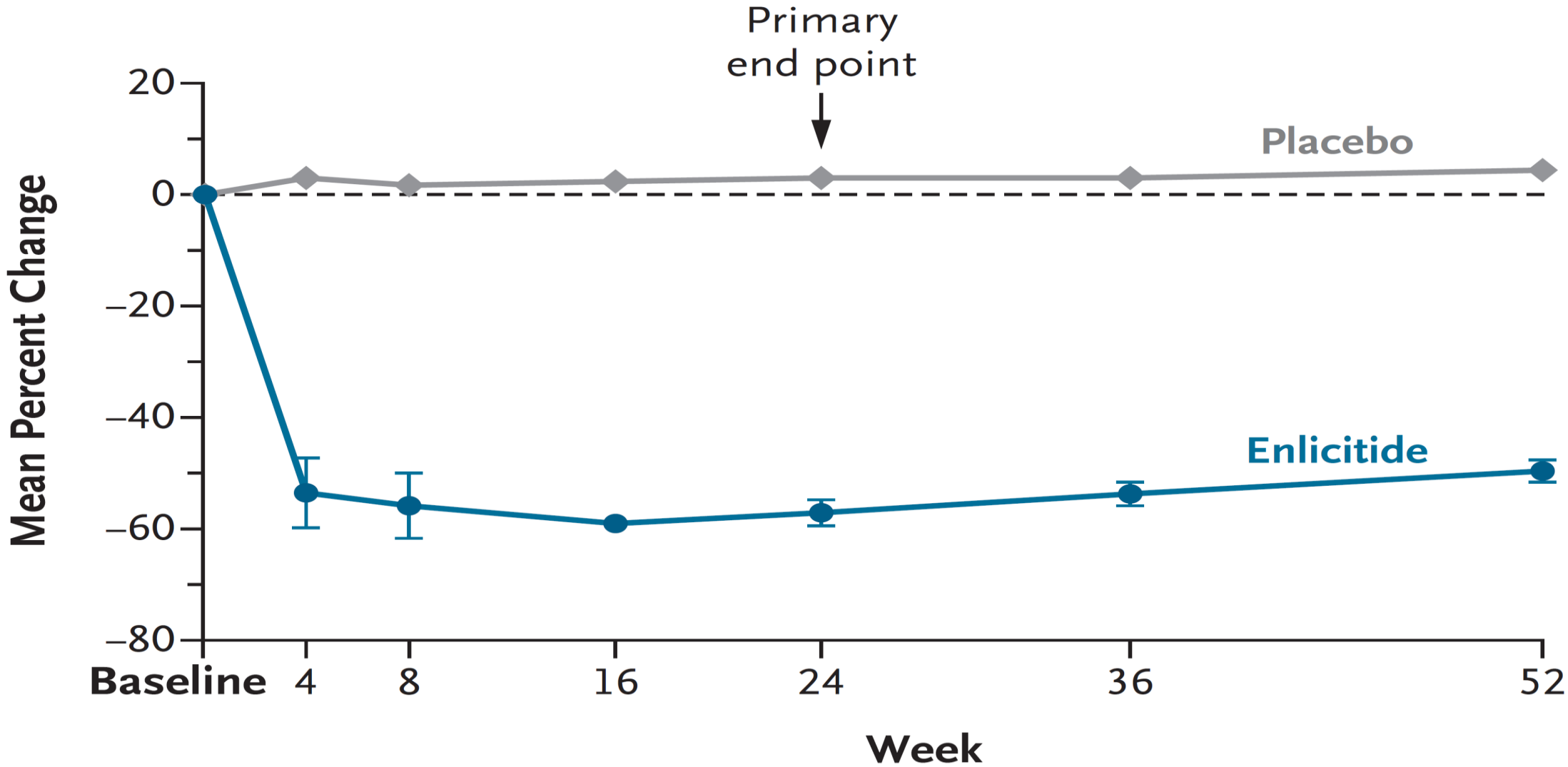
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 5, 2026 VOL. 394 NO. 6

A Placebo-Controlled Trial of the Oral PCSK9 Inhibitor Enlicitide

Ann Marie Navar, M.D., Ph.D.,[1] Elina Mikhailova, M.D., Ph.D.,[2] Alberico L. Catapano, Ph.D.,[3,4] Puja Banka, M.D.,[5] Dirk J. Blom, M.D.,[6] Alberto Cadena, M.D.,[7] Susan Kourpanidis, M.S.,[5] Norman E. Lepor, M.D.,[8,9] Kazuhisa Tsukamoto, M.D., Ph.D.,[10] Geraldine Mendizabal, M.D.,[11] Julio Nunez, M.D.,[12] Wenjuan Zhang, Ph.D.,[13] Pengfei Zhu, D.Phil.,[13] Min Zhuo, M.D., M.P.H.,[5] and Christie M. Ballantyne, M.D.,[14] for the CORALreef Lipids Investigators*

A Change in LDL Cholesterol Levels



No. of Participants							
Placebo	969	933	937	927	923	909	898
Enlicitide	1935	1836	1852	1824	1832	1798	1771

