



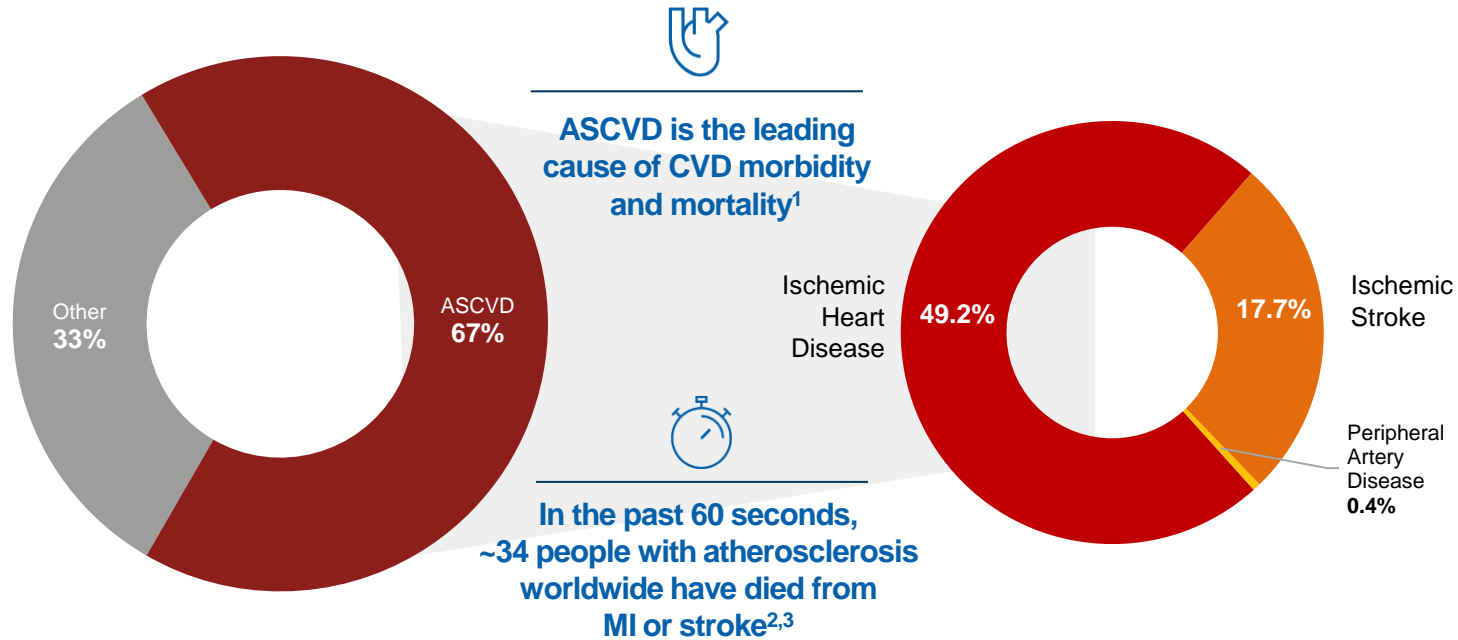
# LIPIDIOLOGY-LIPIDS GOAL LEVEL AND DIFFERENT GUIDELINES

**Dr Evangelos Liberopoulos**

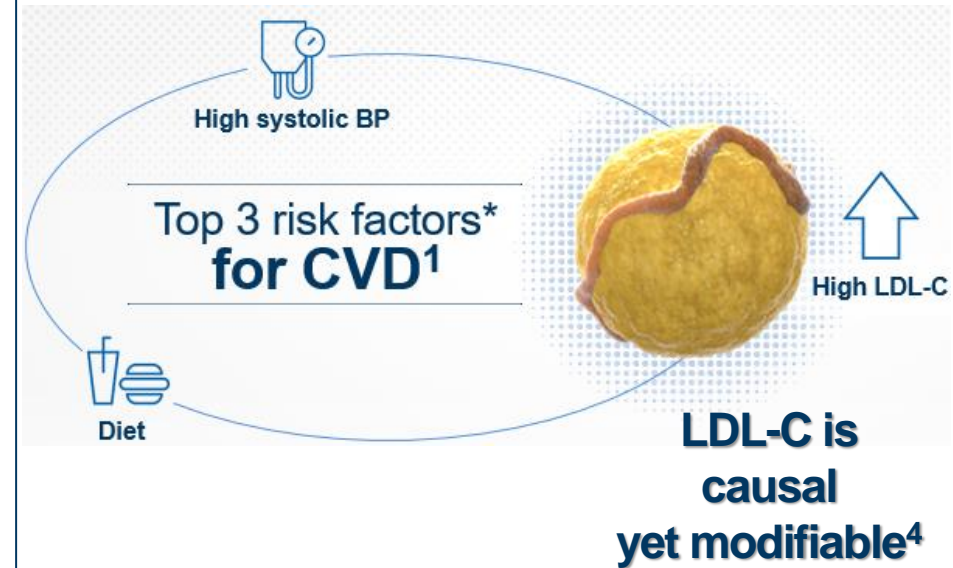
Professor of Medicine-Metabolic Diseases, School of Medicine, National and Kapodistrian University of Athens,  
1<sup>st</sup> Propedeutic Department of Medicine, GHA 'Laiko'

