1ère Année de Médecine

Cas de liaison

Athérosclérose #5

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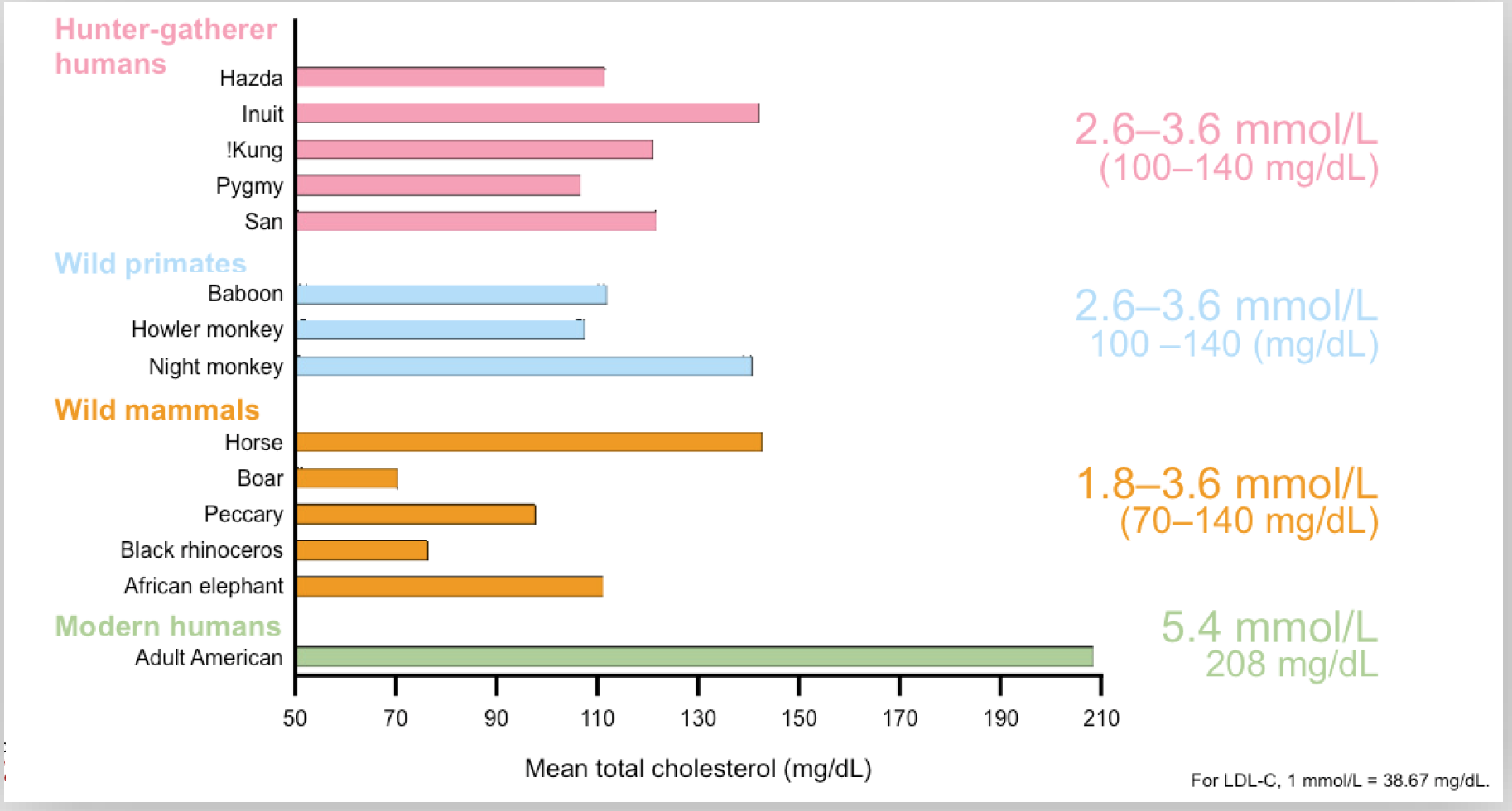
Genève, le 11 décembre 2025

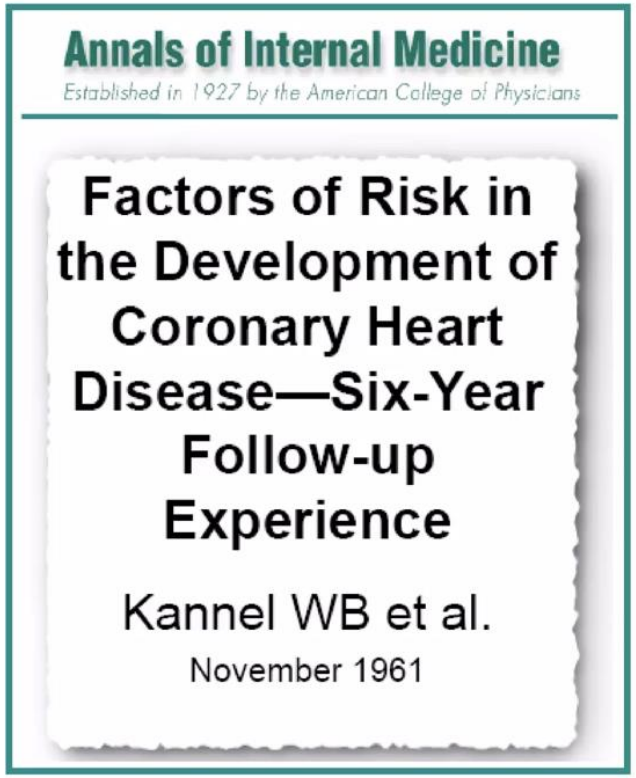
Cholesterol levels: Us versus them…



JACC 2004;43:2142

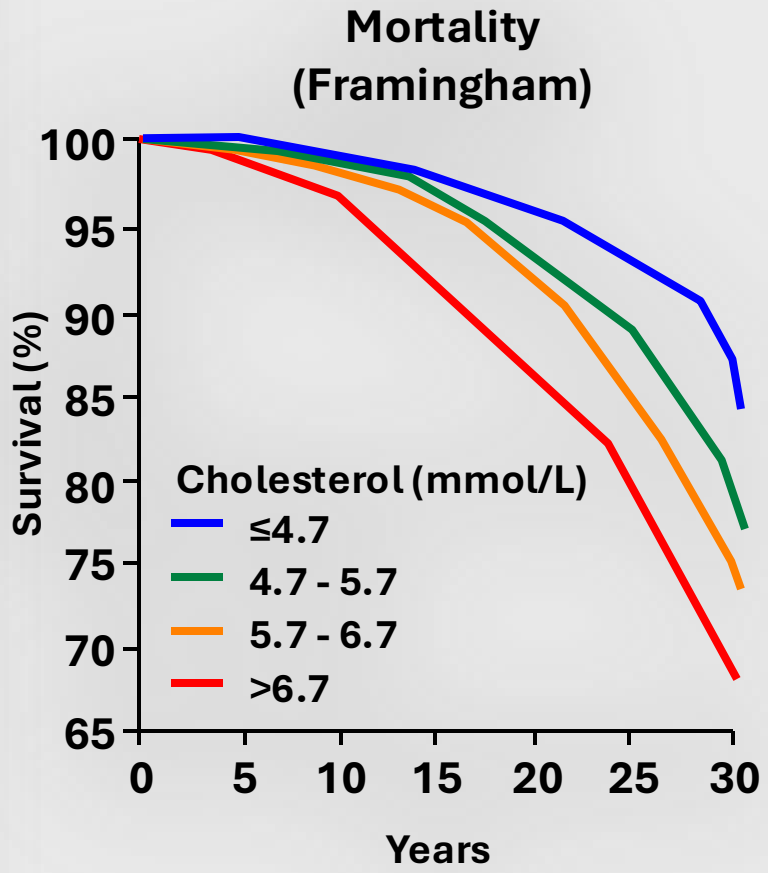
Cholestérol et risque CV

Early Biomarkers: "Factors of Risk"



- High blood pressure
- Increased cholesterol
- Smoking
- Diabetes
- Family history
- Male gender

Source: Kannel WB et al. *Ann Intern Med* 1961;55:33–50.

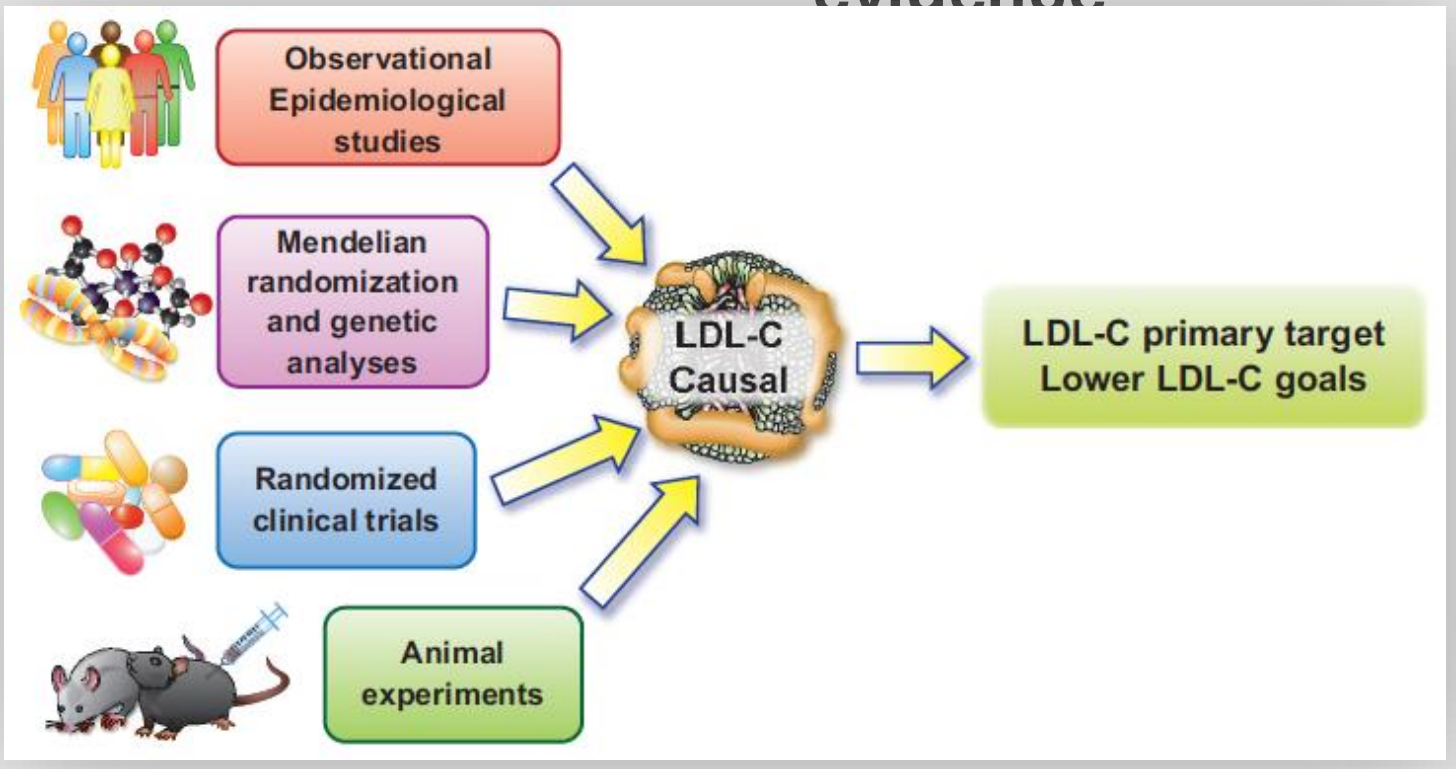


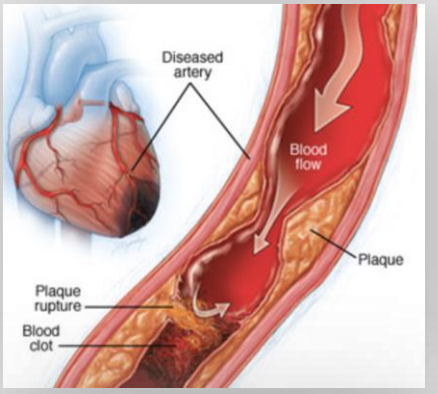
What is a “normal” LDL-cholesterol ?

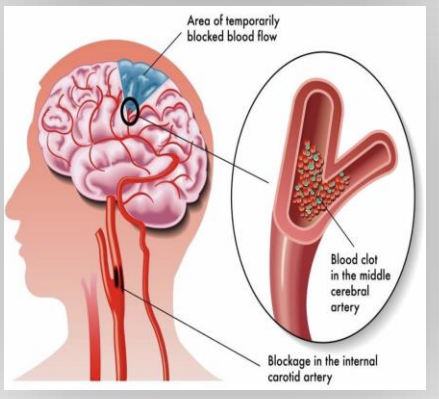
We were all born with a LDL-c value around 1.2 mmol/l

Clear relationship between LDL-C and risk of CV events

LDL-C is the main driver for atherosclerosis: 4 compelling lines of evidence







Eur Heart J 2022;43:3198

Time-exposure to LDL-c

JACC CV HEALTH PROMOTION SERIES

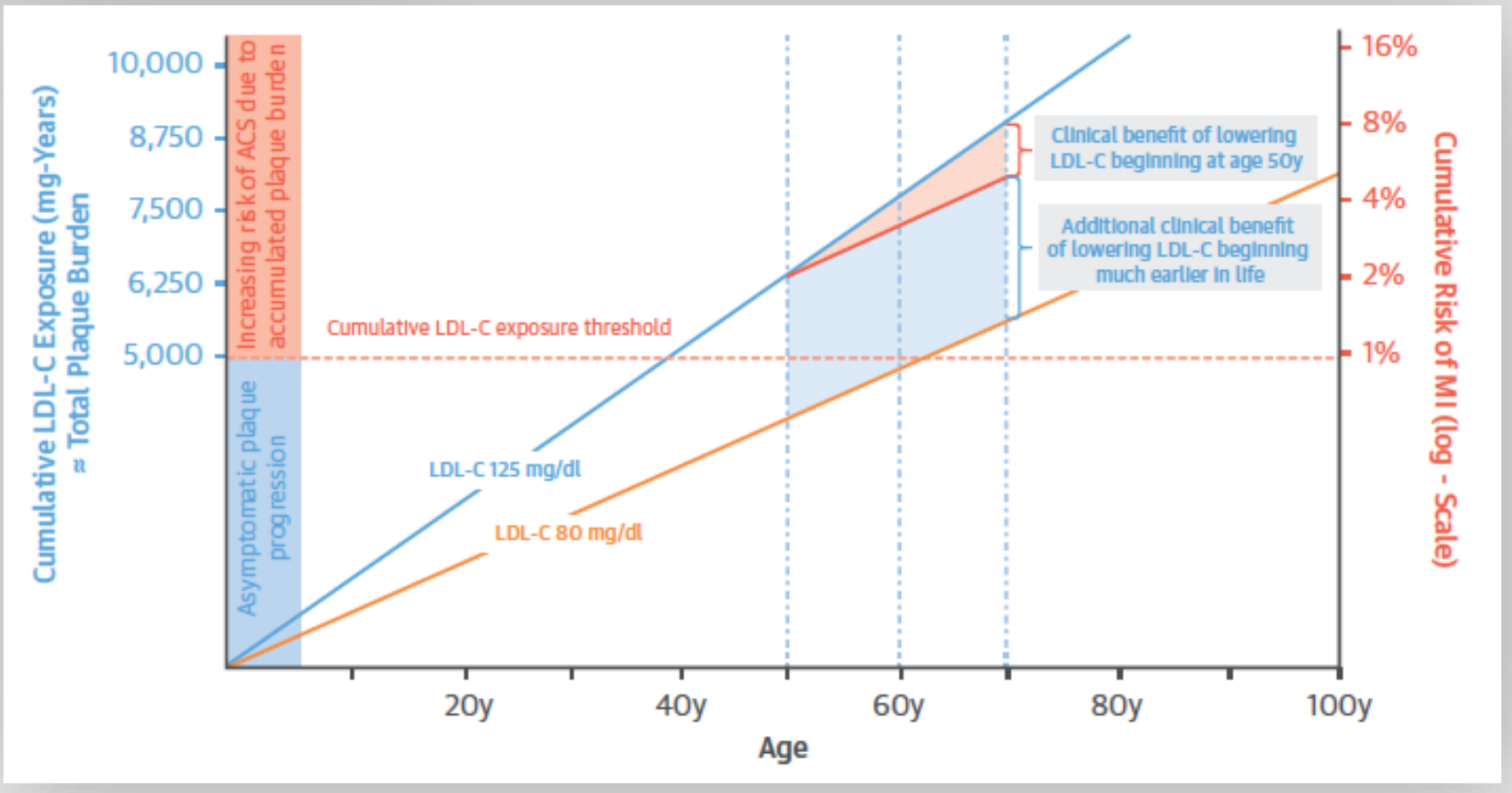
JACC FOCUS SEMINAR

Reprint of: Impact of Lipids on Cardiovascular Health

JACC Health Promotion Series

Brian A. Ference, MD, MPhil, MSc,[a] Ian Graham, MD,[b] Lale Tokgozoglu, MD,[c] Alberico L. Catapano, PhD[d,e]

JACC 2018;72:2890



Cholestérol & Athérosclérose

Dyslipidémies

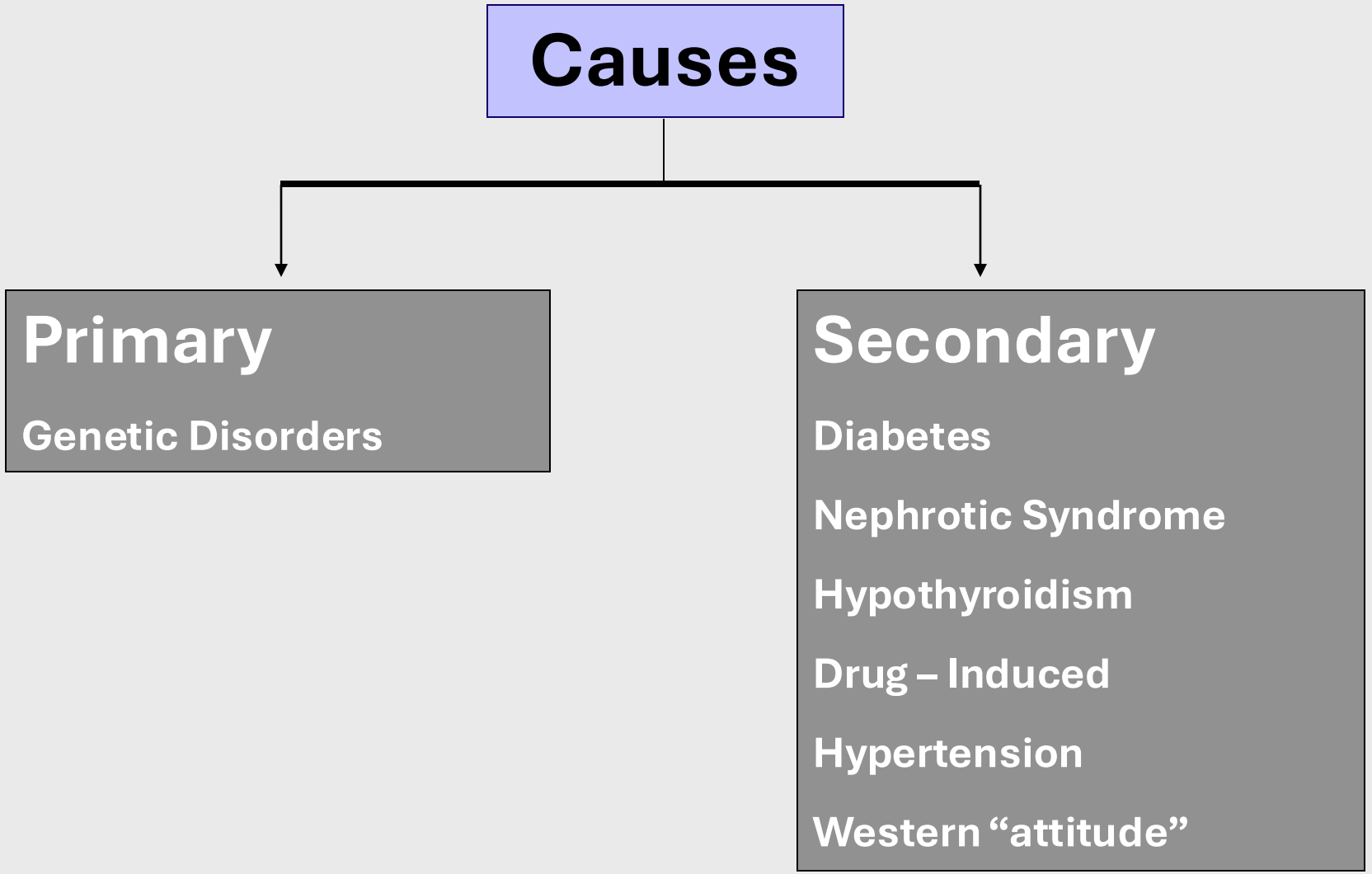
- **Disorder of lipid & lipoprotein metabolism**