Initial safety and efficacy data from single ascending dose portion of Phase 1b heart-1 study expected in 2H23

heart-1

SINGLE ASCENDING DOSE

Starting dose ····· Low dose ····· Intermediate dose ····· High dose

3-6 participants per group with staggering and sentinel dosing

GLOBAL REGULATORY STRATEGY	STUDY ENROLLMENT	INITIAL DATA IN 2H23
• Regulatory clearances in New Zealand and the U.K.	• Recruitment ongoing in New Zealand and the U.K.	• Data from dose escalation portion of the study
Working to resolve Investigational New Drug (IND) application hold and start trial in the U.S.	Enrolling high risk HeFH patients with established ASCVD and LDL not at goal	Safety parameters, blood PCSK9, and blood LDL-C

Source: *Verve Therapeutics*

April 14, 2025 07:00 ET

Verve Therapeutics Announces Positive Initial Data from the Heart-2 Phase 1b Clinical Trial of VERVE-102, an In Vivo Base Editing Medicine Targeting PCSK9

VERVE-102 total RNA dose range	**< 25 mg**	**25 – < 50 mg**	**50 – < 60 mg**
Participants, n	4	7	3
Mean total RNA dose	20 mg	37 mg	55 mg
Mean LDL-C % reduction from baseline	-21%	-41%	-59%

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*

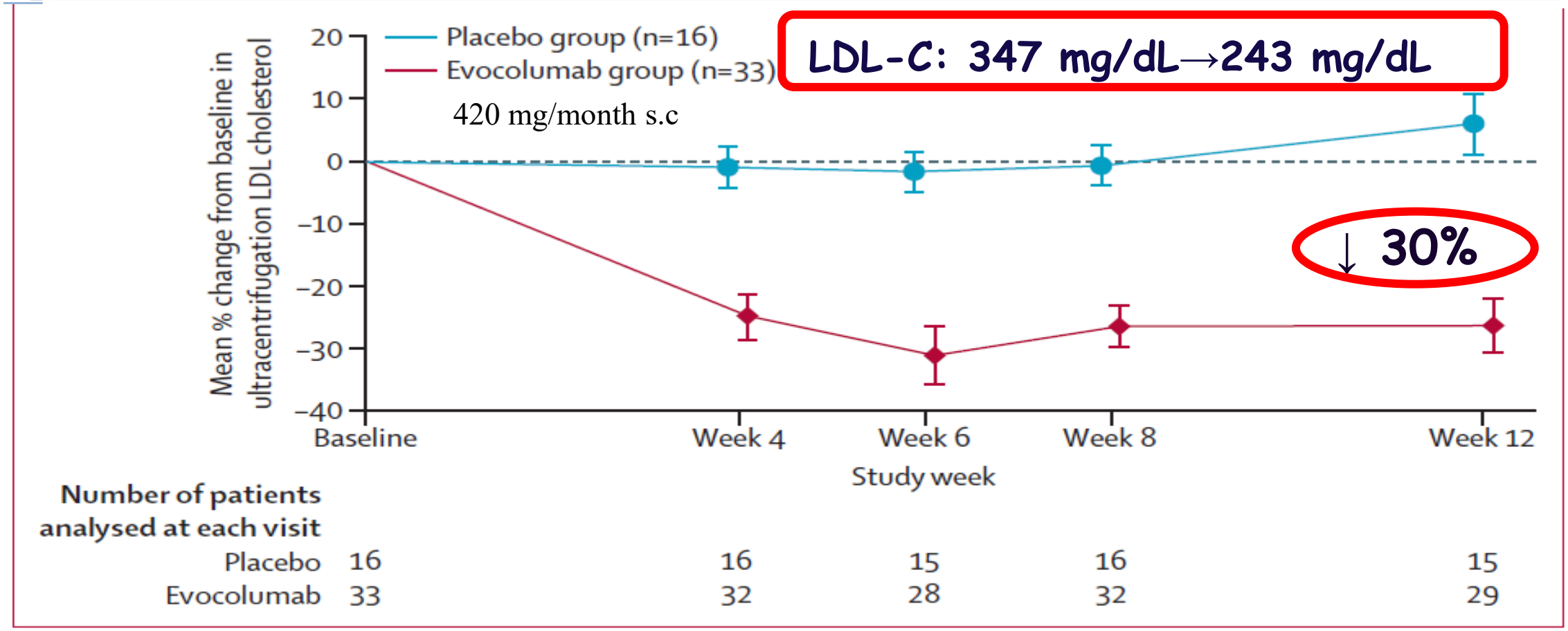
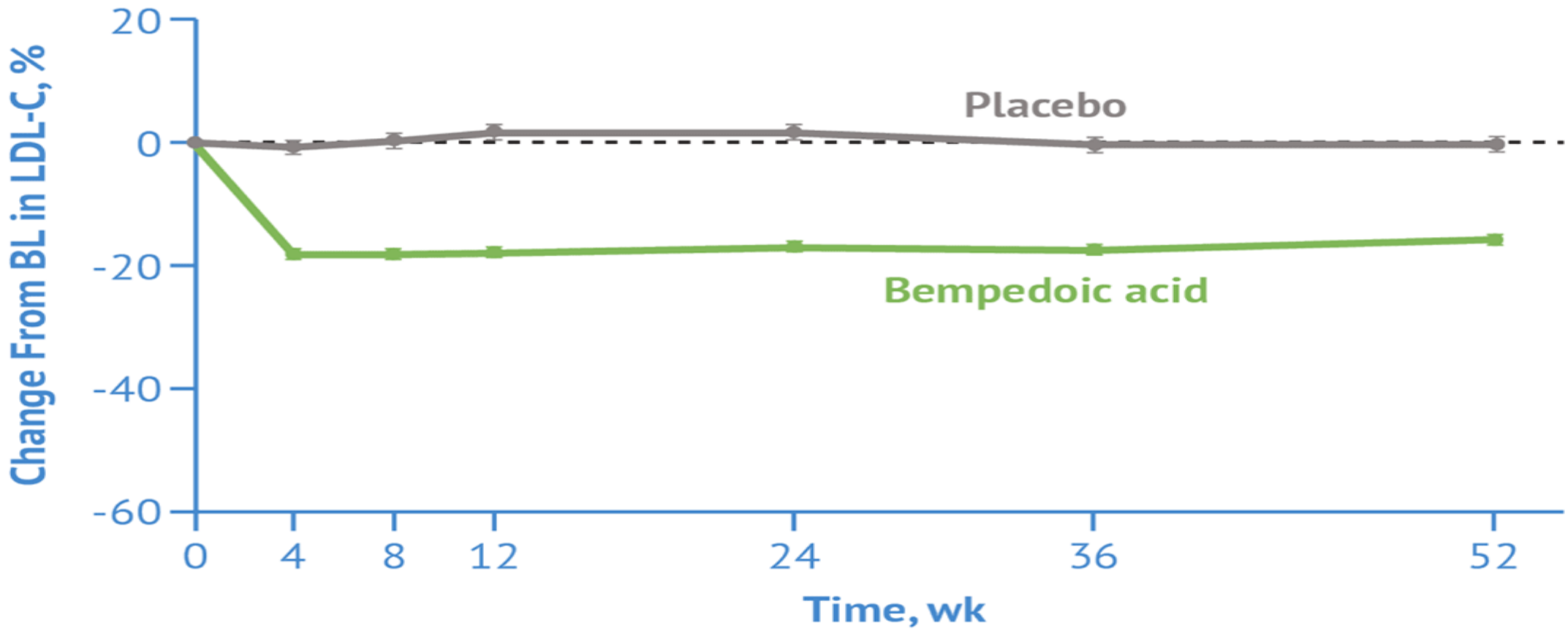