# Most CV deaths are due to ASCVD

18.6 million CV deaths (2019)<sup>1</sup>

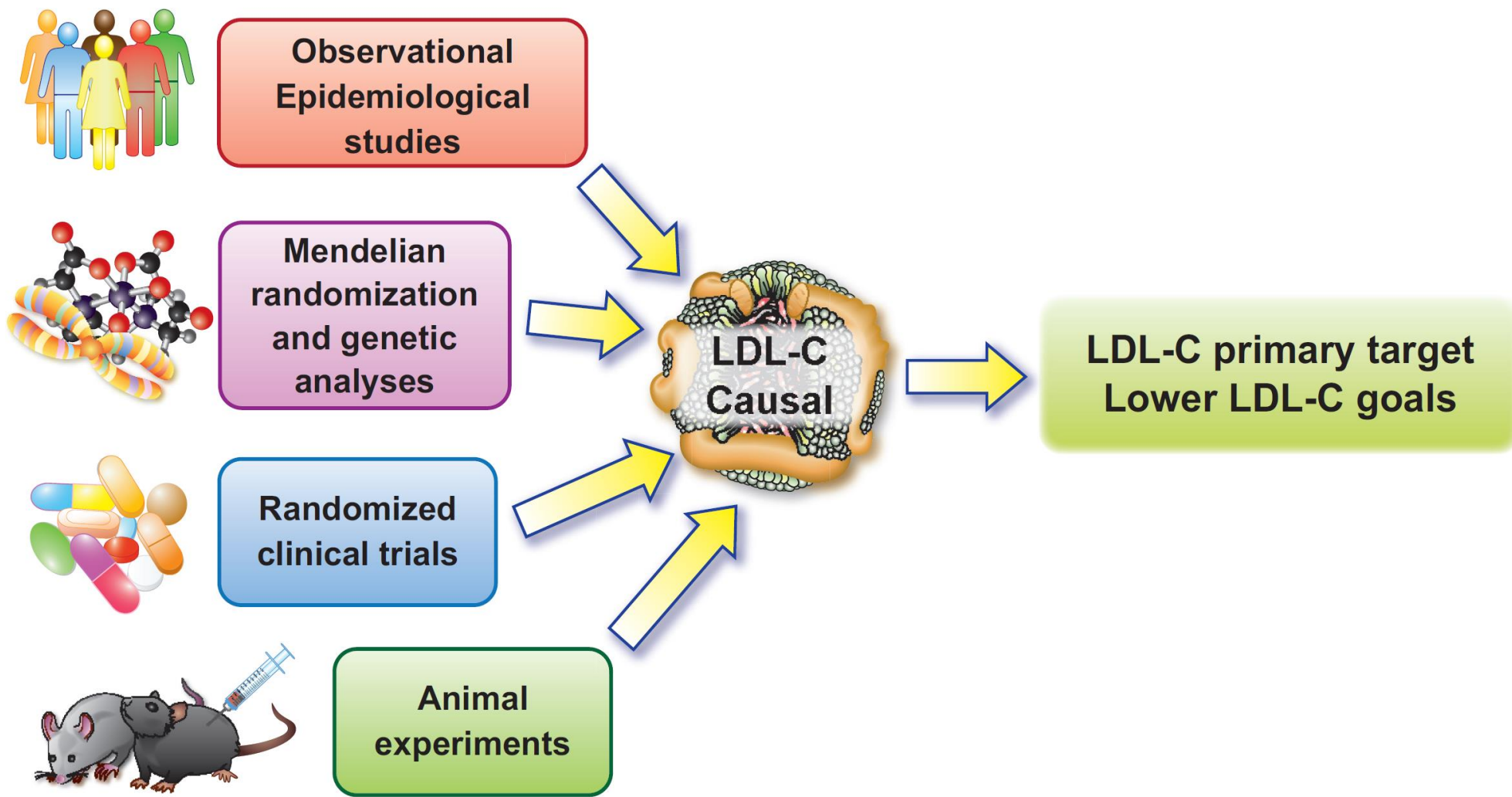


## What if we could reverse the trajectory of CVD?

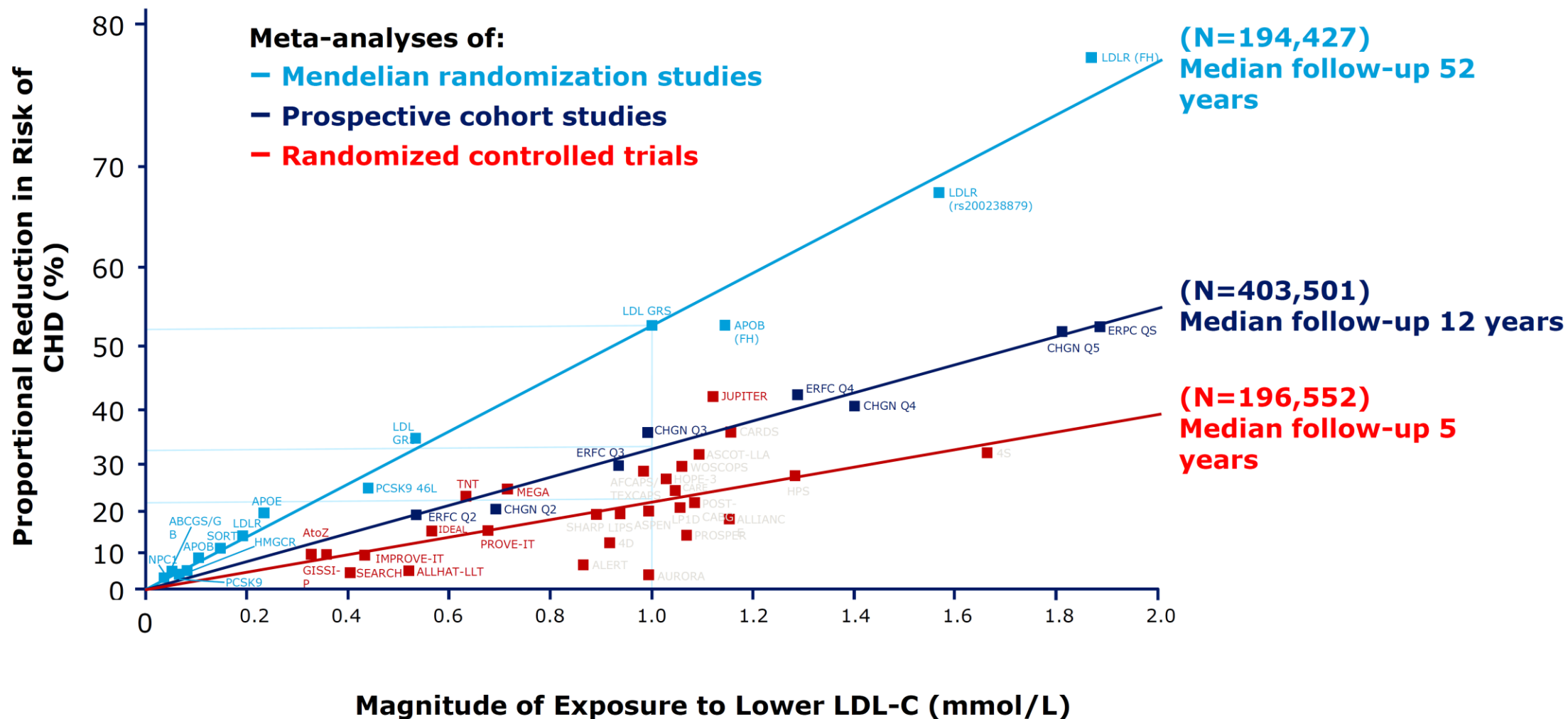


1. Roth GA, et al. *J Am Coll Cardiol.* 2020;76(25):2982-302 2. Barquera S, et al. *Arch Med Res.* 2015;46(5):328-338. 3. Worldometer. World population by year. <https://www.worldometers.info/world-population/world-population-by-year/>. Accessed May 31, 2020.