- **A common form of dyslipidemia is characterized by three lipid abnormalities:**
  - **Elevated triglycerides,**
  - **Elevated LDL and**
  - **Reduced HDL cholesterol**

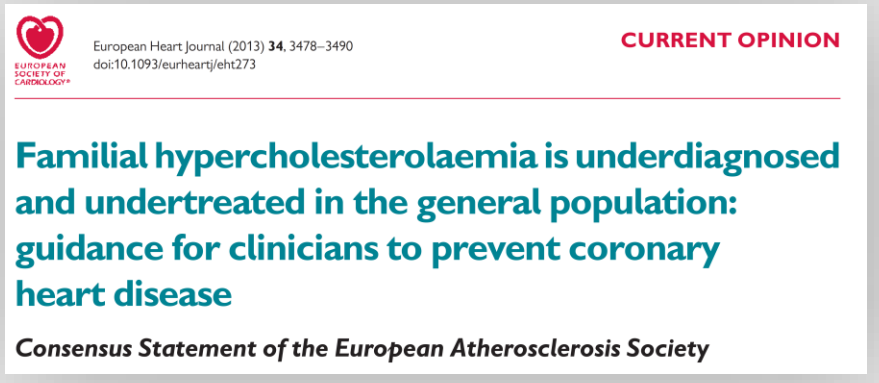
- **Important modifiable risk factor for CAD**

Cholestérol & Athérosclérose

Dyslipidémies



Hypercholestérolémie Familiale



European Heart Journal (2013) **34**, 3478–3490
doi:10.1093/eurheartj/eht273

CURRENT OPINION

Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease

Consensus Statement of the European Atherosclerosis Society

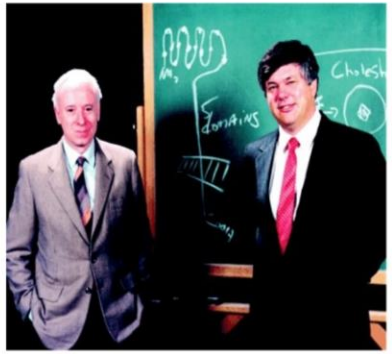
Familial hypercholesterolemia (FH) is a genetically modulated clinical syndrome in which the phenotype is characterized by a high LDL-c level from birth, a propensity to tendon xanthomata, and early onset CHD.

Its established causes are LDLR mutations (most common), gain-of-function PCSK9 mutations, familial defective apoB, and Lp(a) mutations.

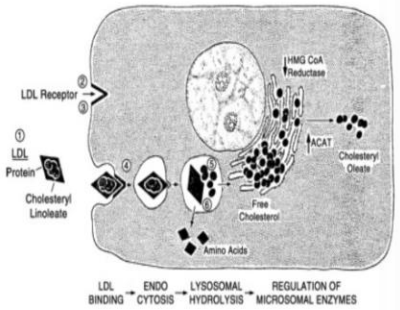
Eur Heart J 2013;34:3478

HoFH have normal organ development and behavior

Familial Hypercholesterolemia is a Defect in the LDL Receptor



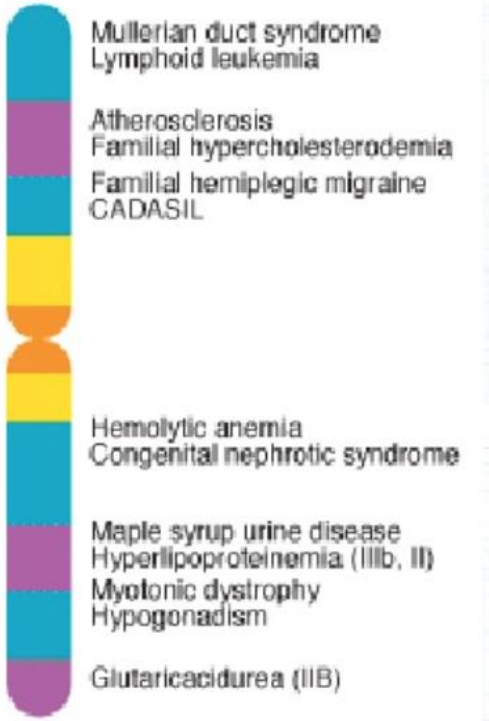
Joseph Goldstein and Michael Brown



LDL Receptor Pathway, 1976

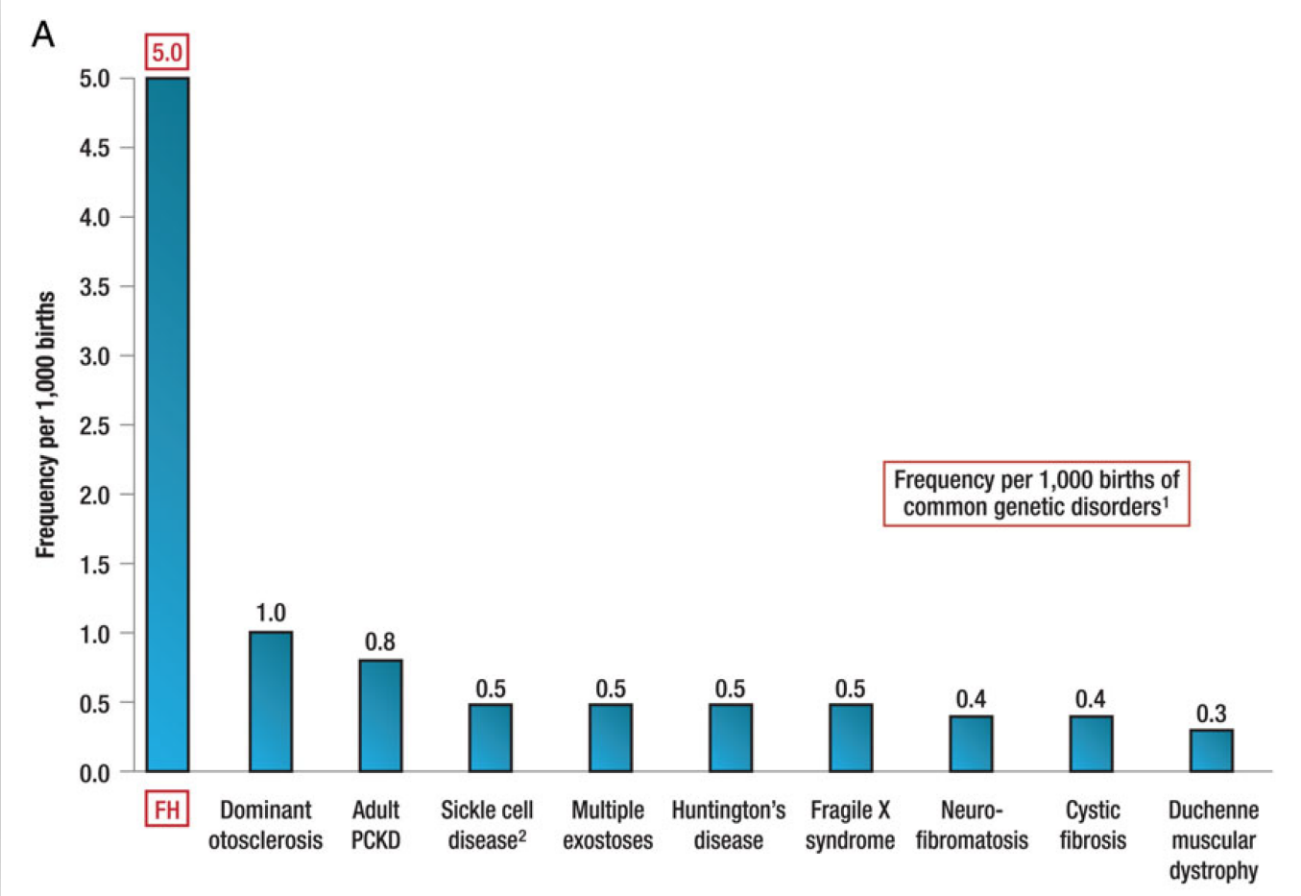
- chromosome 19

LDLR, APOB, LDLRAP1, PCSK9



Hypercholestérolémie Familiale

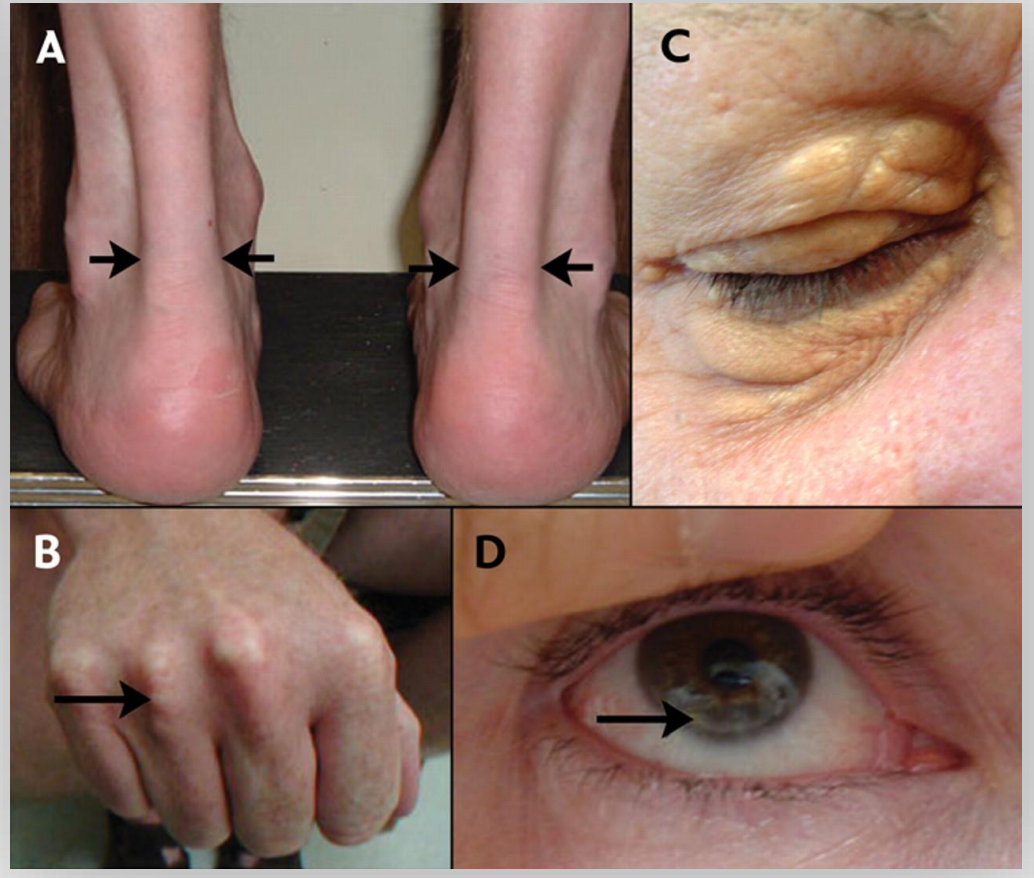
The most frequent of rare diseases…



Eur Heart J 2013;34:3478

Hypercholestérolémie Familiale

Six year-old girl with homozygous Familial Hypercholesterolemia. Bumps on skin are deposits of cholesterol derived from LDL.



Clear relationship between LDL-C and risk of CV events

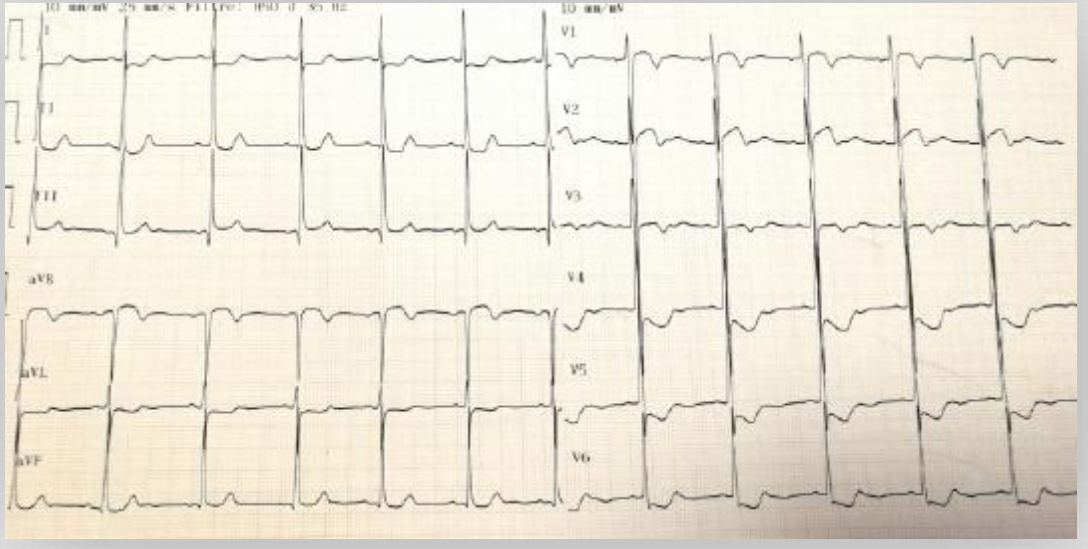
ESC European Society of Cardiology
European Heart Journal - Case Reports
doi:10.1093/ehjcr/ytz233

GRAND ROUND
Coronary heart disease

A case report of an acute coronary syndrome in a 10-year-old boy with homozygous familial hypercholesterolaemia

Thibault Leclercq [1]*, Sylvie Falcon-Eicher[1], Michel Farnier[1,2], Emmanuel Le Bret [3], Raphaëlle Maudinas[4], Stéphanie Litzler-Renault[5], Christiane Mousson[6], Luc Lorgis[1], and Yves Cottin[1]

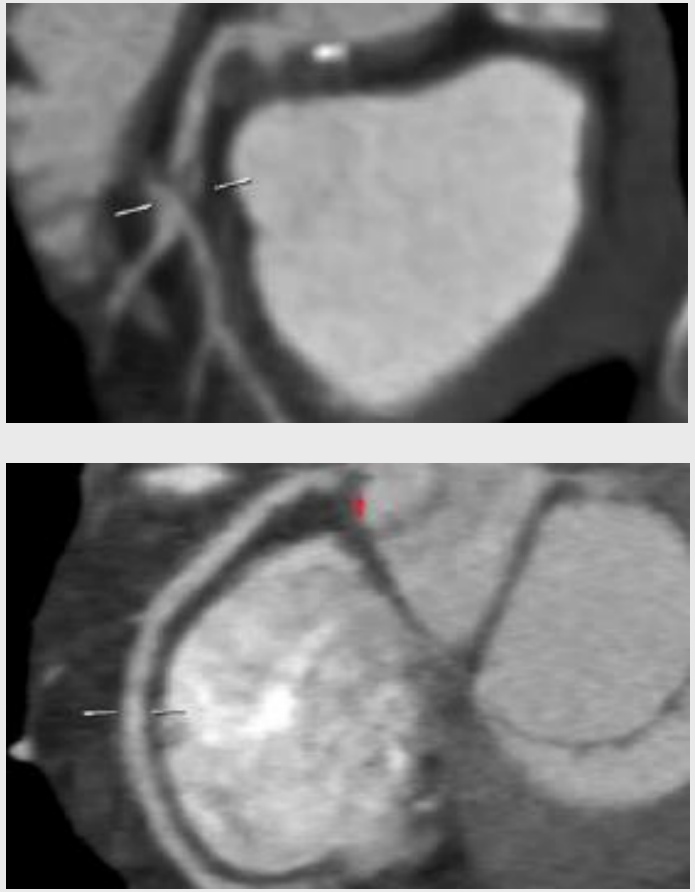
Three years prior to presentation	Appearance of xanthomas (*Figure 1*)
	LDL cholesterol (LDL-C): 802 mg/dL (20.73 mmol/L)
	Lipoprotein A: 124 mg/dL (4.43 µmol/L)
	Genetic diagnosis
One year prior presentation	Patient put on rosuvastatin 10 mg and ezetimibe 10 mg, LDL-C 650 mg/dL (16.8 mmol/L)



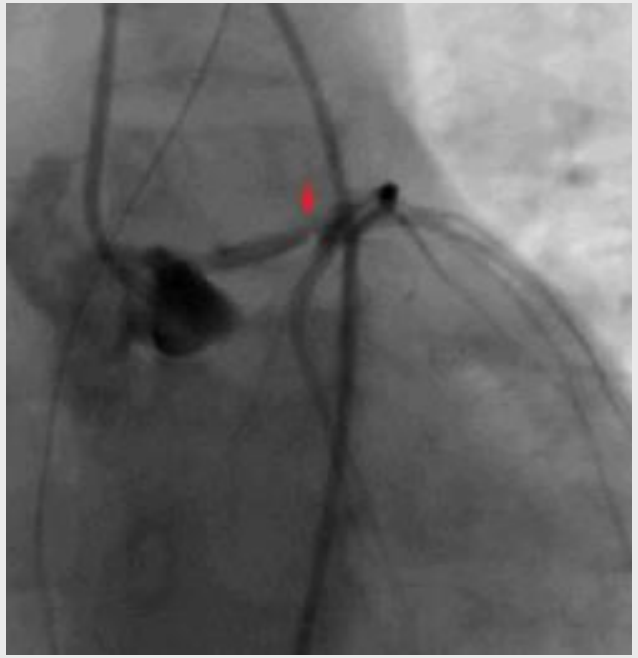
Eur Heart J Case Rep 2020;4:1

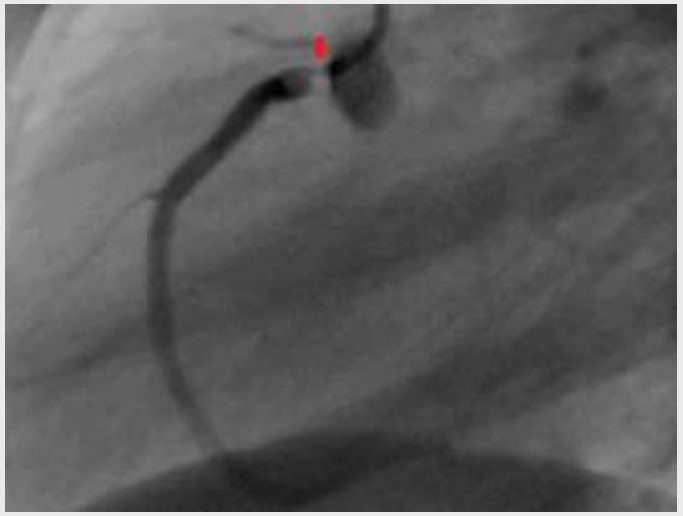
Clear relationship between LDL-C and risk of CV events