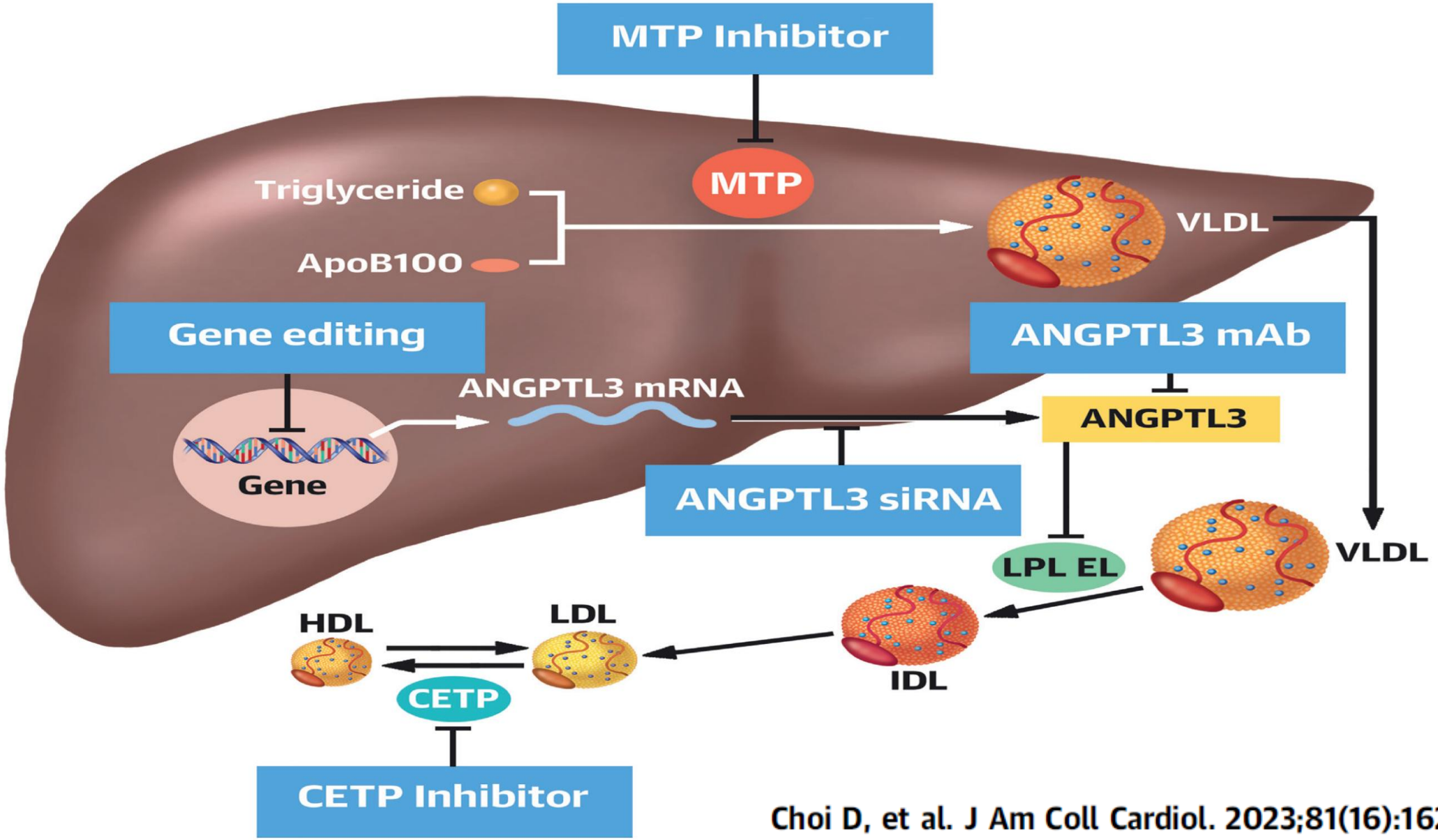
Figure 2: Mean percentage change in ultracentrifugation LDL cholesterol concentration from baseline to week 12

www.thelancet.com Published online October 2, 2014

Bempedoic Acid and Reduction in LDL-C in HeFH[16]

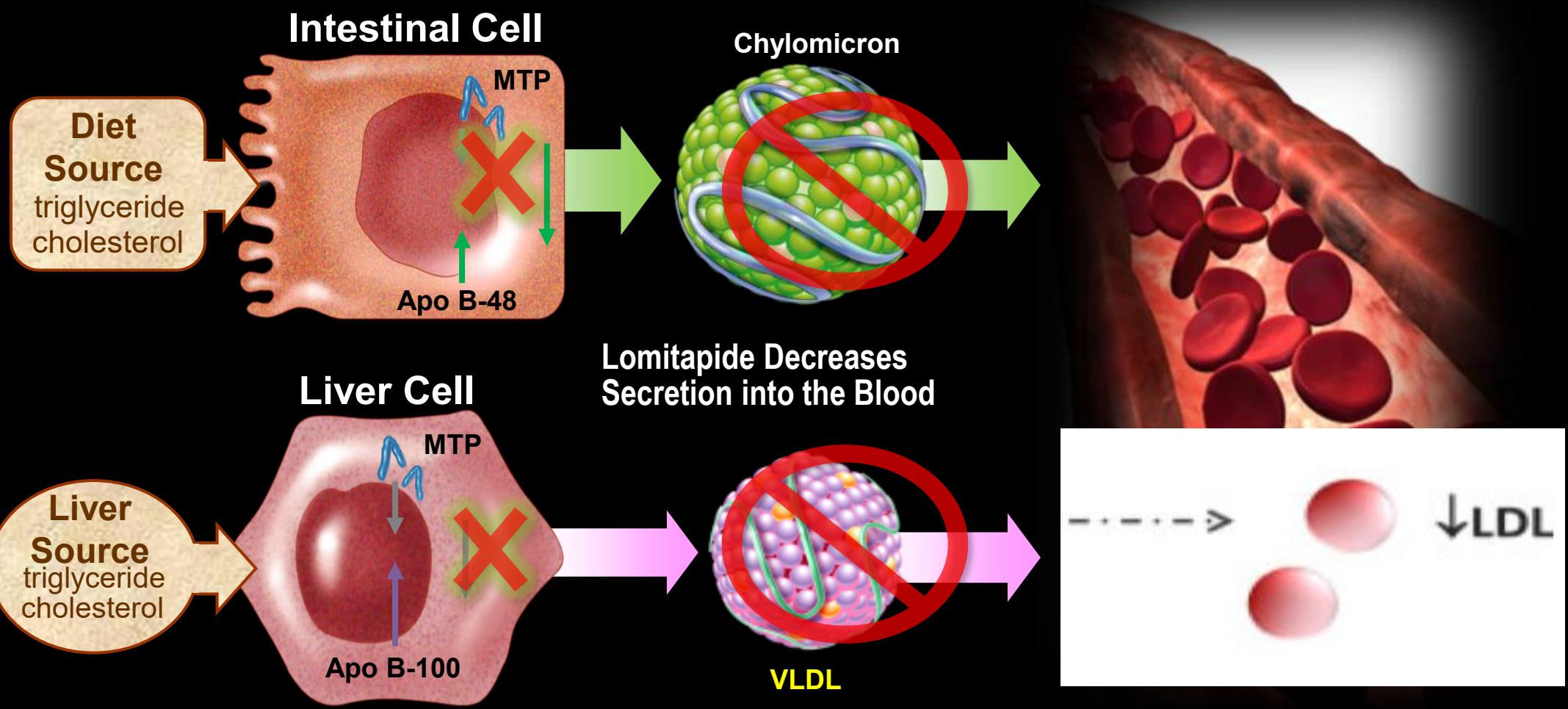


LDL-R INDEPENDENT TREATMENTS

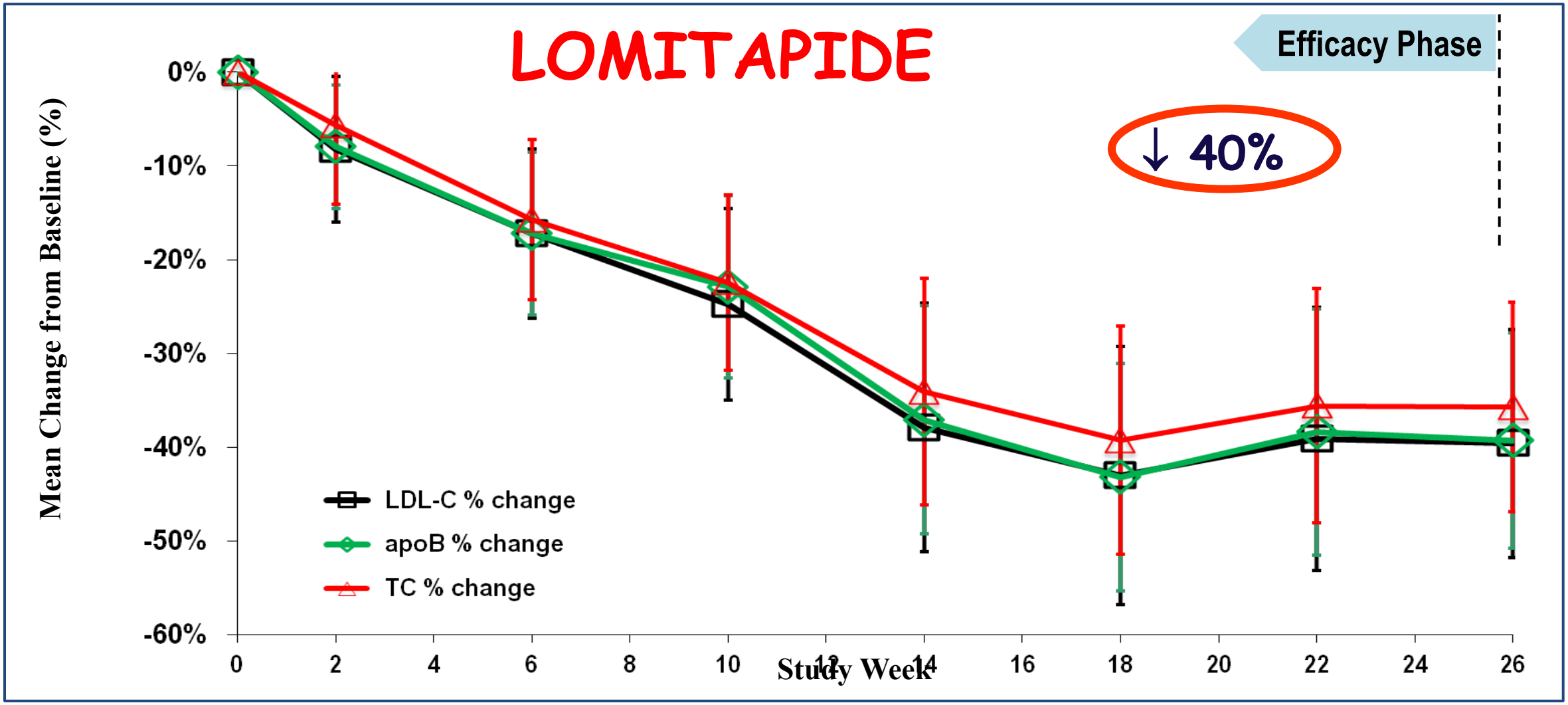


Choi D, et al. J Am Coll Cardiol. 2023;81(16):1621-1632.