Cardiac CT-Scan



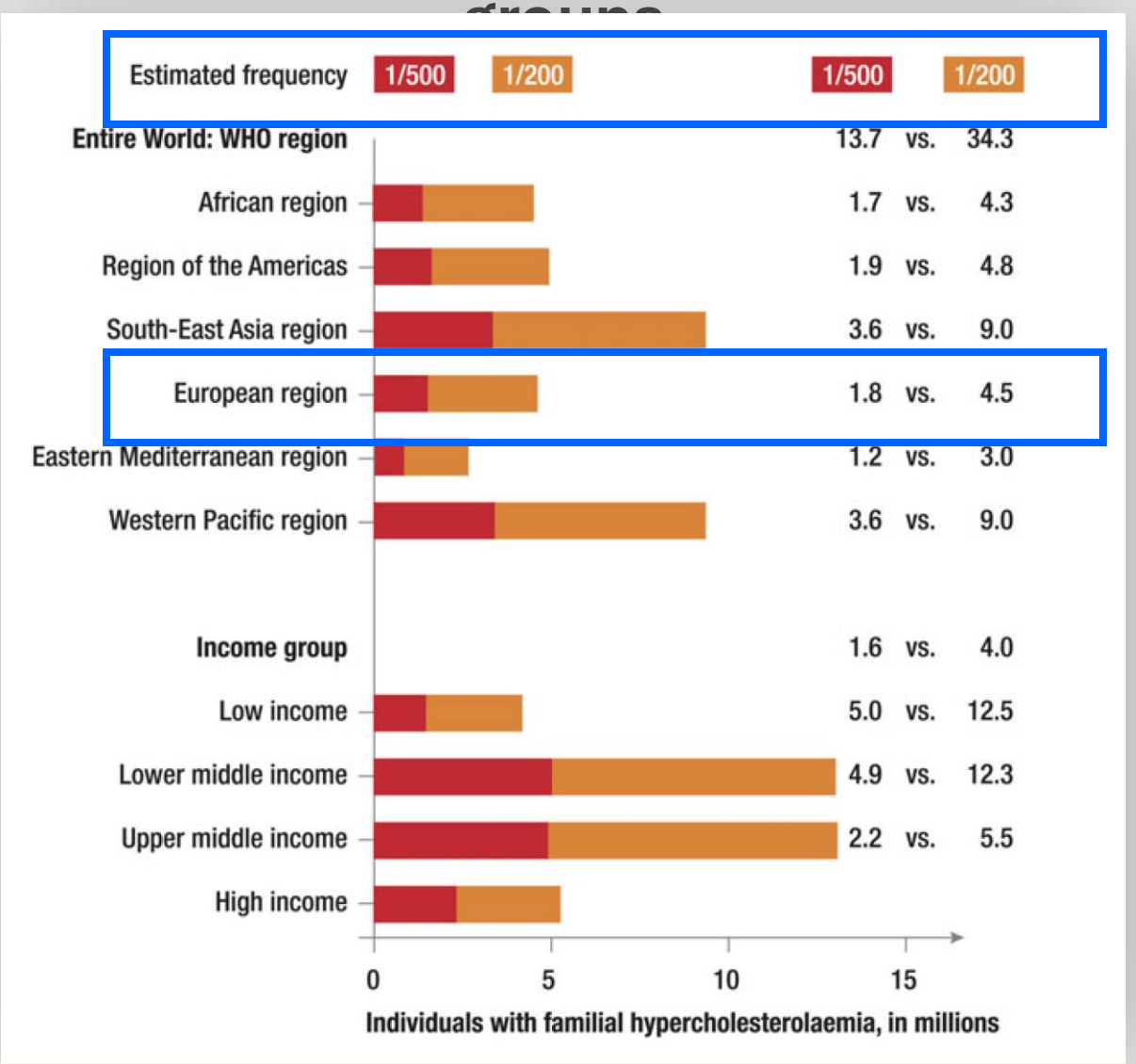
Coronary angiography





Eur Heart J Case Rep 2020;4:1

Estimated millions of individuals worldwide with familial hypercholesterolaemia by WHO regions and by income groups



Eur Heart J 2013;34:3478

Frequency of Familial Hypercholesterolemia

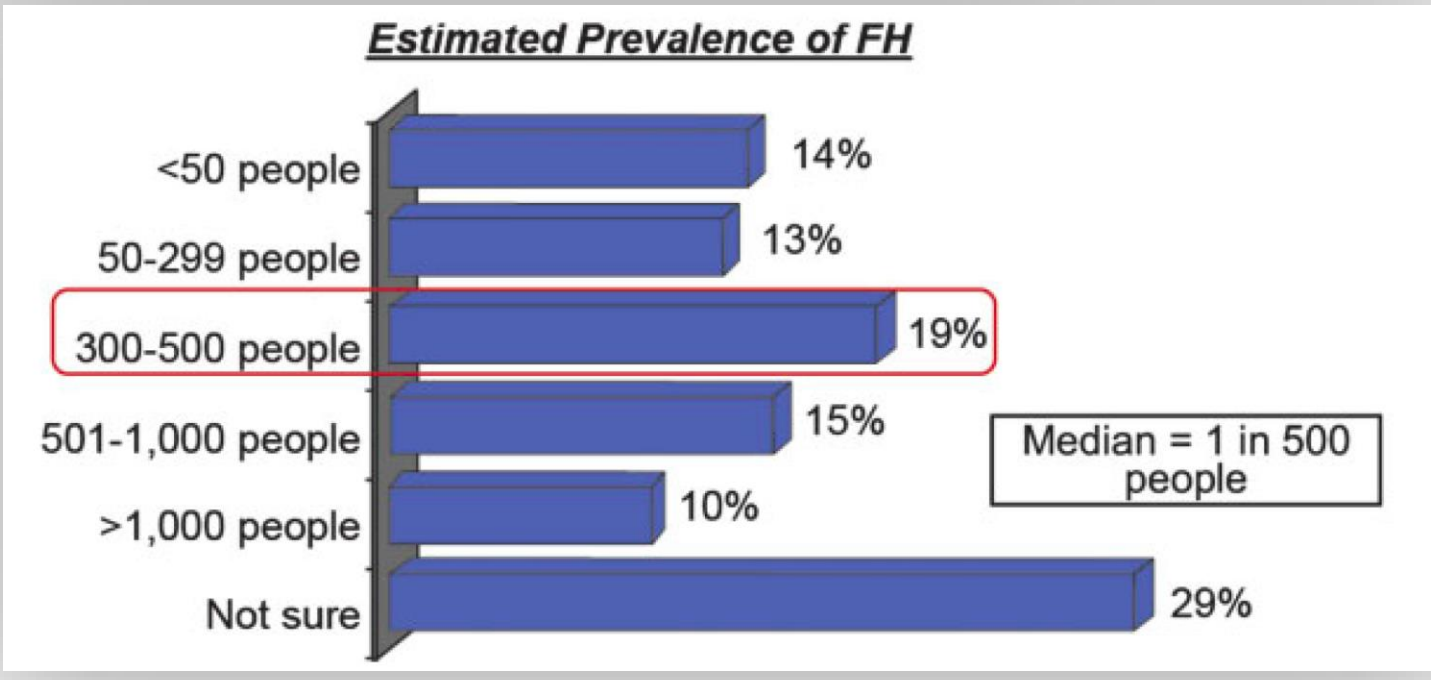
Reviews

PREVENTION

Familial Hypercholesterolemia: An Under-recognized but Significant Concern in Cardiology Practice

JoAnne M. Foody, MD, FACC, FAHA
Cardiovascular Wellness Program, Brigham & Women's Hospital and Harvard Medical School, Boston, Massachusetts

Address for correspondence:
JoAnne M. Foody, MD
Associate Professor,
Harvard Medical School
Director, Cardiovascular Wellness Program Brigham & Women's Hospital, 75 Francis Street, PB-136
Boston, MA 02115
jfoody@partners.org

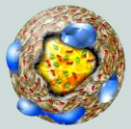


Clin Cardiol 2014;37:119

Diagnosis of Familial Hypercholesterolemia

Dutch FH criterias

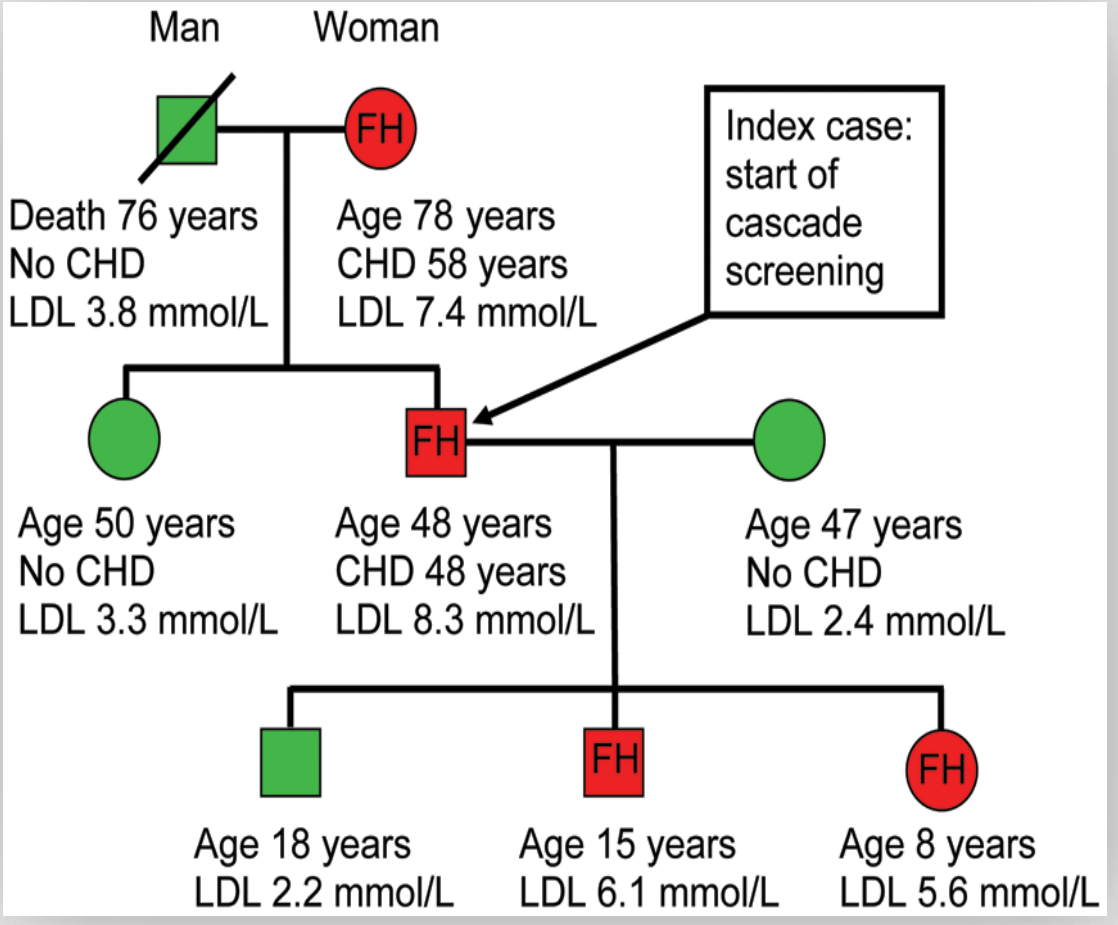
Feature	Score
Family history	
First-degree relative with known premature coronary and/or vascular disease (men <55 years, females <60 years) OR First-degree relative with known LDL-C above the 95th percentile for age and sex	1
First-degree relative with tendinous xanthomata and/or arcus cornealis OR 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) – 8.5 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:

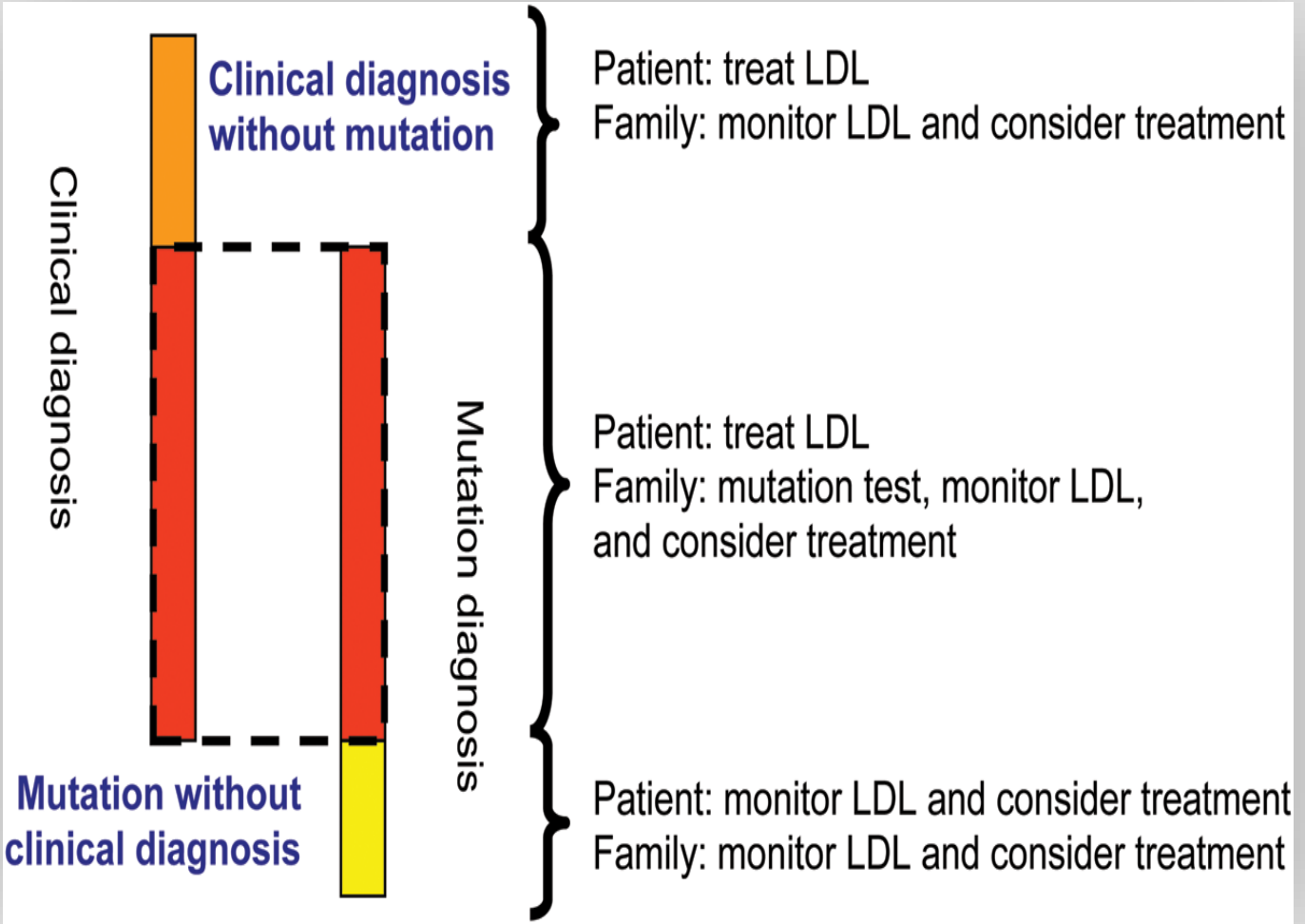
- Definite FH = total score greater than 8
- Probable FH = total score between 6 and 8
- Possible FH = total score between 3 and 5
- Unlikely FH = total score of less than 3

Familial Hypercholesterolemia – cascade screening



Eur Heart J 2013;34:3478

Familial Hypercholesterolemia – cascade screening



Eur Heart J 2013;34:3478

Familial Hypercholesterolemia in Switzerland

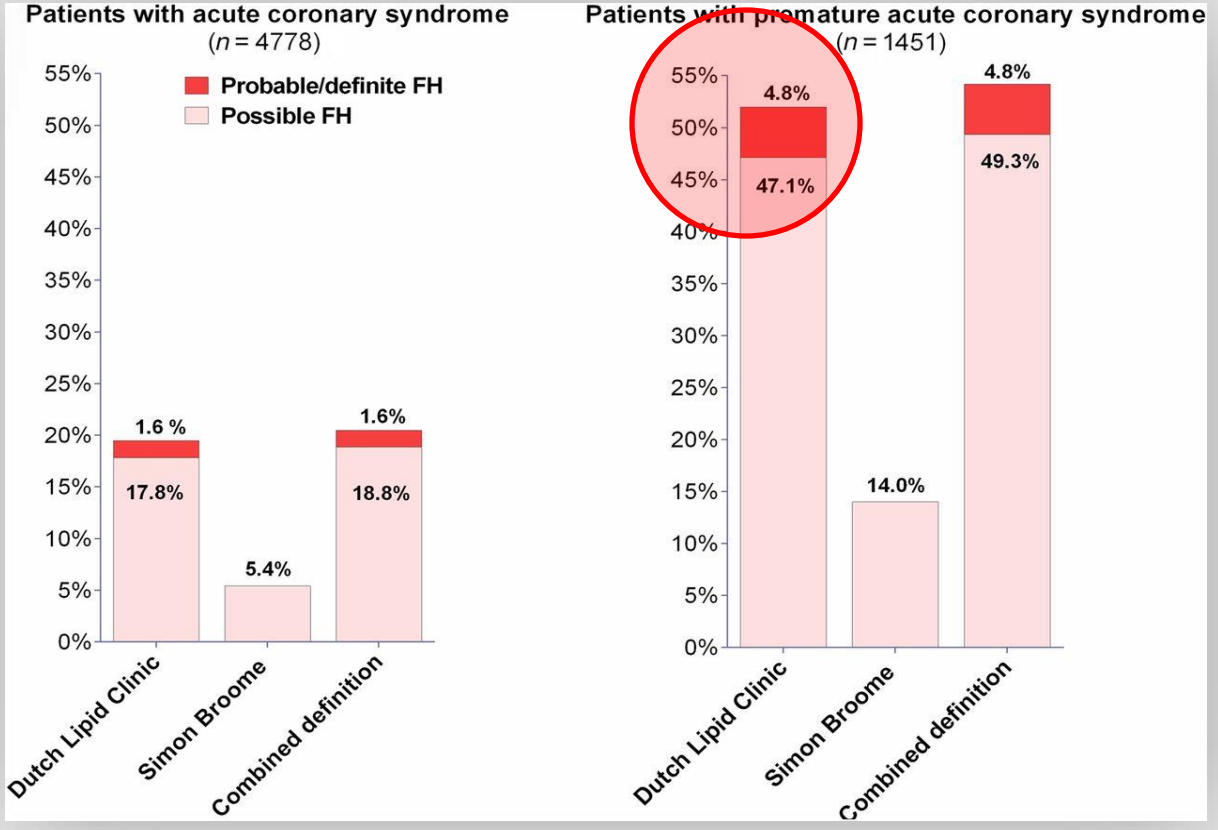
European Heart Journal
doi:10.1093/eurheartj/ehv289

CLINICAL RESEARCH
Lipids

Prevalence and management of familial hypercholesterolaemia in patients with acute coronary syndromes

David Nanchen[1]*, Baris Gencer[2], Reto Auer[1], Lorenz Räber[3], Giulio G. Stefanini[3], Roland Klingenberg[4], Christian M. Schmied[4], Jacques Cornuz[1], Olivier Muller[5], Pierre Vogt[5], Peter Jüni[6], Christian M. Matter[4], Stephan Windecker[3], Thomas F. Lüscher[4], François Mach[2], and Nicolas Rodondi[7]

What is the prevalence of FH in ACS patients ?



Eur Heart J 2015;36:2438

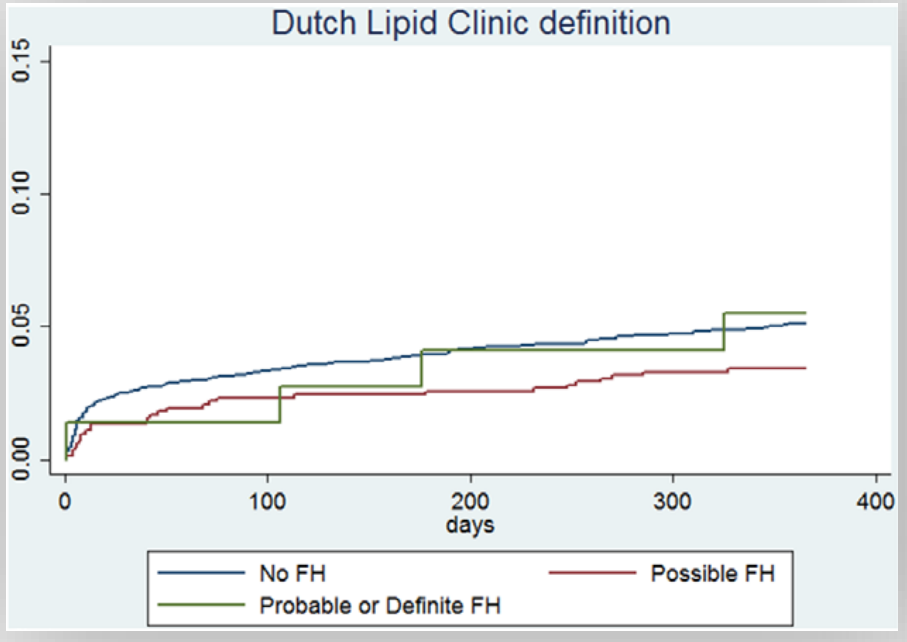
Familial Hypercholesterolemia in Switzerland

ORIGINAL RESEARCH ARTICLE

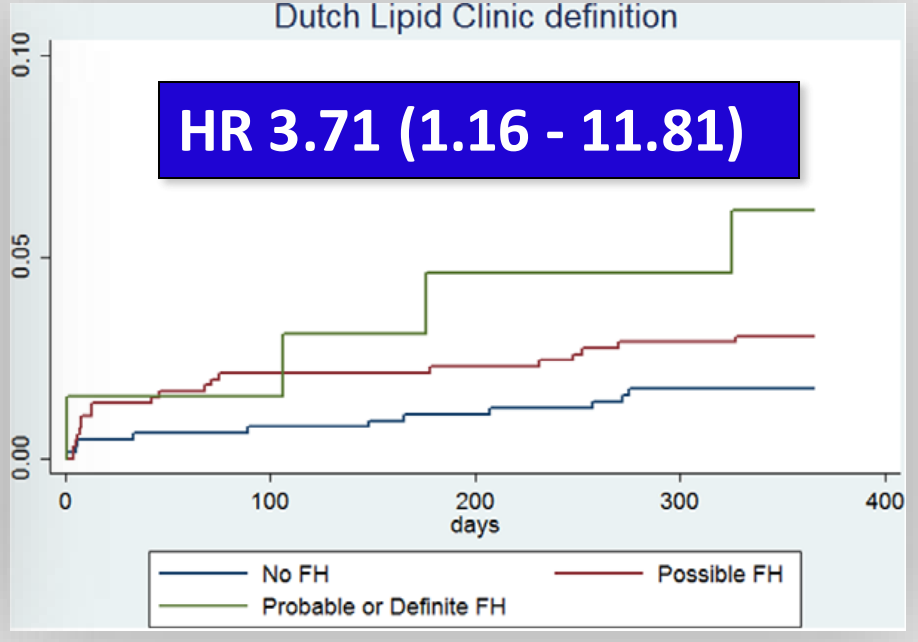
Prognosis of Patients With Familial Hypercholesterolemia After Acute Coronary Syndromes

Prognosis of Familial Hypercholesterolemia in Switzerland

Incidence of recurrent coronary events after ACS, by presence of FH (n=4'534)



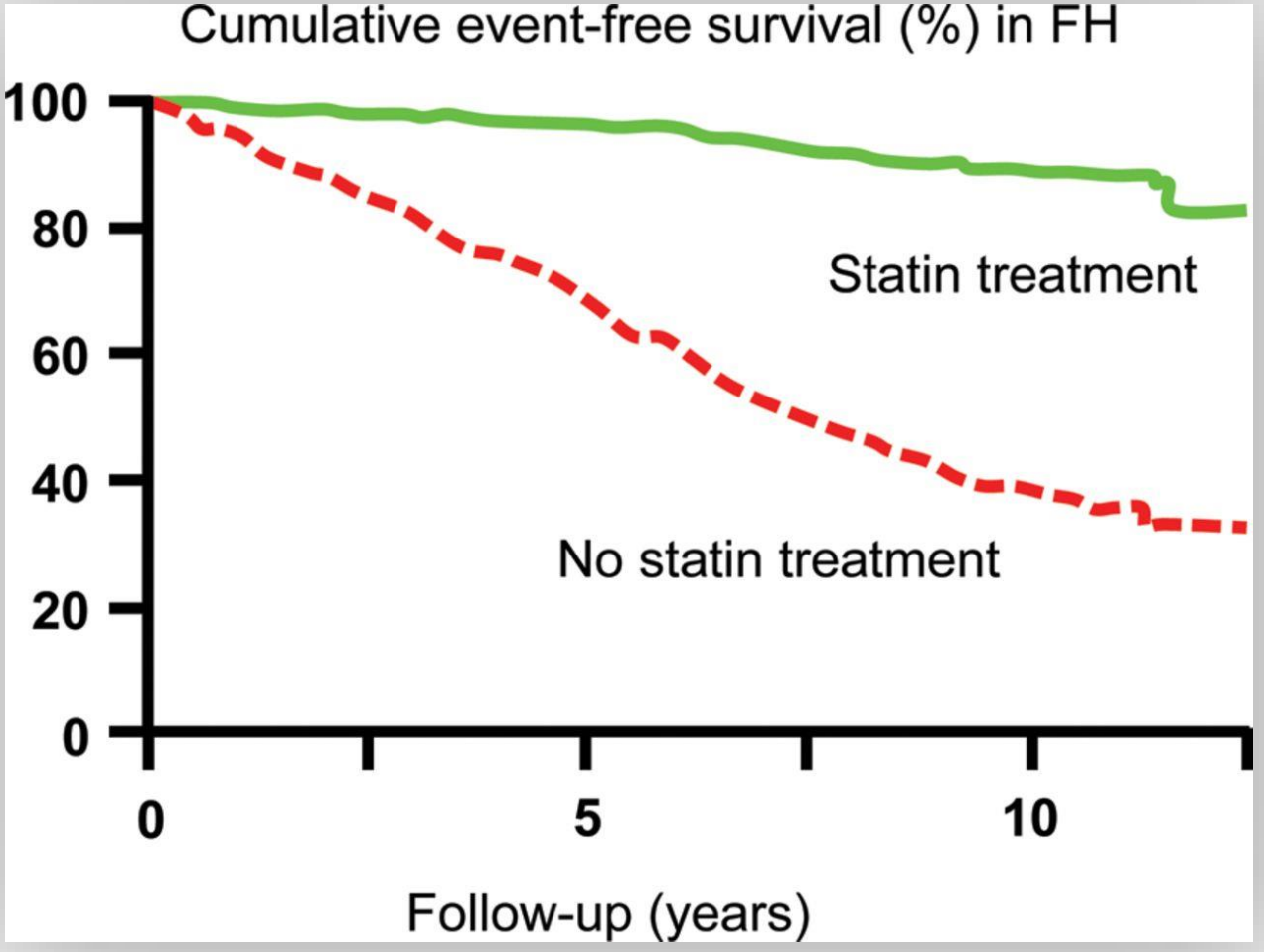
Incidence of recurrent coronary events in young patients with premature ACS, by presence of FH (n=1'369)



Circulation 2016;134:698

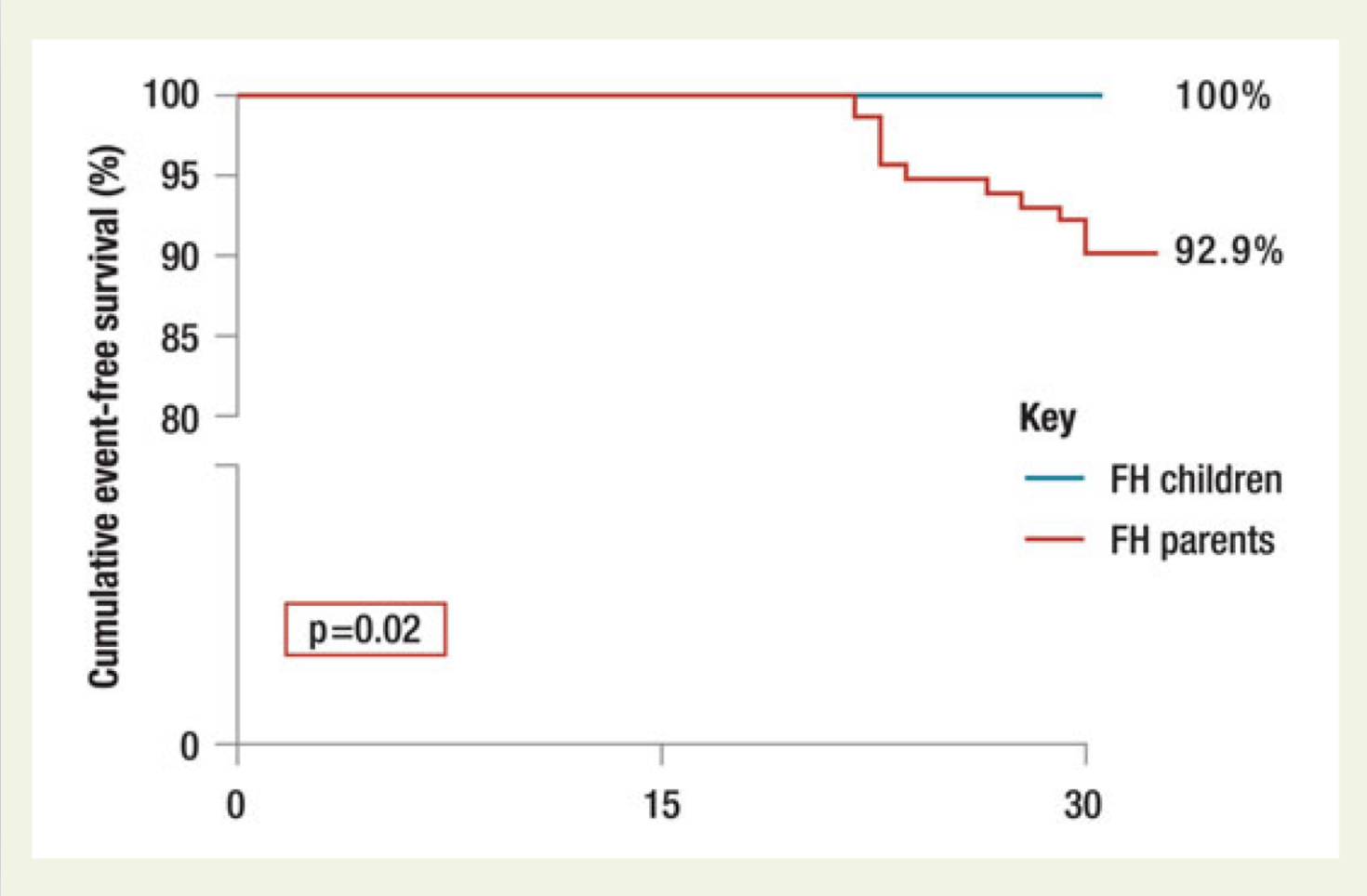
Treatment of Familial Hypercholesterolemia

Kaplan–Meier curve estimates of cumulative CHD-free survival among individuals with familial hypercholesterolemia according to statin treatment



Eur Heart J 2013;34:3478

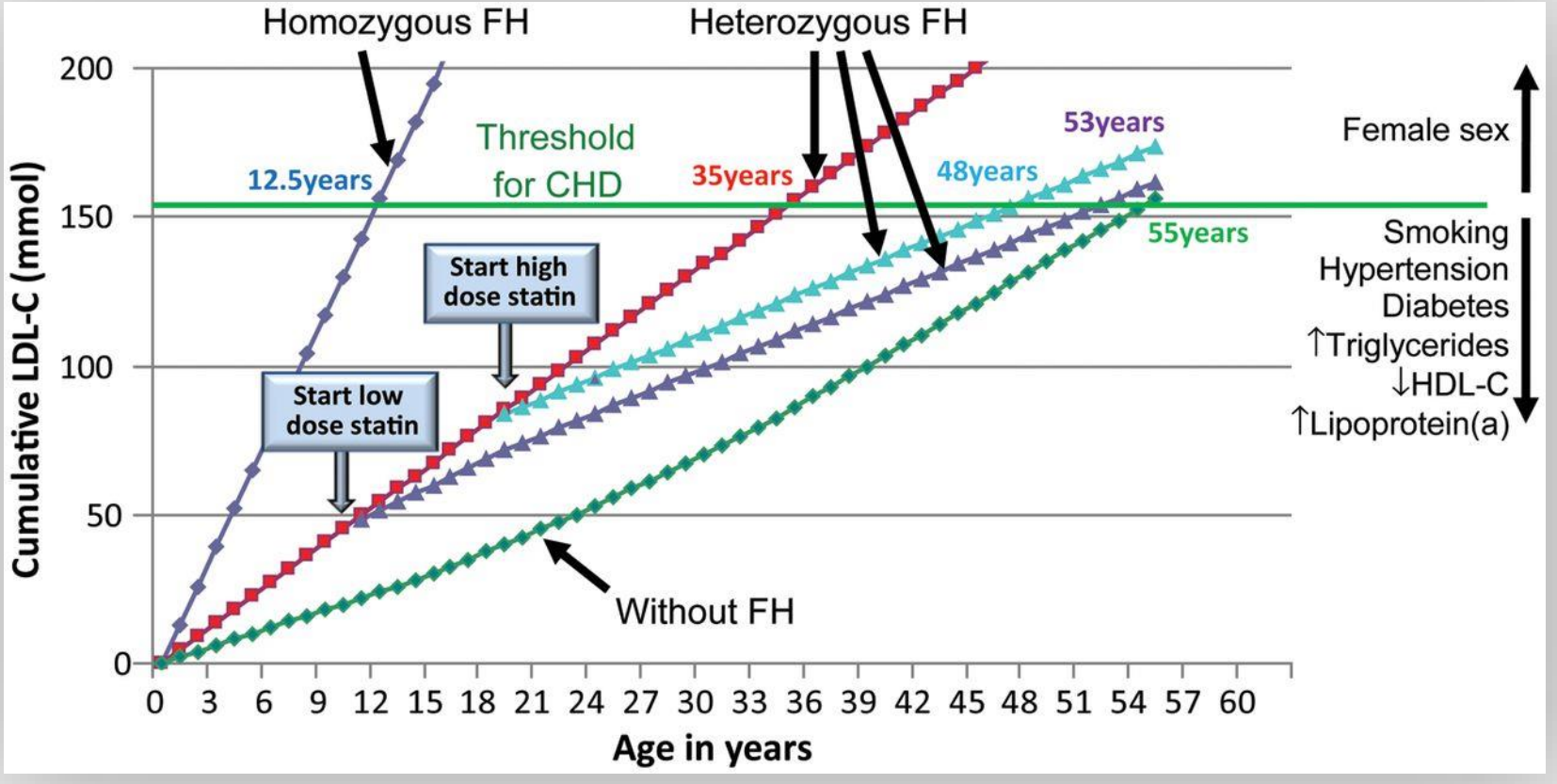
Treatment of Familial Hypercholesterolemia



Eur Heart J 2015;36:2425

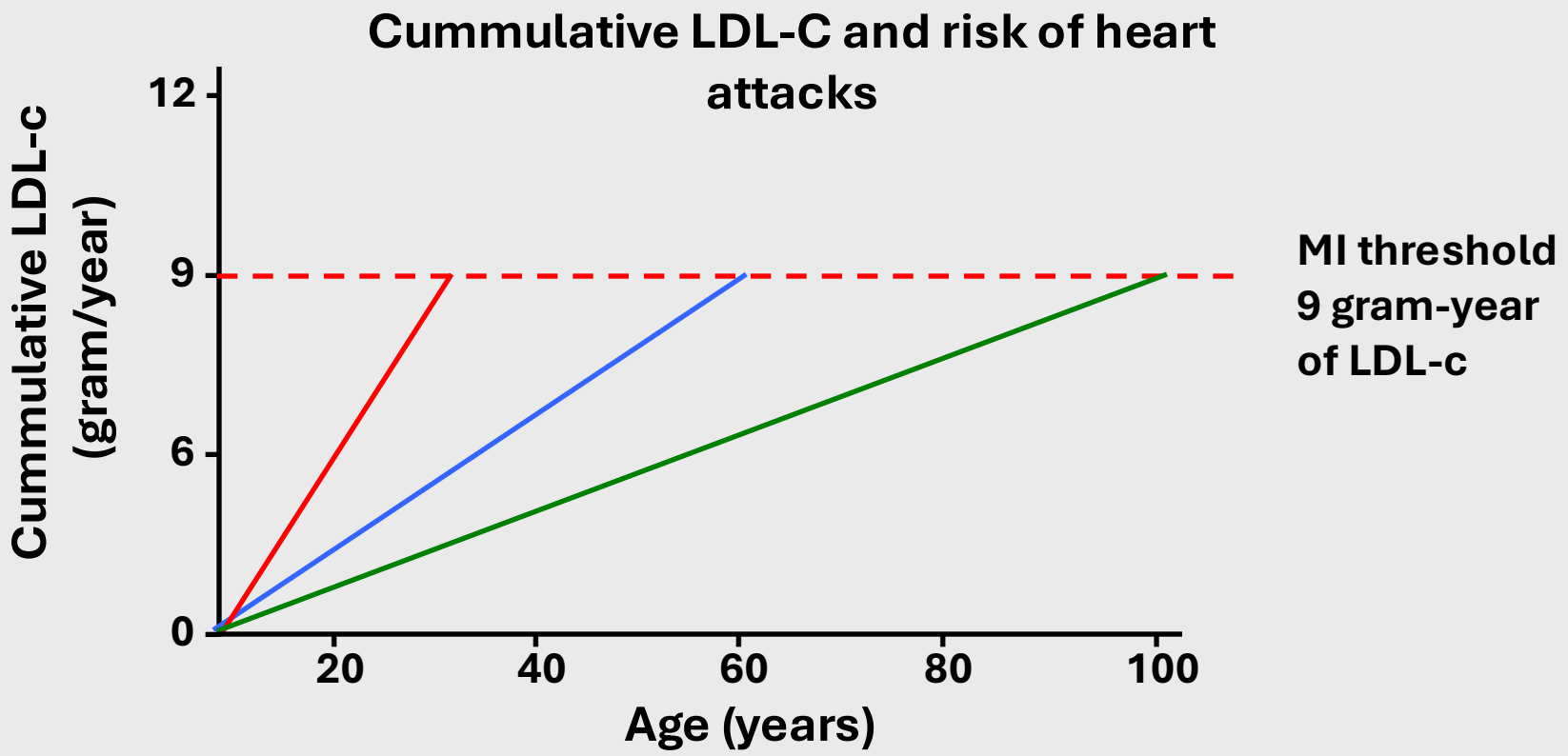
The lower the better, but also the sooner the better

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



Eur Heart J 2013;34:3478

The lower the better, but also the <u>sooner</u> the better



Typical MI in a 60 y.o. men with 150mg/dl = 9 gram-year of LDL-C

A 30 y.o. FH men with 300mg/dl (9 gram-year of LDL-C at the age of 30 !!!)

A 50 y.o. women with PCSK9$^{-/+}$ and 70mg/dl (9 gram-year of LDL-C at the age of 100 !!!)