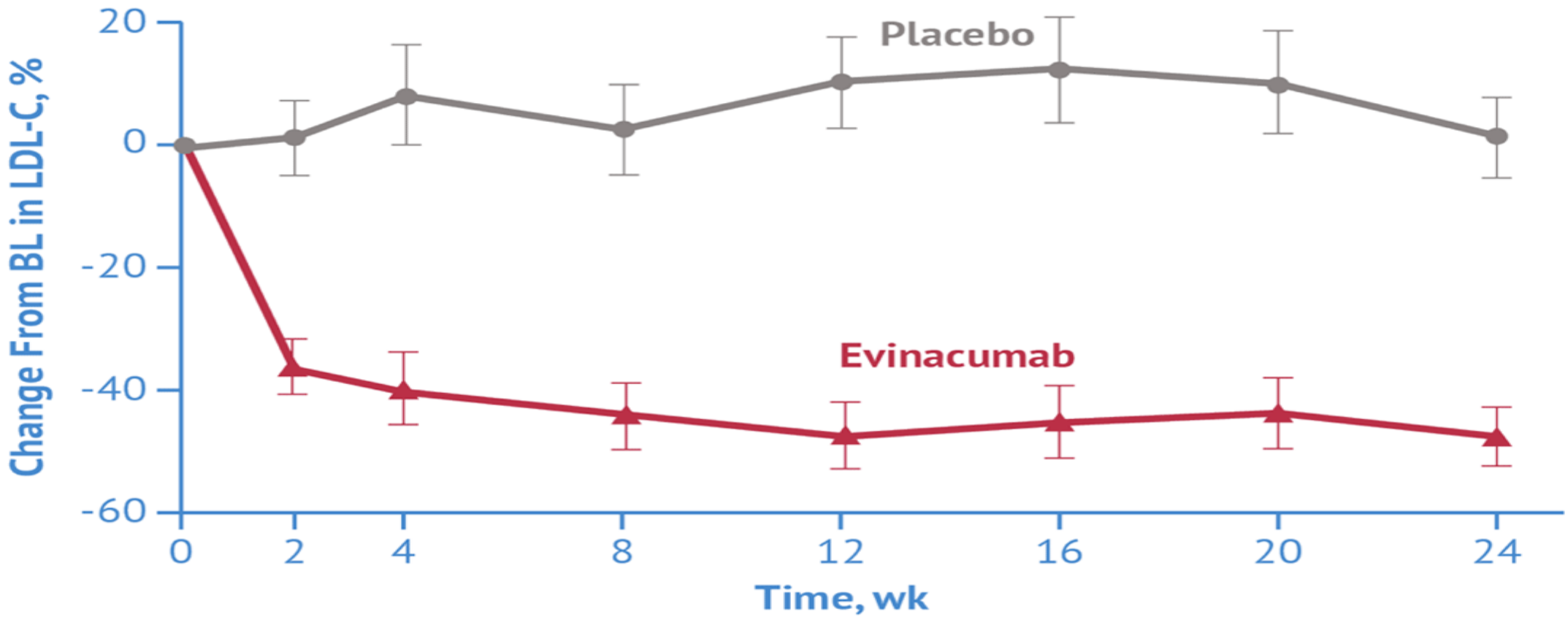
MTP Inhibition Predicted to Reduce Production of Both Chylomicrons and VLDL



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



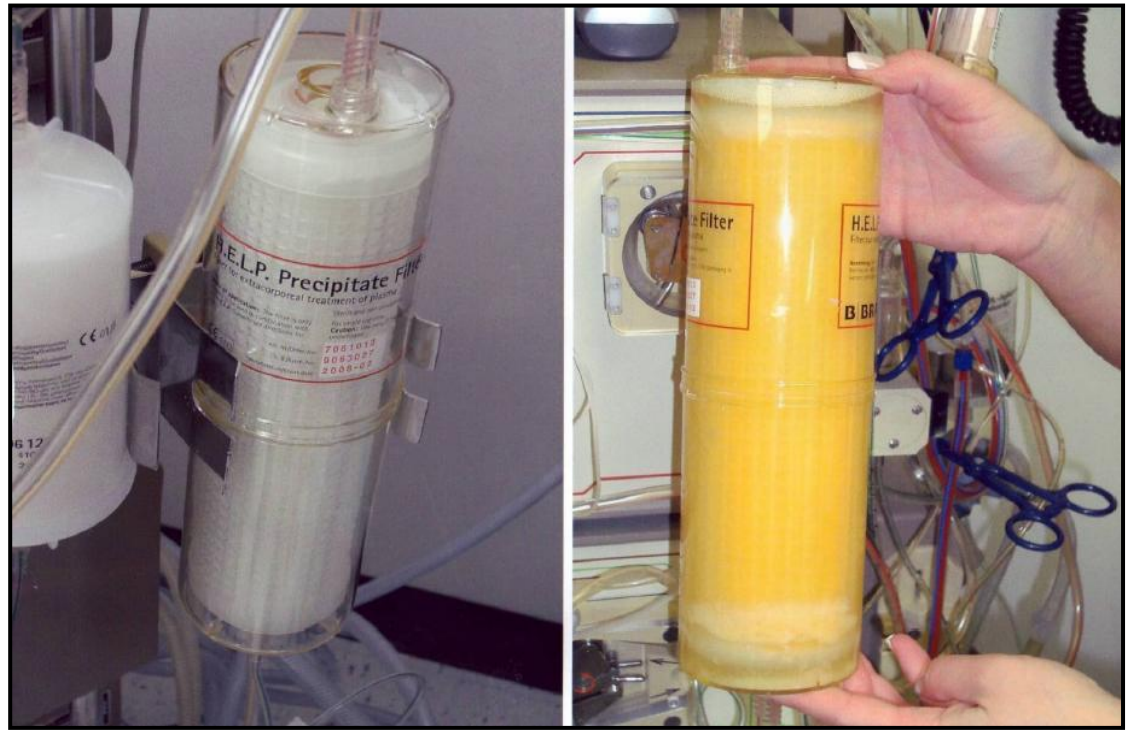
Evinacumab and Reduction in LDL-C in HoFH[13]



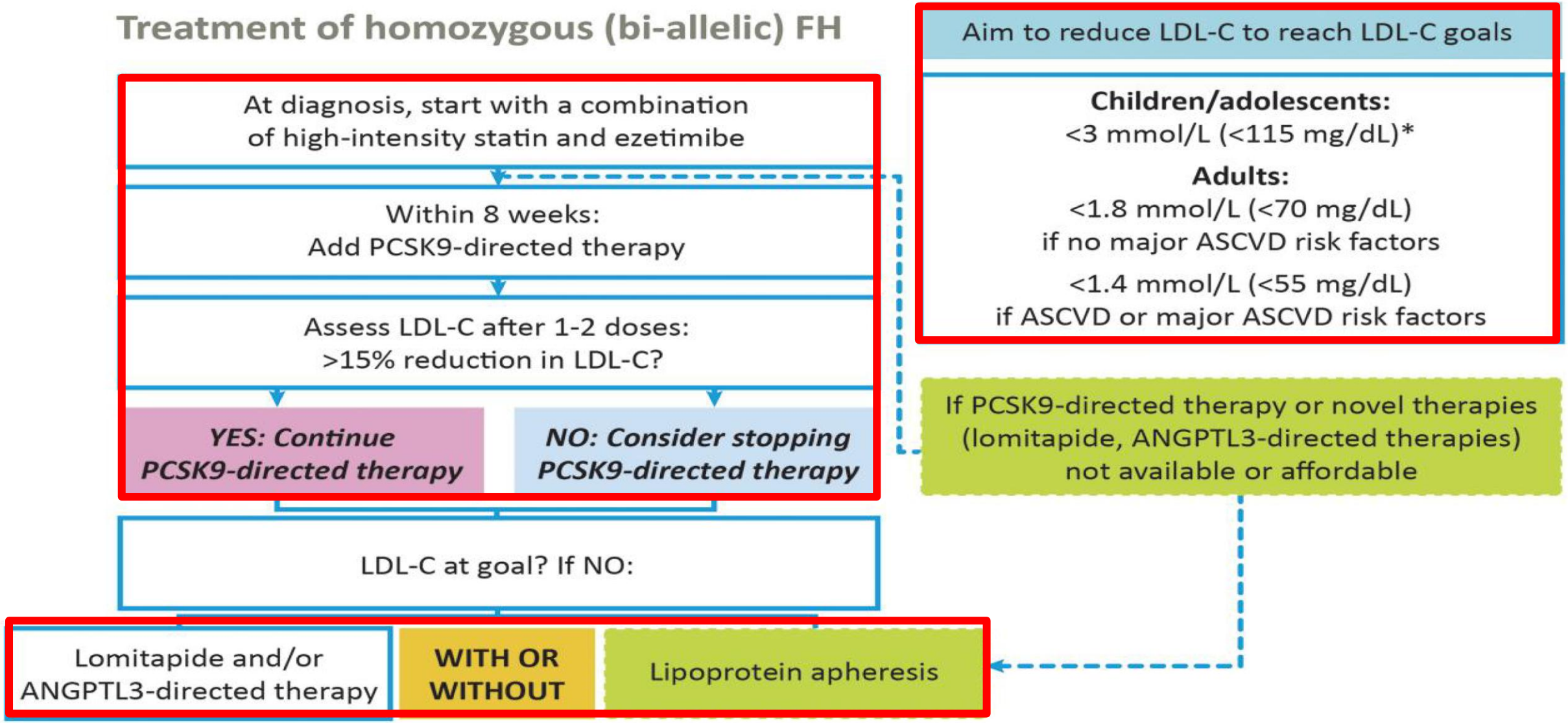
LDL-C was lower in the evinacumab group vs placebo for both null-null and non-null variants

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 of homozygous (bi-allelic) FH



*Lower goals may require imaging

Liver transplant may have a role in severely affected HoFH patients refractory to the above treatment options or when these options are not available or affordable.

EAS

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

Zodasiran, an RNAi therapeutic targeting ANGPTL3, for treating patients with homozygous familial hypercholesterolaemia (GATEWAY): an open-label, randomised, phase 2 trial

Frederick J Raal, Jean Bergeron, Daniel Gaudet, Robert S Rosenson, David R Sullivan, Traci Turner, Robert A Hegele, Christie M Ballantyne, Joshua W Knowles, Nicholas J Leeper, Ira J Goldberg, Rong Zhou, Ma'an Muhsin, Jennifer Hellawell, James Hamilton, Gerald F Watts

Lancet Diabetes Endocrinol 2025

Published Online
December 18, 2025
https://doi.org/10.1016/
S2213-8587(25)00290-6