Treatment of Familial Hypercholesterolemia

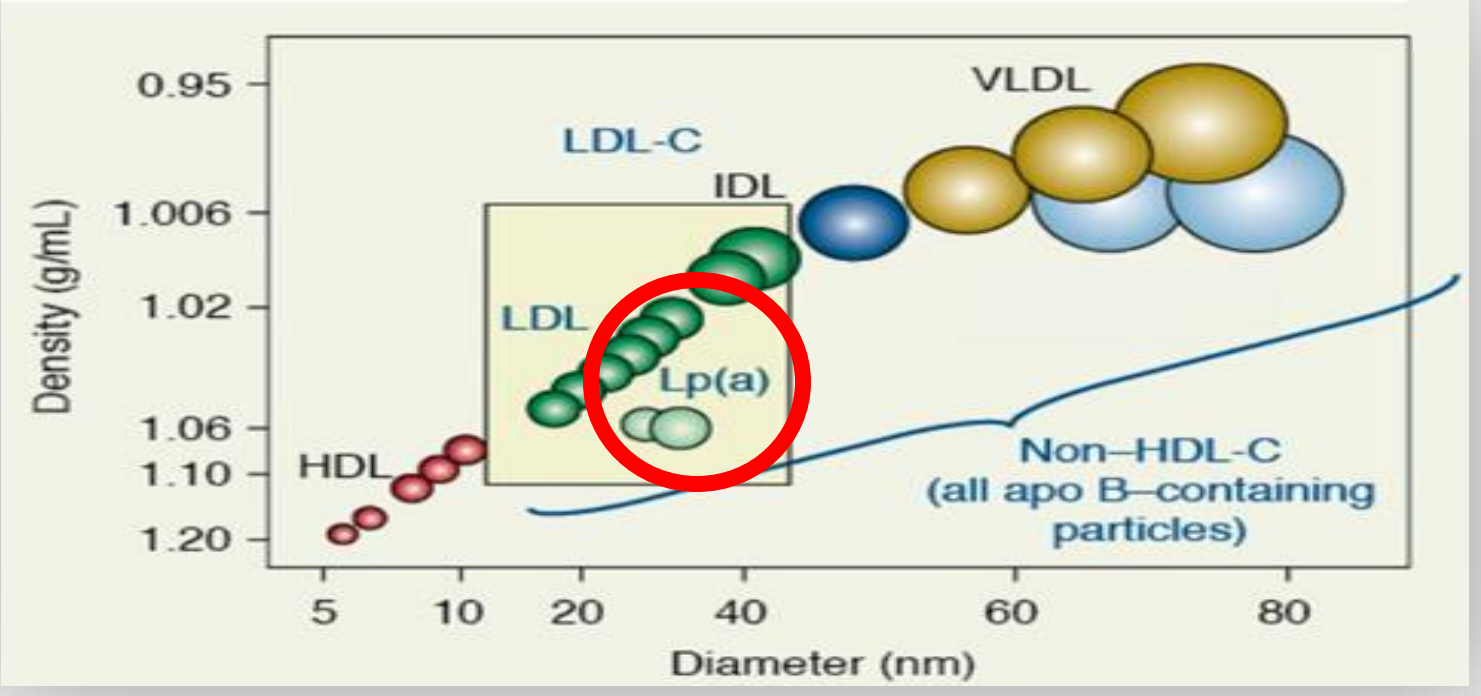
We recommend:

children, adults, and families should be screened for FH if:

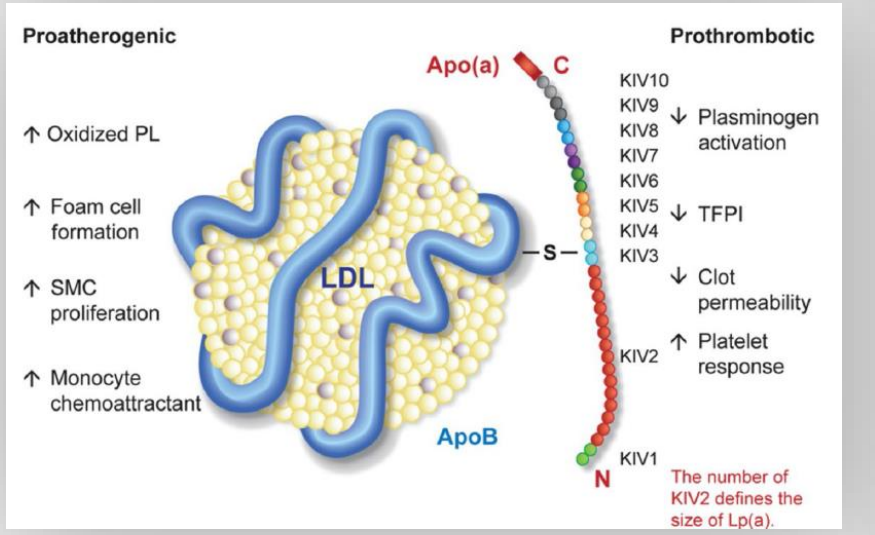
- Family member presents with FH
- Total cholesterol in adult ≥ 8mmol/L
- Total cholesterol in child ≥ 6mmol/L
- Premature CHD
- Tendon xanthomas
- Sudden premature cardiac death

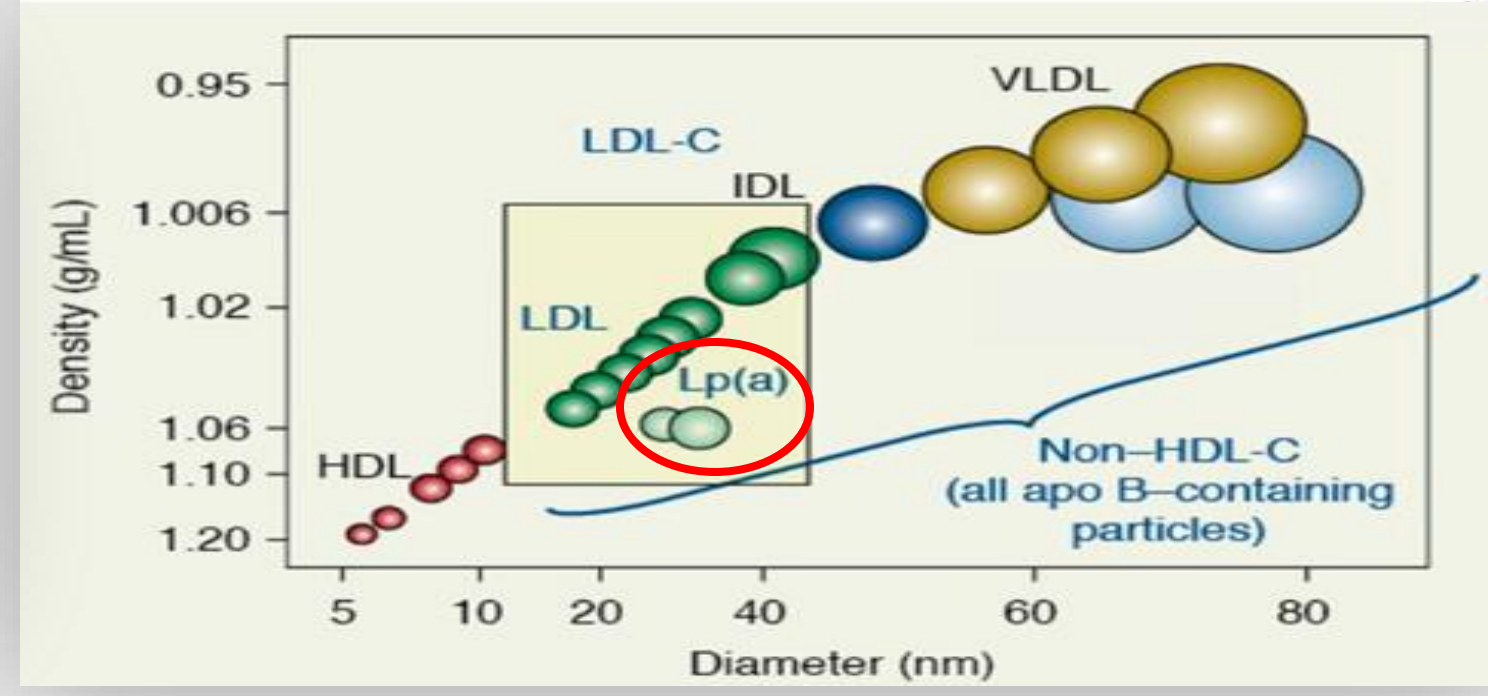
Eur Heart J 2013;34:3478

Caractéristiques des lipoprotéines



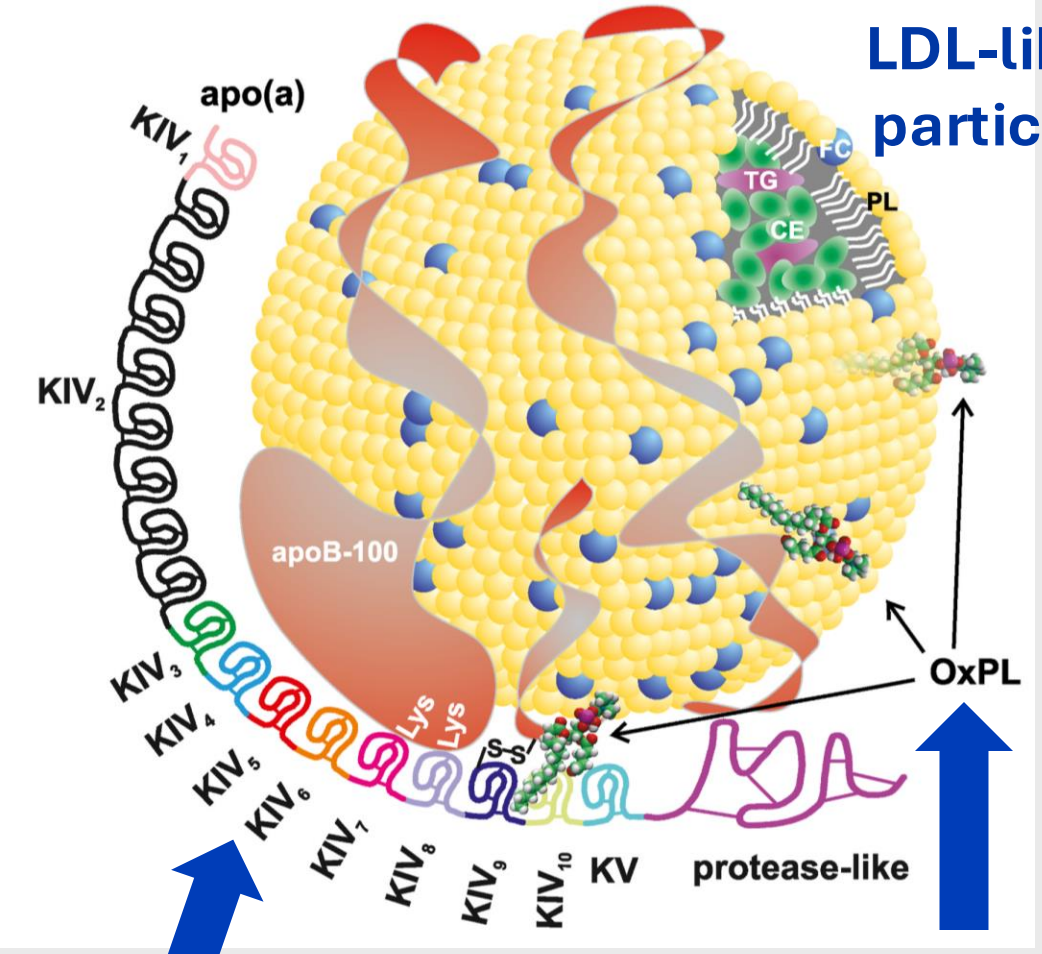
Caractéristiques des lipoprotéines





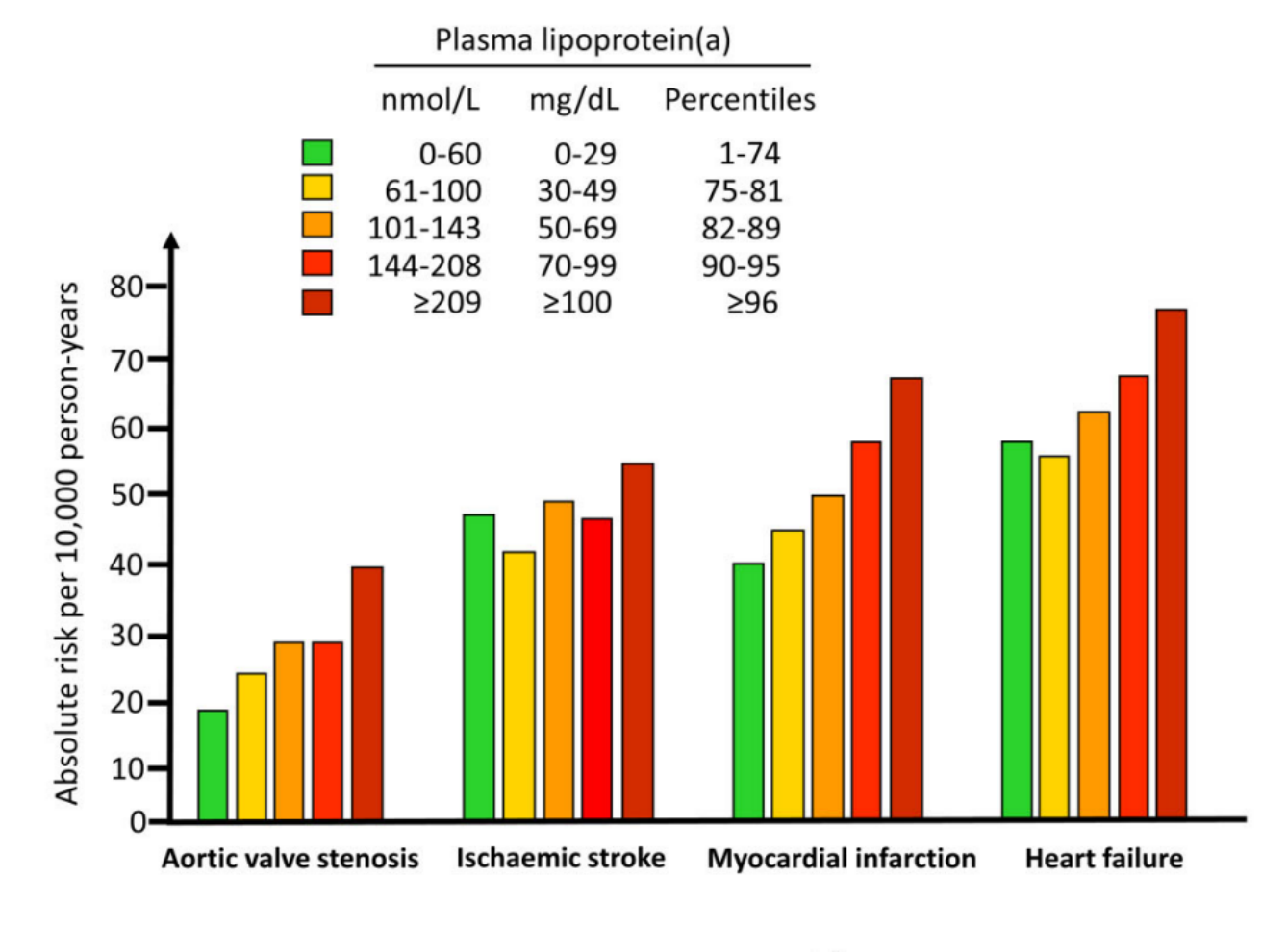
Lipoprotein(a)

Lp(a) - the next target to fight cardiovascular disease



- Described by K. Berg in 1963
- An independent risk factor for cardiovascular disease
- Shows only minor correlations with other lipoproteins (if any)
- Concentrations are mainly genetically determined
- One of the most important genetic risk factors for CVD

Risk of CVD as a function of increasing plasma Lp(a) concentration in the general population



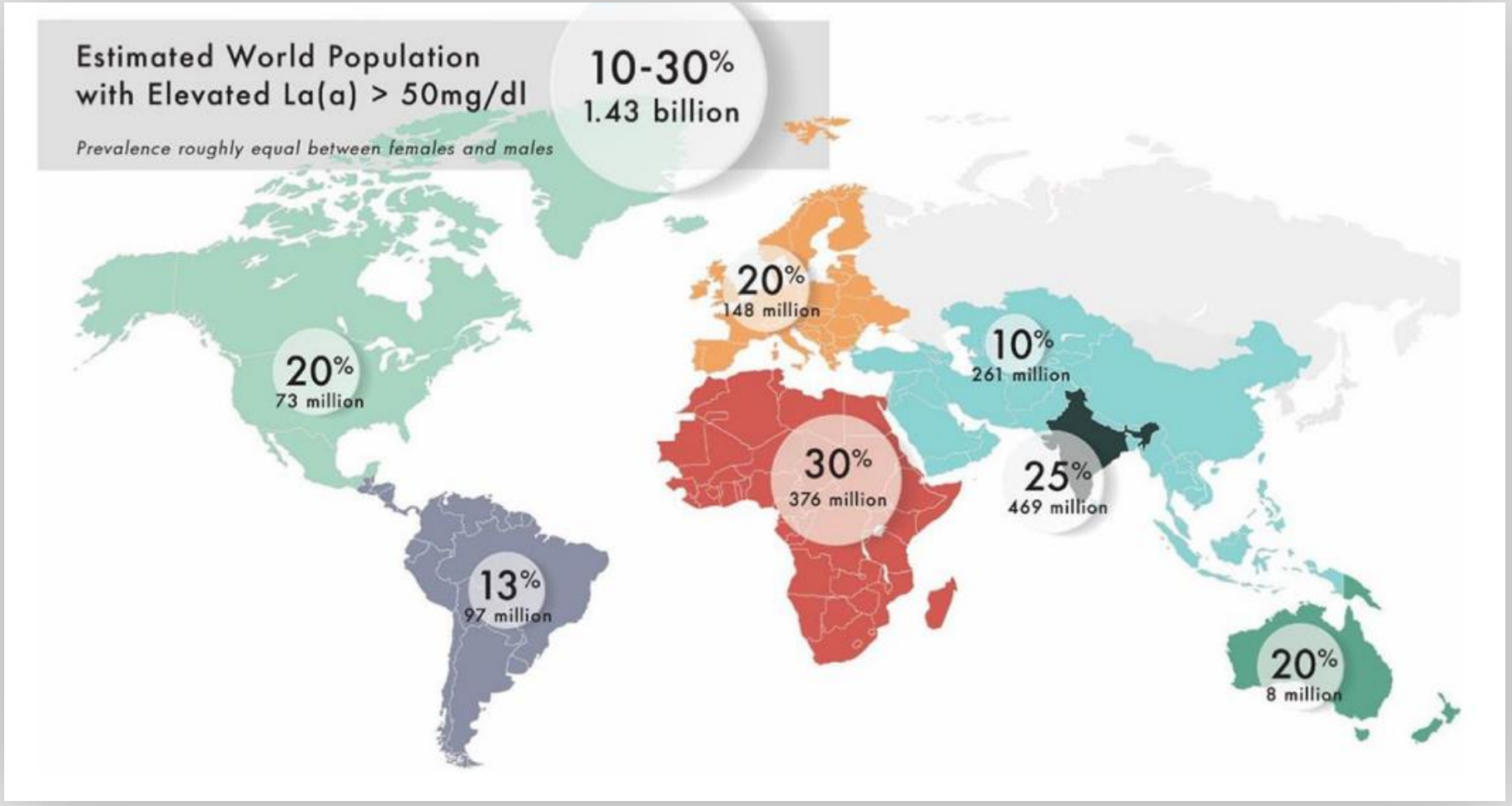
>75th percentile: increased the risk for AVS and myocardial infarction

>90th percentile: increased risk for heart failure

>95th percentile: increased risk for cardiovascular mortality and ischaemic stroke