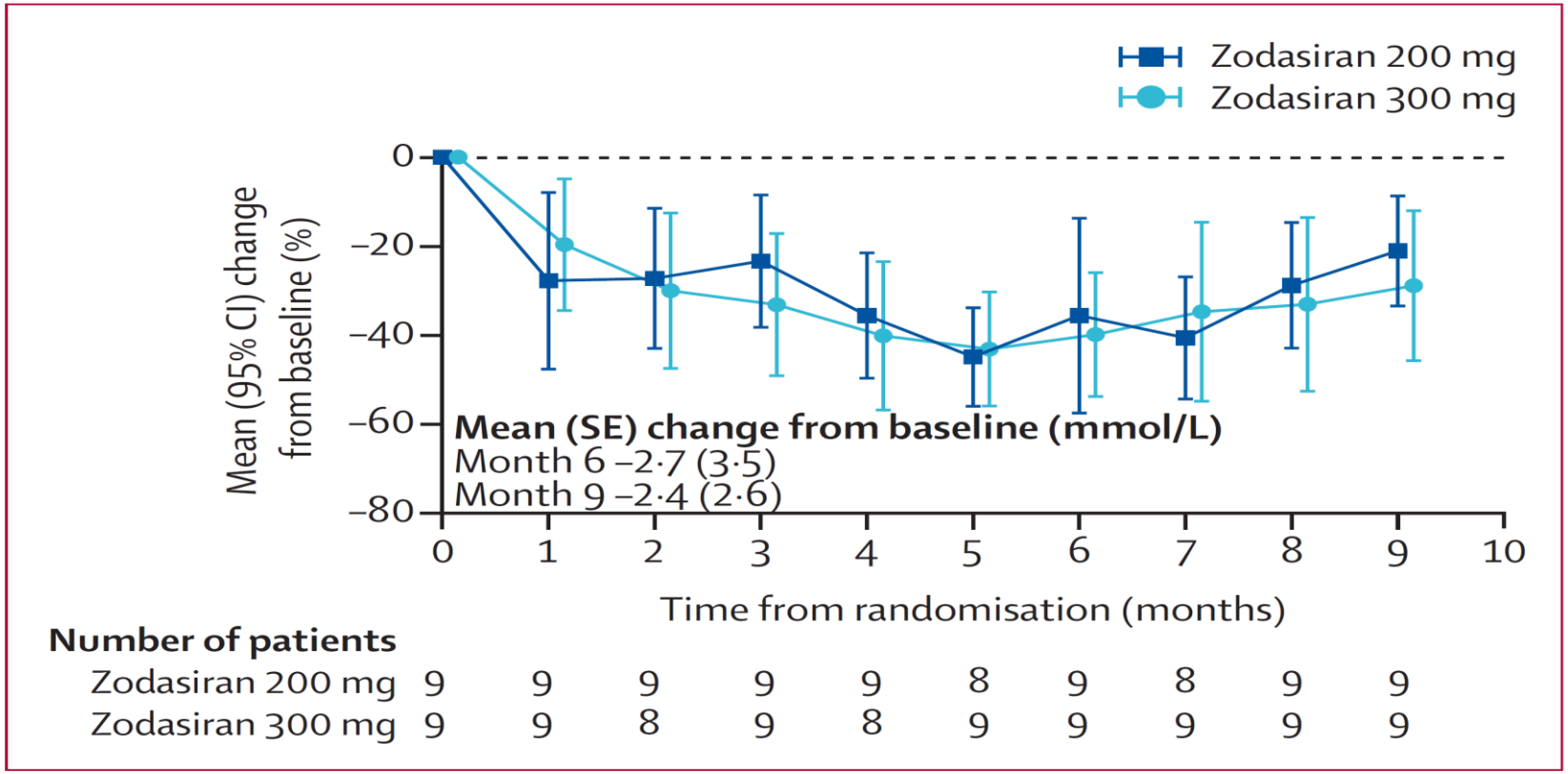


Figure 2: **Percentage change from baseline in fasting LDL cholesterol (preparative ultracentrifugation) through the randomised treatment period**

JACC VOL. ■, NO. ■, 2025

Effect of ANGPTL3 Inhibition With Solbinsiran in Preclinical and Early Human Studies

Kausik K. Ray, FMedSci,[a] Helle Linnebjerg, PhD,[b] Laura F. Michael, PhD,[b] Xi Shen, PhD,[b] Xiaosu Ma, PhD,[b] Shufen Lim, PhD,[b] Eugene Y. Zhen, PhD,[b] Henryk Dudek, PhD,[c] Marc Abrams, PhD,[c,d] Utsav Saxena, PhD,[c] Anton Turanov, PhD,[c] Stephen J. Nicholls, PhD,[e] Giacomo Ruotolo, MD[b]

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 1 Trial of CRISPR-Cas9 Gene Editing Targeting ANGPTL3

Luke J. Laffin, M.D.,[1,2] Stephen J. Nicholls, M.B., B.S., Ph.D.,[3] Russell S. Scott, M.B., Ch.B., Ph.D.,[4] Peter M. Clifton, M.B., B.S., Ph.D.,[5] John Baker, M.D.,[6] Ashish Sarraju, M.D.,[1,2] Shweta Singh, Ph.D.,[7] Qiuqing Wang, M.S.,[2] Kathy Wolski, M.P.H.,[2] Huansheng Xu, Ph.D.,[7] Jen Nielsen, M.S.,[7] Naimish Patel, M.D.,[7] Jason M. Duran, M.D., Ph.D.,[7] and Steven E. Nissen, M.D.[1,2]

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