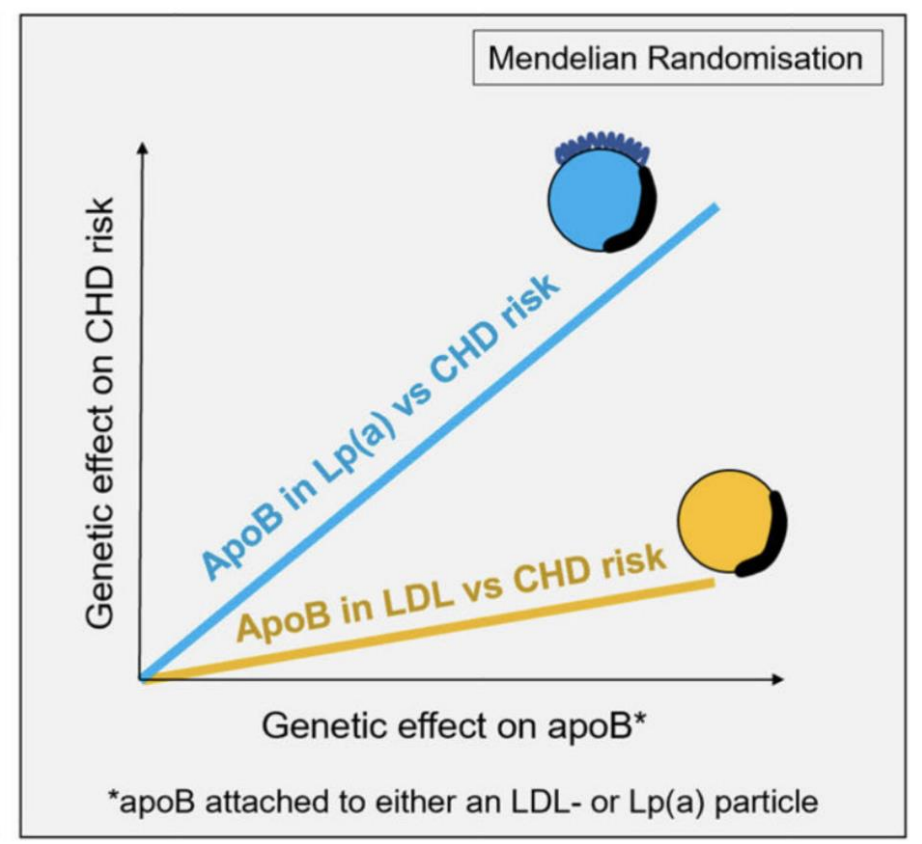
Eur Heart J. 2022;43:3925

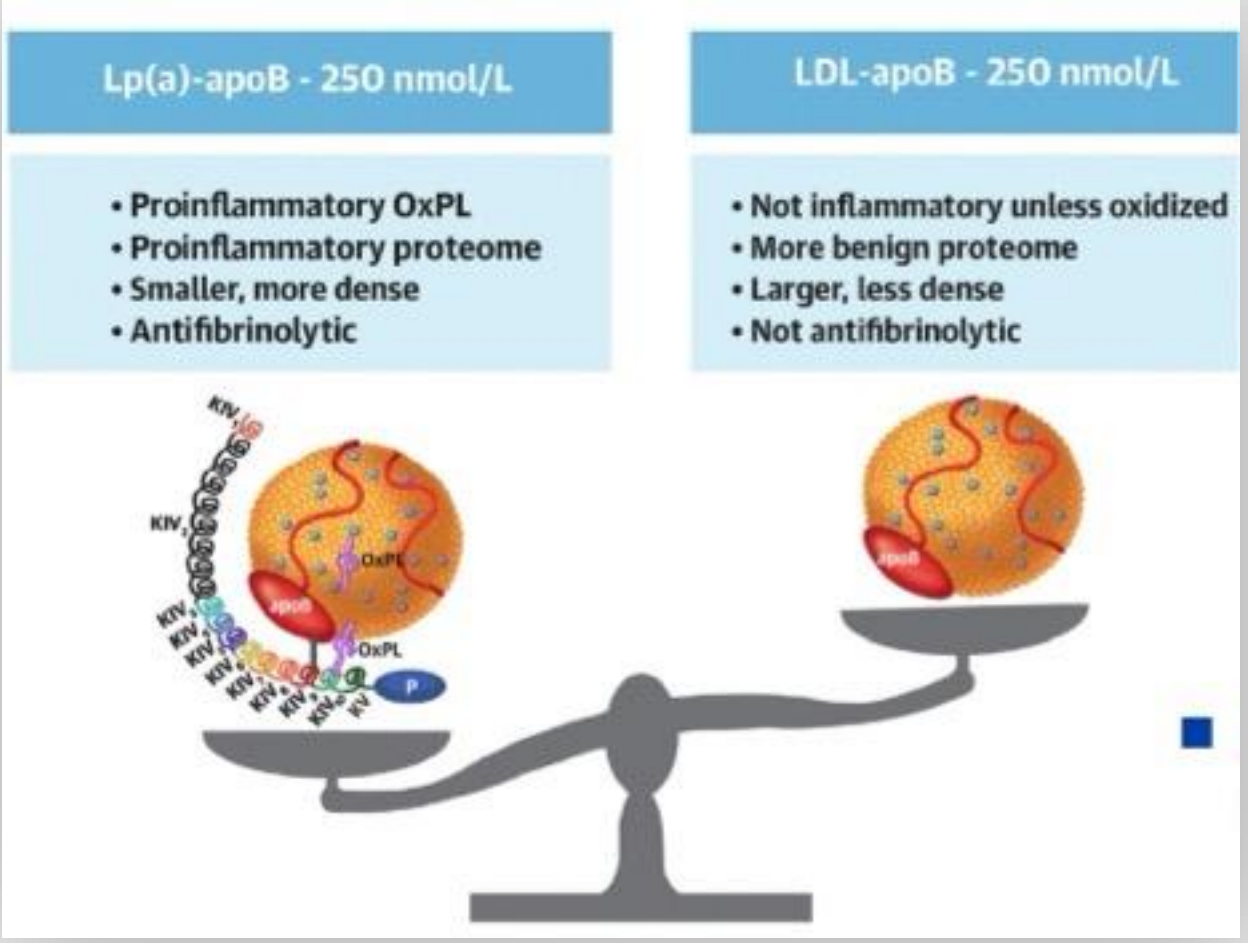
Estimated prevalence of elevated lipoprotein(a) globally



Current Cardiovascular Risk Reports https://doi.org/10.1007/s12170-022-00698-8

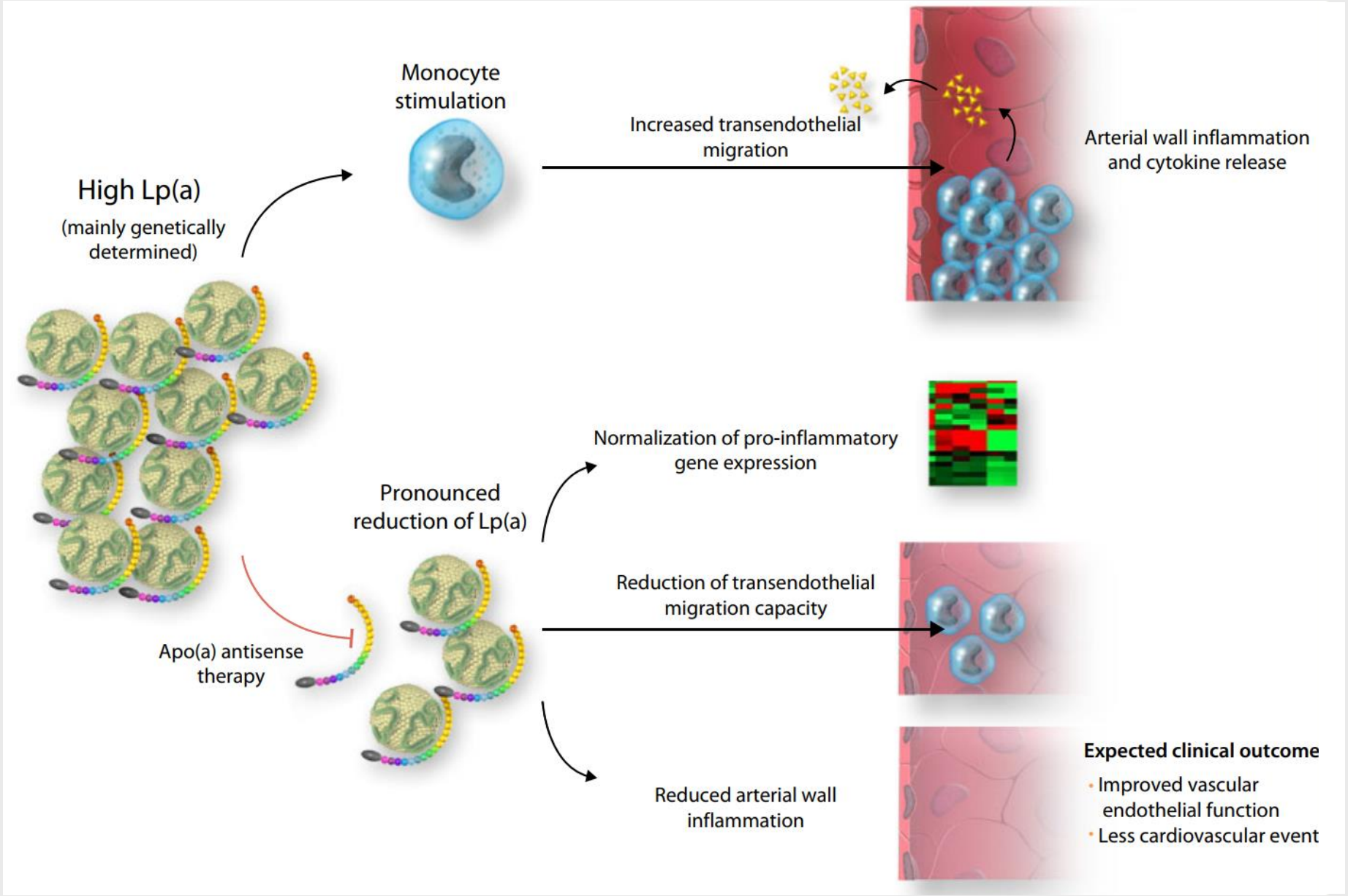
Is Lp(a) more atherogenic than LDL-C ?





J Am Coll Cardiol. 2024;83:385

Lp(a) and arterial wall inflammation

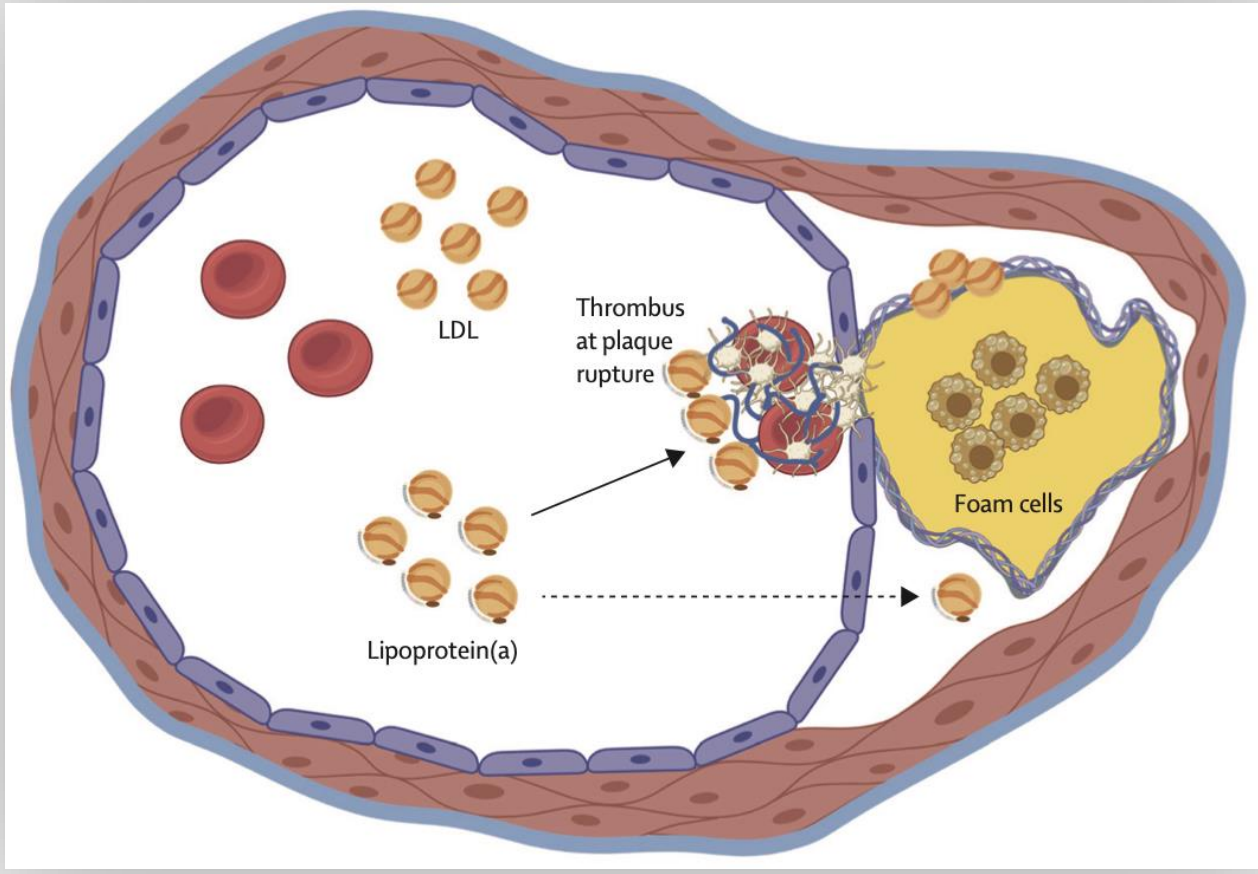


Eur Heart J 2020;41:2272

Eur Heart J 2020;41:2262

Pathophysiology of Lp(a)

Suggested role of high plasma lipoprotein(a) concentrations in thrombus growth at sites of atherosclerotic plaque rupture

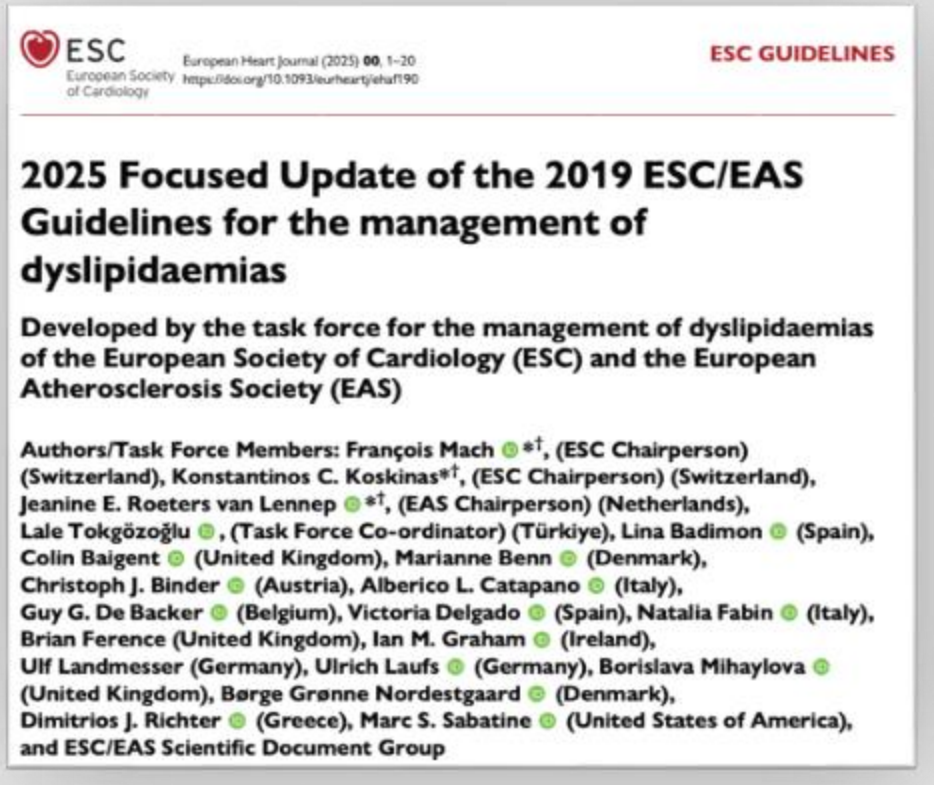


Lancet September 12, 2024

Lipoprotein(a)

Figure 3

Association between Lp(a) levels and lifetime risk of major cardiovascular events.



ESC European Society of Cardiology

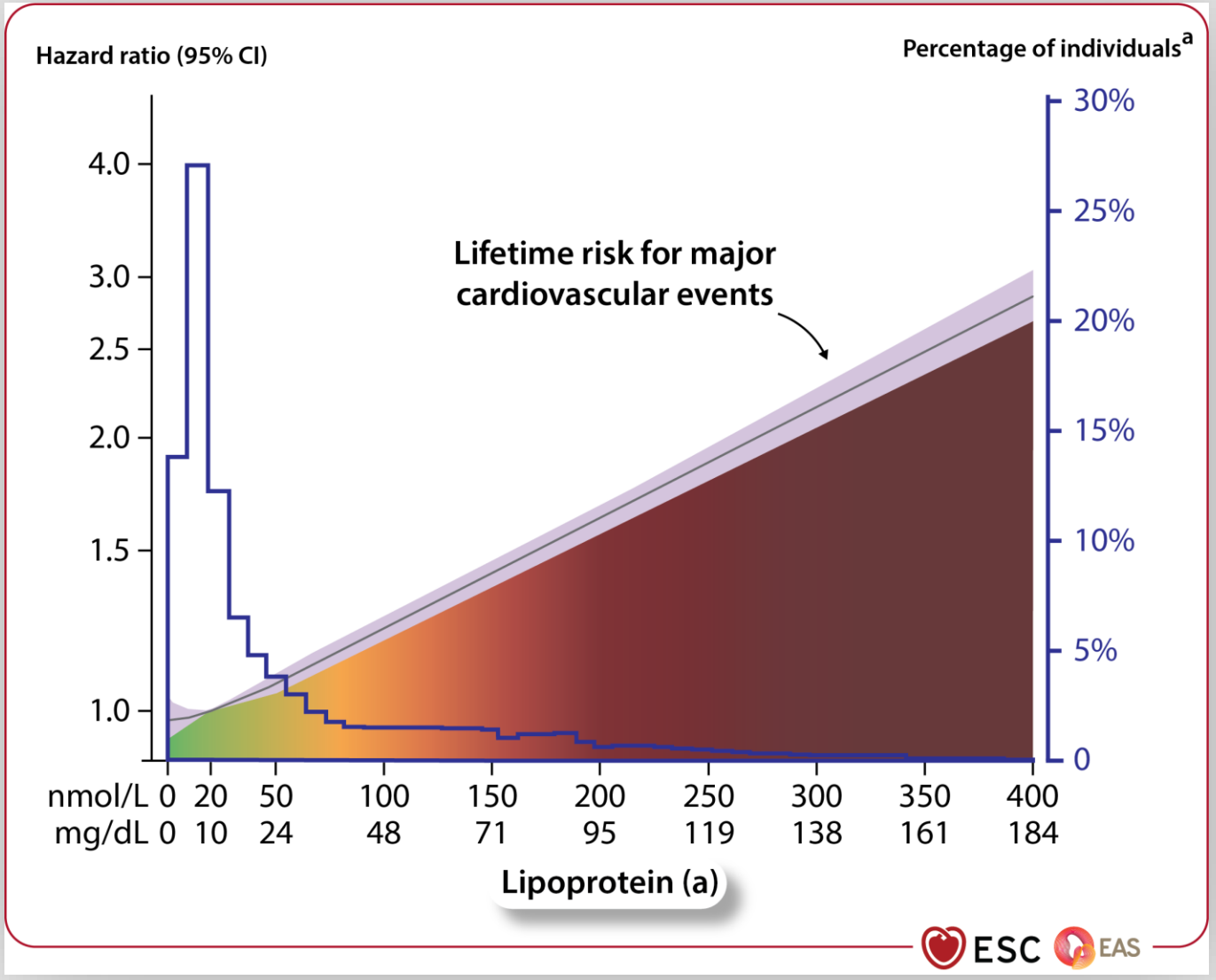
European Heart Journal (2025) 00, 1–20
https://doi.org/10.1093/eurheartj/ehaf190

ESC GUIDELINES

2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias

Developed by the task force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

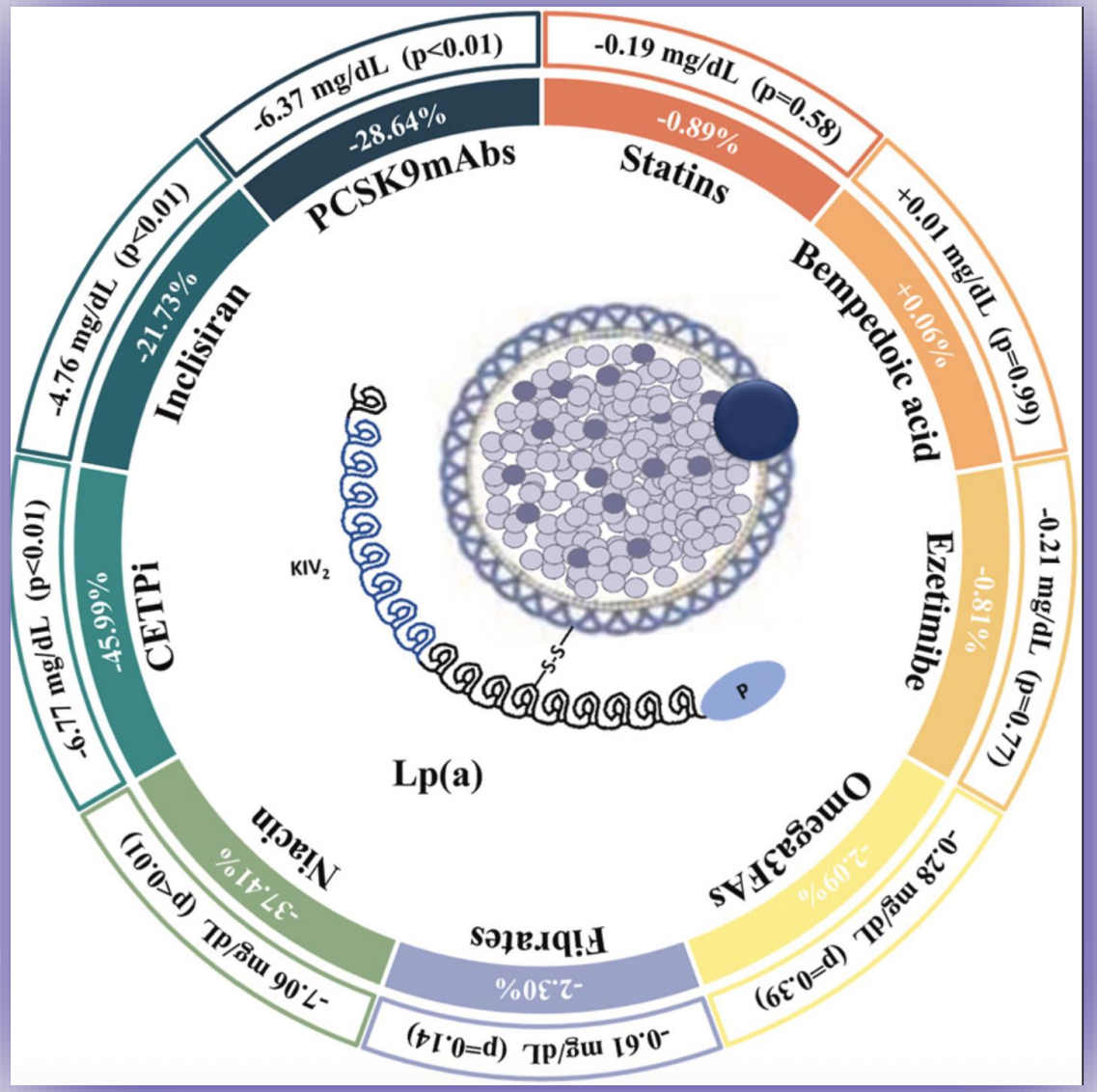
Authors/Task Force Members: François Mach *†, (ESC Chairperson) (Switzerland), Konstantinos C. Koskinas*†, (ESC Chairperson) (Switzerland), Jeanine E. Roeters van Lennep *†, (EAS Chairperson) (Netherlands), Lale Tokgözoğlu, (Task Force Co-ordinator) (Türkiye), Lina Badimon (Spain), Colin Baigent (United Kingdom), Marianne Benn (Denmark), Christoph J. Binder (Austria), Alberico L. Catapano (Italy), Guy G. De Backer (Belgium), Victoria Delgado (Spain), Natalia Fabin (Italy), Brian Ference (United Kingdom), Ian M. Graham (Ireland), Ulf Landmesser (Germany), Ulrich Laufs (Germany), Borislava Mihaylova (United Kingdom), Børge Grønne Nordestgaard (Denmark), Dimitrios J. Richter (Greece), Marc S. Sabatine (United States of America), and ESC/EAS Scientific Document Group



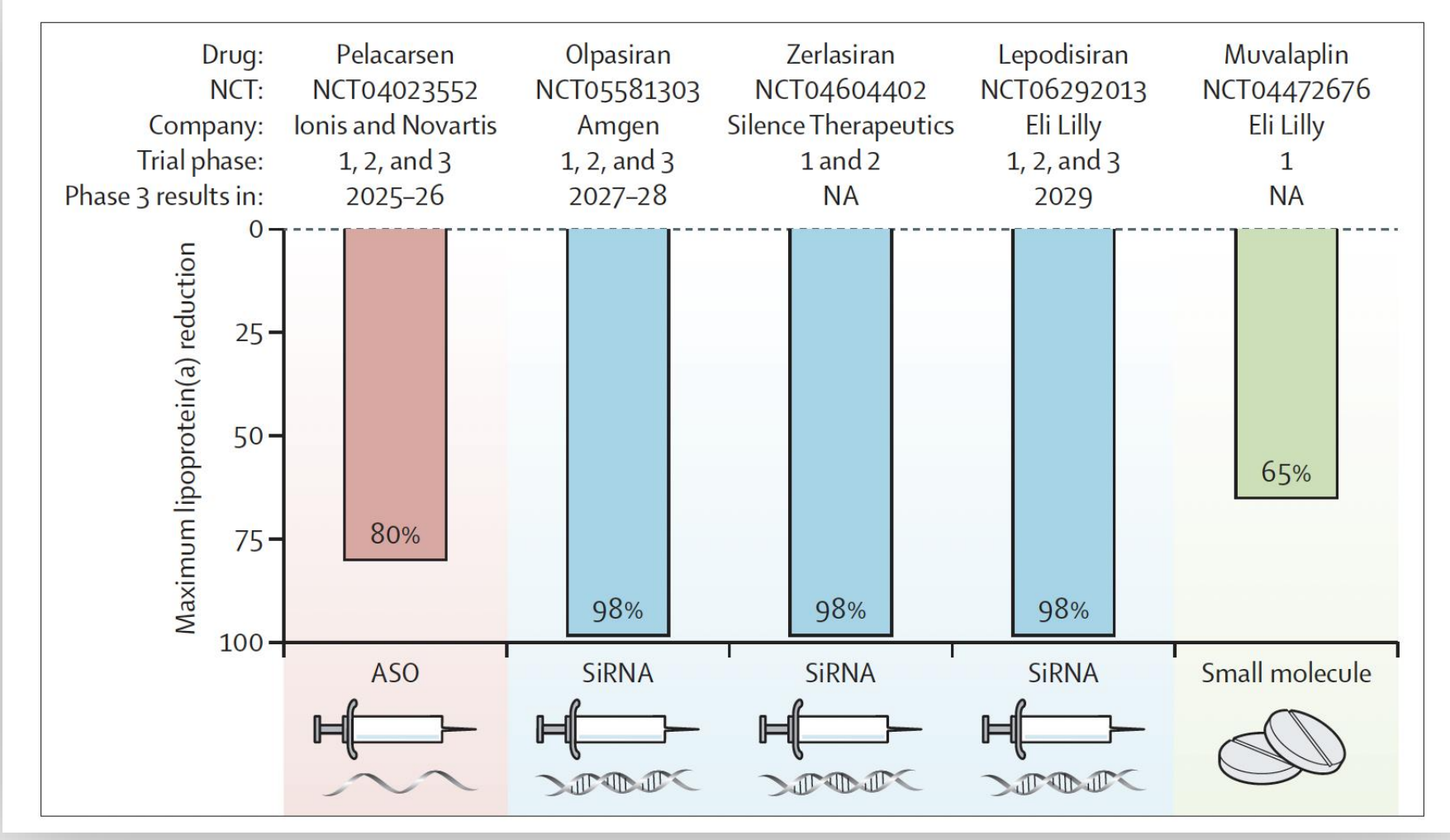
Effect of lipid lowering therapies on Lp(a)

- Lifestyle: No change
- High-intensity statin: No change
- Ezetimibe, Bempedoic acid : No change
- PCSK9 inhibitor: decrease by 25%
- Niacin: decrease by 25% but no clinical benefit
- Obicetrapib: decrease by 30-50 % ?

- Apheresis: decrease up to 70 %
- Specific Lp(a) lowering therapies awaited



Specific Lp(a)-lowering medications tested in randomized clinical trials



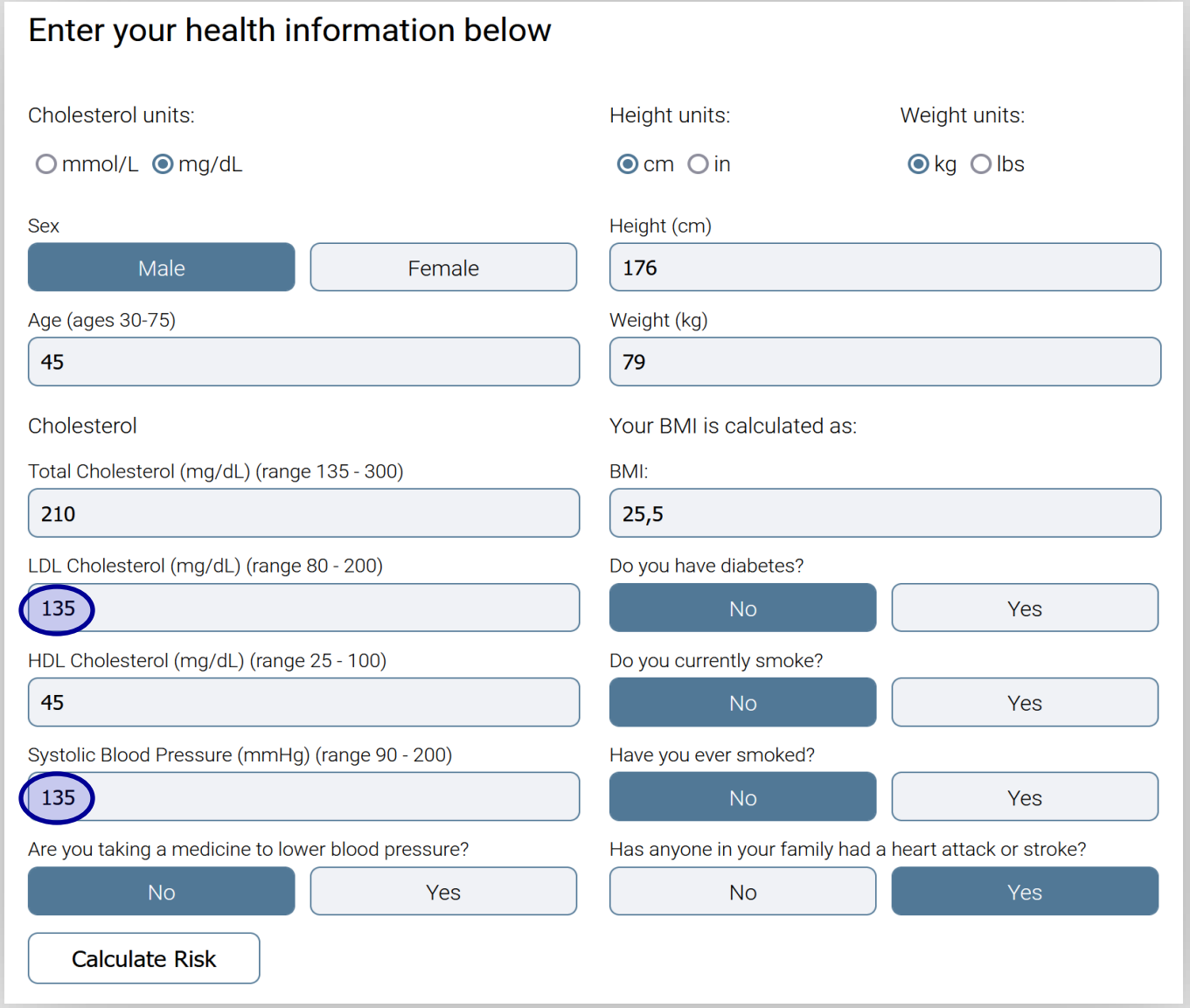
Lancet 2024 https://doi.org/10.1016/S0140-6736(24)01

Time-exposure to LDL-c

powered by

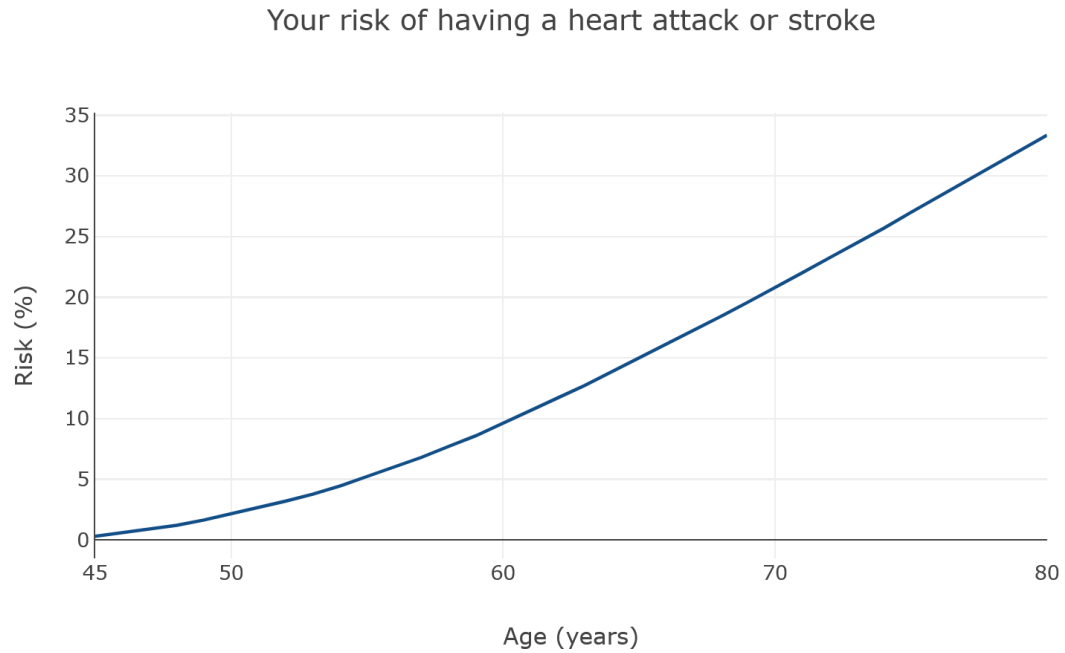
DeepCausalAI

Lp(a) Clinical Guidance



http://www.eas-society.org/LPA_risk_and_benefit_algorithm *Eur Heart J.* 2022;43:3925

Time-exposure to LDL-c



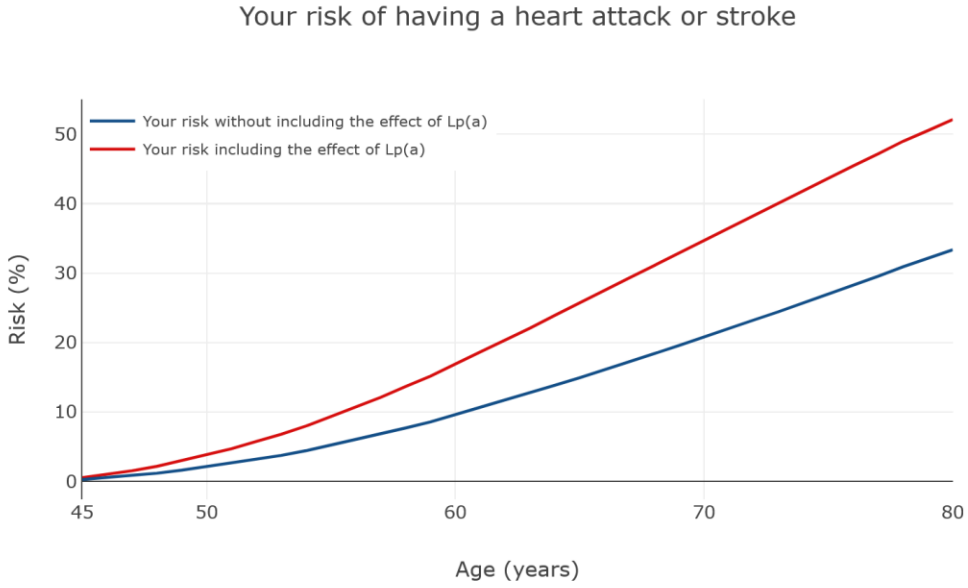
Your risk of having a heart attack or stroke up to age 80 is: 33.4%

Lp(a) units:

nmol/L mg/dL

Enter your Lp(a) level below to see how much it increases your risk of heart attack and stroke.

100



Your risk of having a heart attack or stroke up to age 80 is: 33.4%

With an Lp(a) level of 100 mg/dL, your estimated risk of having a heart attack or stroke up to age 80 changes from 33.4% to: 52.1%

When the light blue line and the dark blue line overlap, this is the amount you have to reduce your LDL or blood pressure in order to compensate for the increased risk caused by your Lp(a) levels.

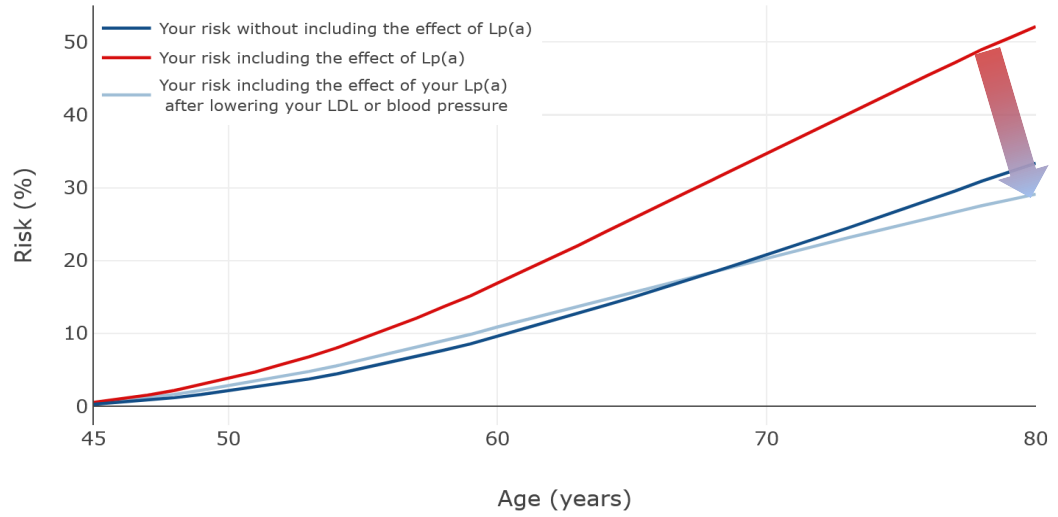
How much should I lower my LDL? - 40

0 80

How much should I lower my blood pressure? - 5

0 20

Your risk of having a heart attack or stroke



With an Lp(a) level of 100 mg/dL, your estimated risk of having a heart attack or stroke up to age 80 changes from 33.4% to:

52.1%

With an Lp(a) of 100 mg/dL and an estimated risk of NaN%, lowering your LDL by 40 mg/dL and your SBP by 5 mmHg beginning at age 45 will reduce your risk of having a heart attack or stroke to:

29.1%

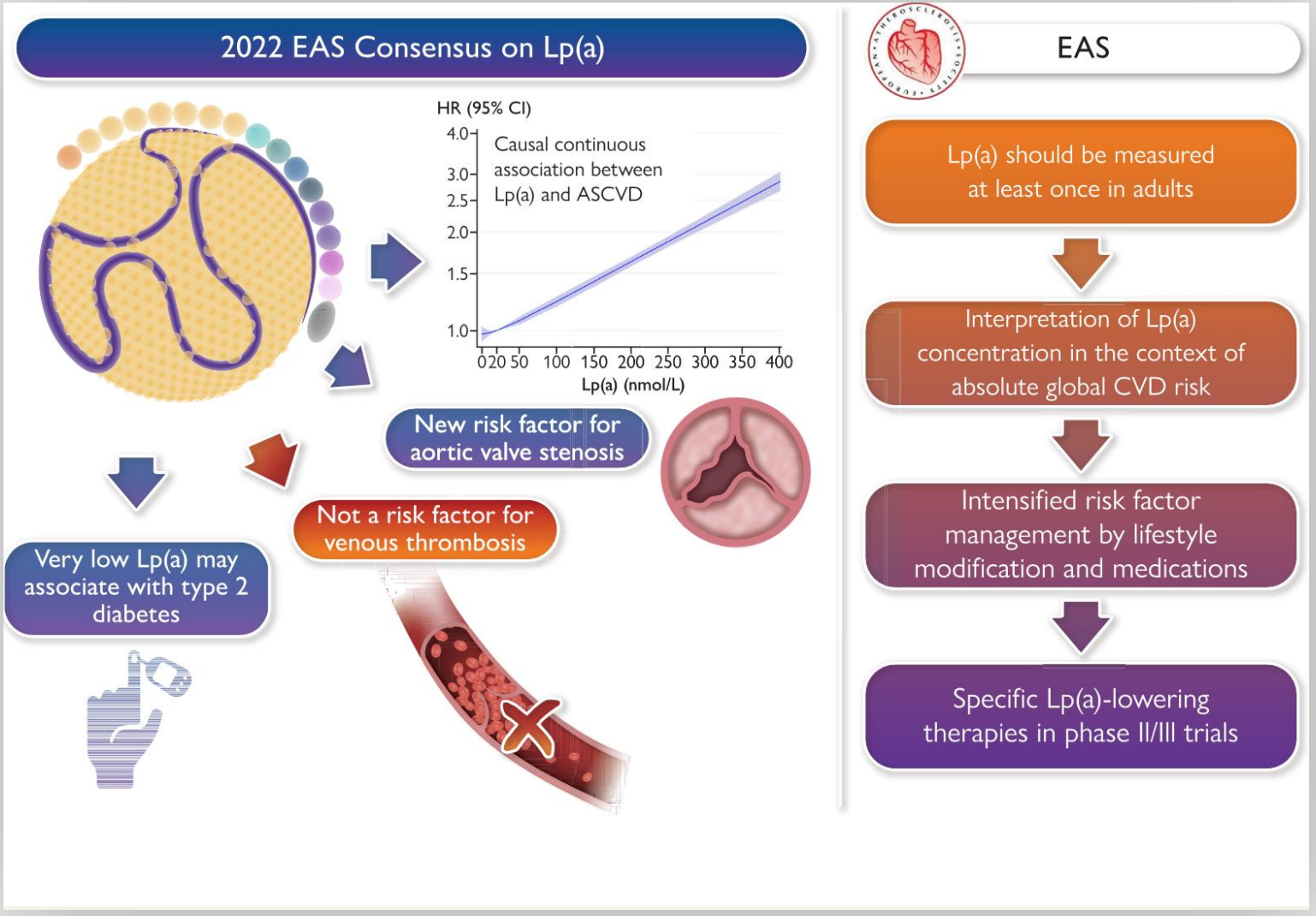
Remember patient has:

LDL-C 135 mg/dL

Syst. BP 135 mmHg

Lipoprotein(a)

Lipoprotein(a) is a CV risk factor



Eur Heart J 2022;43:3925

Alimentation & Cholestérol

Contenu en cholestérol en mg pour 100 g			
Cervelle	3.000	Viande de porc, de bœuf	90
Jaune d'œuf	1.400	Volailles	70
Œuf entier	470	Viande d'agneau	65
Foie/rognons	350	Hareng	60
Beurre	280	Truite	50
Cœur/langue	140	Fromages à 20–40% de mat. grasse	20–50
Saucisses/crème	100	Lait	12
Fromages à 60% mat, gr.	100	Margarine/huile végétale	0

Alimentation & Cholestérol

Lipides cachés en gramme par portion			
Avocat	47	Noisettes	9
Cacahuètes, grillées	25	Gouda (45%)	8
Pommes frites	22	Crème a la nougatine	6
Tourte forêt noire au kirsch	22	Chips aux cacahuètes	2
Chips de pomme de terre	20	Chocolat au lait	2
Poulet rôti	12	Poudre de cacao, partiellement dégraissée	1
Salami allemand	10	Olives (vertes, marinées)	0,4
Crème glacée	9		

Alimentation & Cholestérol

Produit	indiqué	contre-indiqué
Lait/produits laitiers	lait allégé, lait maigre, petit-lait, babeurre, séré maigre, fromage cottage, fromage du Harz, fromages maigres a moins de 10% de mat. grasse	lait entier, crème, crème double, lait condensé riche en graisse, yaourt entier, sortes de fromage à plus de 30% de mat. grasse
Œufs	blanc d'œuf	jaune d'œuf, œufs brouillés, œufs au plat, omelette
Poissons	poissons maigres tels que cabillaud, carrelet, truite, colin	anguille, anguille fumée, fricadelle carpe grasse, poisson pané
Saucisses	sortes de saucisse à plus de 20% de mat.gr., jambon cuit sans couenne, jambonneau de dinde, saucisse de volaille	sortes de saucisses à plus de 20% de mat.gr., saucisses fumées, saucisses au foie, pâte à tartiner sous forme de saucisse
Viandes	viande de veau, lapin, gibier, volaille sauvage, poulet (sans peau)	viande grasse de porc, de bœuf ou d'agneau, abats, lard, oie, canard
Pommes de terre	cuites ou en robe des champs, boulettes de p. de terre, purée	p.de terre rôties, pommes frites, pommes chips
Sauces	sauces allégées, sauces au citron ou au yaourt maigre, sauce à salade allégée	mayonnaise, rémoulade, sauce à salade à la crème, au beurre, au fromage
Entremets	flan au lait allégé flan aux fruits, gelées	desserts au beurre à la crème ou au lait entier, crème à la nougatine, branches au chocolat, pralinés
Patisseries confiseries	produits faits à partir de lait allégé et de graisses végétales sans jaune d'œuf	tourte, gâteaux cuits au saindoux ou à l'huile, biscuits au beurre, gâteaux salés et au fromage
Boissons	café filtre, thé, eau minérale, jus de fruits ou de légumes sans sucre	limonades et sirops sucrés, crème et liqueur à l'œuf, café sans filtre, irish coffee

Alimentation & Cholestérol

Le métabolisme du cholestérol sera nettement amélioré si le niveau énergétique est augmenté d'au moins 1000 kcal, optimalement 2000 kcal/semaine, par l'activité physique régulière

Consommation de 150 kcal en minutes			
nettoyer la voiture	45–60	aller à bicyclette (8 km)	30
nettoyer les fenêtres	45–60	danser	30
passer l' aspirateur	45–60	ratisser les feuilles	30
jouer au volleyball	45	sauter à la corde	15
travaux jardiniers	30–45	pelletter la neige	15
marcher (2,8 km)	35	monter les escaliers	15

Quels sports, combien de calories brulées ?

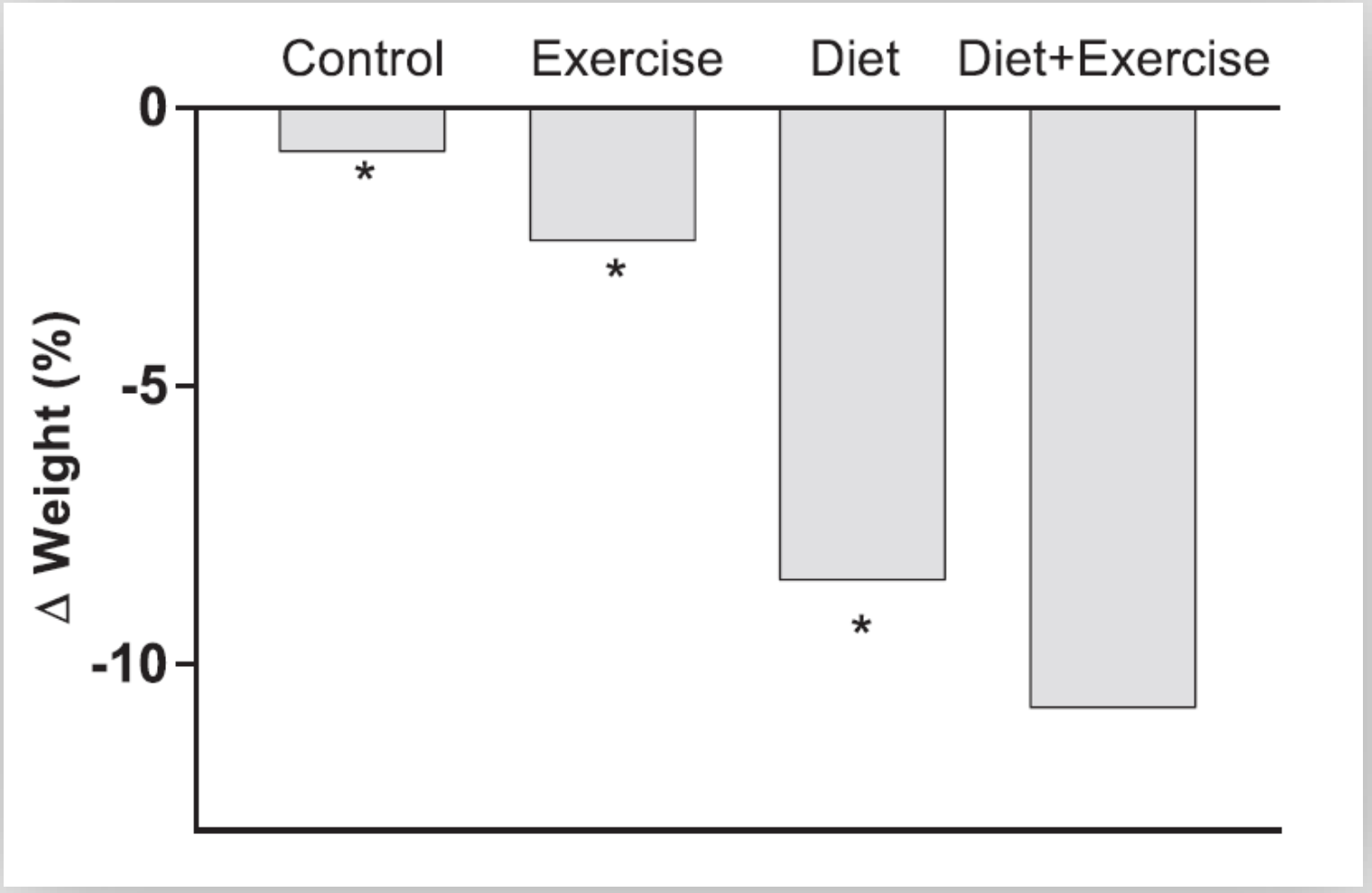
- Nage (brasse): 458 kcal/ 30‘
- High Intensity Interval Training: 444 kcal/ 30‘
- Jogging: 394 kcal/ 30‘
- Zumba: 271 kcal/ 30‘
- Vélo de course: 300 kcal/ 30’

458 kcal

244 kcal

52 kcal

Stratégie optimale pour perdre du poids: Combinaison de moins de calories et plus bouger



Obesity 2012;20:1628

Bénéfices cardiovasculaires grace à l'activité physique (2020 WHO guidelines)

1. Any physical activity is better than no physical activity.
2. Adults should engage in at least 150–300 min of moderate aerobic exercise per week, or at least 75–150 min of vigorous aerobic exercise per week, or equivalent combinations thereof. In explanation, if personal exertional capacity is rated on a 0–10 scale, a rating of 5–6 is moderate aerobic activity, and 7–8 is vigorous aerobic activity.
3. Adults should also engage in at least moderate intensity muscle-strengthening exercise of all major muscle groups at a frequency of at least twice a week.
4. The minutes that contribute toward this guidance do not need to accrue from leisure time exercise conducted specifically for the purpose of health; they can accrue from everyday household activities, during movement from place to place, and as work-related activities.
5. The minutes that contribute toward this guidance can accrue in periods of any duration across the course of the day and do not need to accrue in sessions of a minimum duration.

Sédentarité - Intervention

Wolters Kluwer Health | Lippincott Williams & Wilkins

EUROPEAN SOCIETY OF CARDIOLOGY®

Original Scientific Paper

Stairs instead of elevators at workplace: cardioprotective effects of a pragmatic intervention

Philippe Meyer[a], Bengt Kayser[e], Michel P. Kossovsky[b], Philippe Sigaud[a], David Carballo[a], Pierre-F. Keller[a], Xavier Eric Martin[c], Nathalie Farpour-Lambert[c], Claude Pichard[d] and François Mach[a]

[a]Cardiology Service, [b]Department of Community Medicine, [c]Department of Pediatrics, [d]Nutrition Unit, University Hospital of Geneva and [e]Institute of Movement Sciences and Sports Medicine, University of Geneva, Geneva, Switzerland

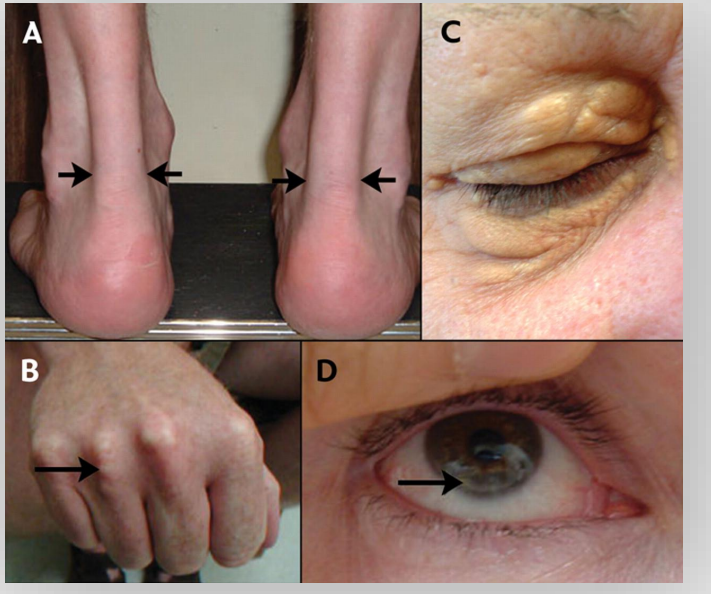
Received 31 July 2009 Accepted 11 February 2010

Conclusion Encouraging stair use at work is effective for improving fitness, body composition, blood pressure, and lipid profile in asymptomatic individuals with an inactive lifestyle and thus may be a simple way to significantly reduce cardiovascular disease risk at the population level. Eur J Cardiovasc Prev Rehabil 00:000–000 © 2010 The European Society of Cardiology

Conclusions/Messages

L'hypercholestérolémie Familiale (HF) est la plus fréquente des maladies rares, environ 1/250-300 habitants en Suisse.

L'HF est très largement sous-diagnostiquée en prévention primaire, et en prévention secondaire.



European Heart Journal (2013) **34**, 3478–3490
doi:10.1093/eurheartj/eht273

CURRENT OPINION

Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease

Consensus Statement of the European Atherosclerosis Society

Conclusions/Messages

Le score Dutch lipid network permet de très bien documenter la présence d'une HF.

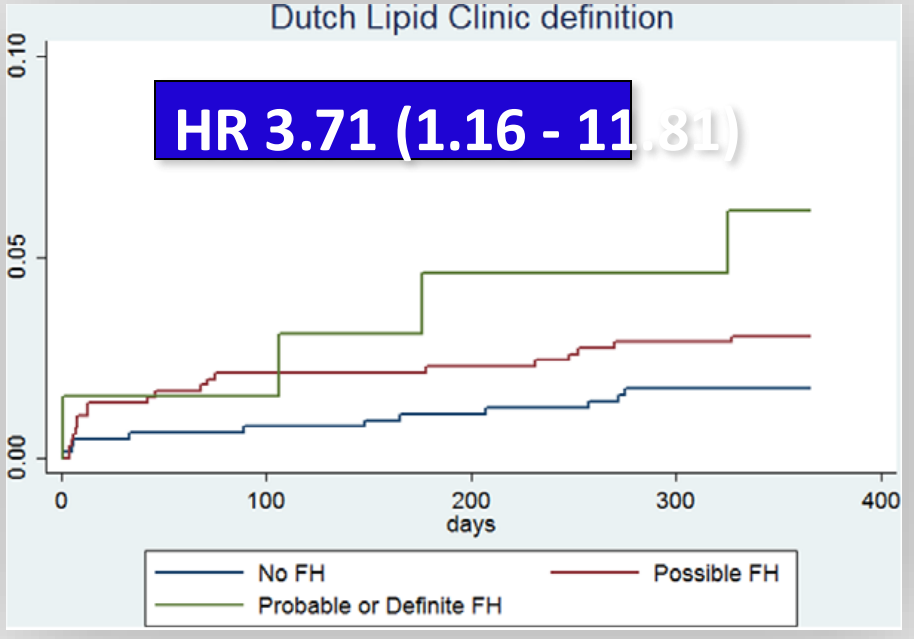
Table 19 Diagnostic criteria for the clinical diagnosis of HeFH according to MedPed and WHO[158]

	Criteria	Score
Family history	First-degree relative known with premature CAD[a] and/or first-degree relative with LDL-C >95th centile	1
	First-degree relative with Tx and/or children <18 with LDL-C >95th centile	2
Clinical history	Patient has premature CAD*	2
	Patient has premature cerebral/ peripheral vascular disease	1
Physical examination	Tx	6
	Arcus cornealis below the age of 45 years	4
LDL-C	>8.5 mmol/L (more than ~330 mg/dL)	8
	6.5–8.4 mmol/L (~250–329 mg/dL)	5
	5.0–6.4 mmol/L (~190–249 mg/dL)	3
	4.0–4.9 mmol/L (~155–189 mg/dL)	1
Definite FH		Score >8
Probable FH		Score 6-8
Possible FH		Score 3-5
No diagnosis		Score <3

[a]Premature CAD: male before 55, women before 60 years of age.
CAD = coronary artery disease; FH = familial hypercholesterolaemia; HeFH = heterozygous familial hypercholesterolaemia; LDL-C = low-density lipoprotein-cholesterol; Tx = tendon xanthomata; WHO = World Health Organization.

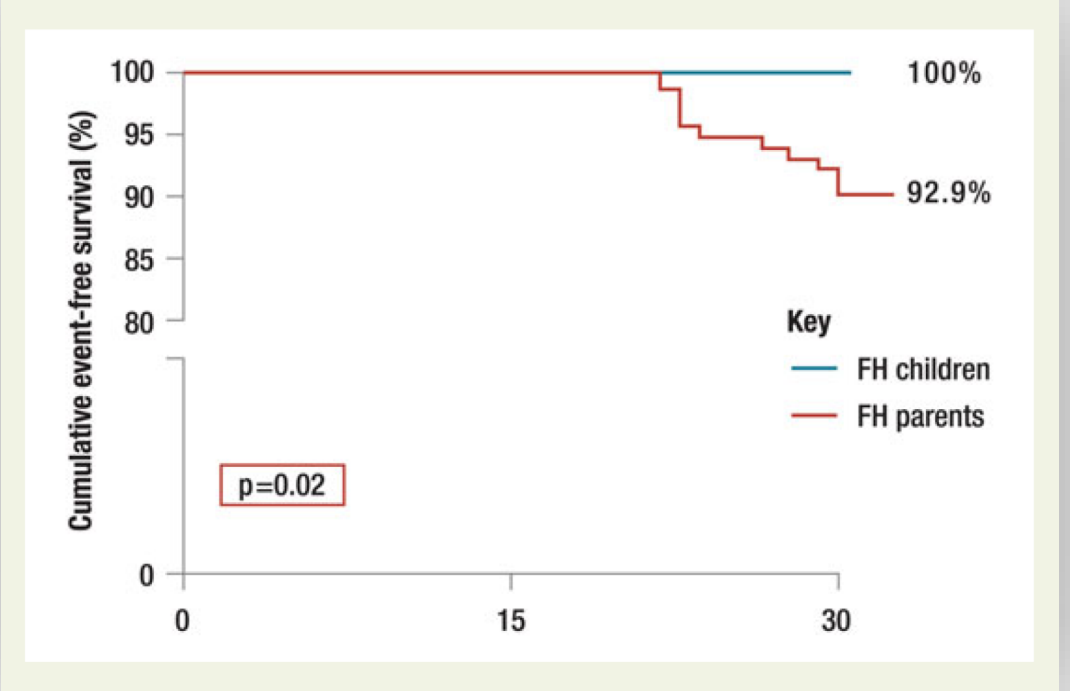
Conclusions/Messages

Le diagnostique d'HF est un facteur de mauvais pronostique après une syndrome coronarien aigu (infarctus du myocarde).



Conclusions/Messages

En présence d'une HF, un traitement hypolipémiant efficace permet de diminuer significativement la survenue de futurs événements CV.



Conclusions/Messages

La Lipoprotéine(a) Lp(a) est une LDL-like lipoprotéine avec une addition de apo(a), ce qui lui confer un défaut de reconnaissance par le LDLR.

La Lp(a) a de nombreuses propriétés augmentant l'athérogénèse et la thrombogénèse.

Son augmentation dans le sang est principalement liée à des mutations génétiques.

ESC European Society of Cardiology

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EDITORIAL

Lipoprotein(a): the perpetual supporting actor

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