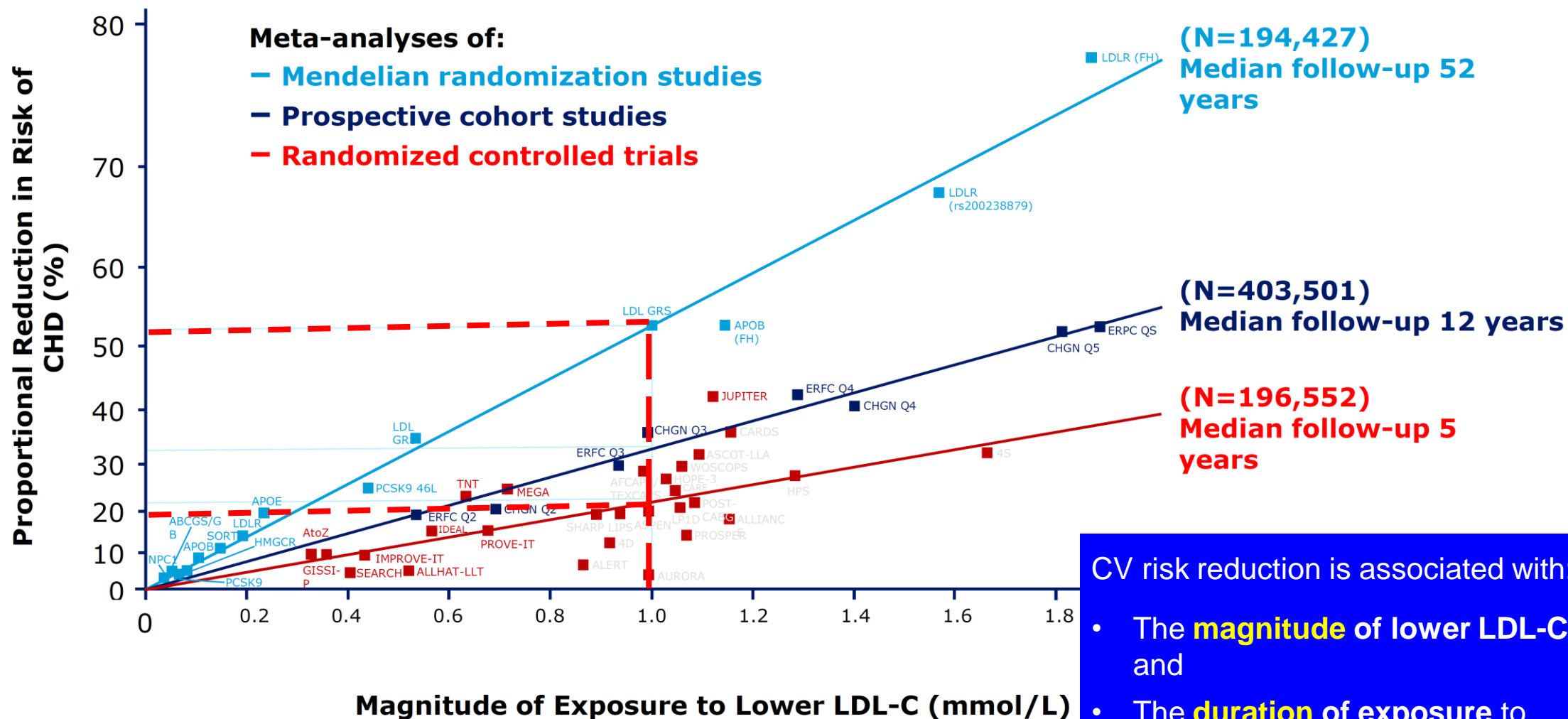
4. Ference BA, et al. *J Am Coll Cardiol.* 2018;72(10):1141-1156



# Over a 5 year time horizon we need greater absolute LDL-C reductions to achieve greater risk reductions



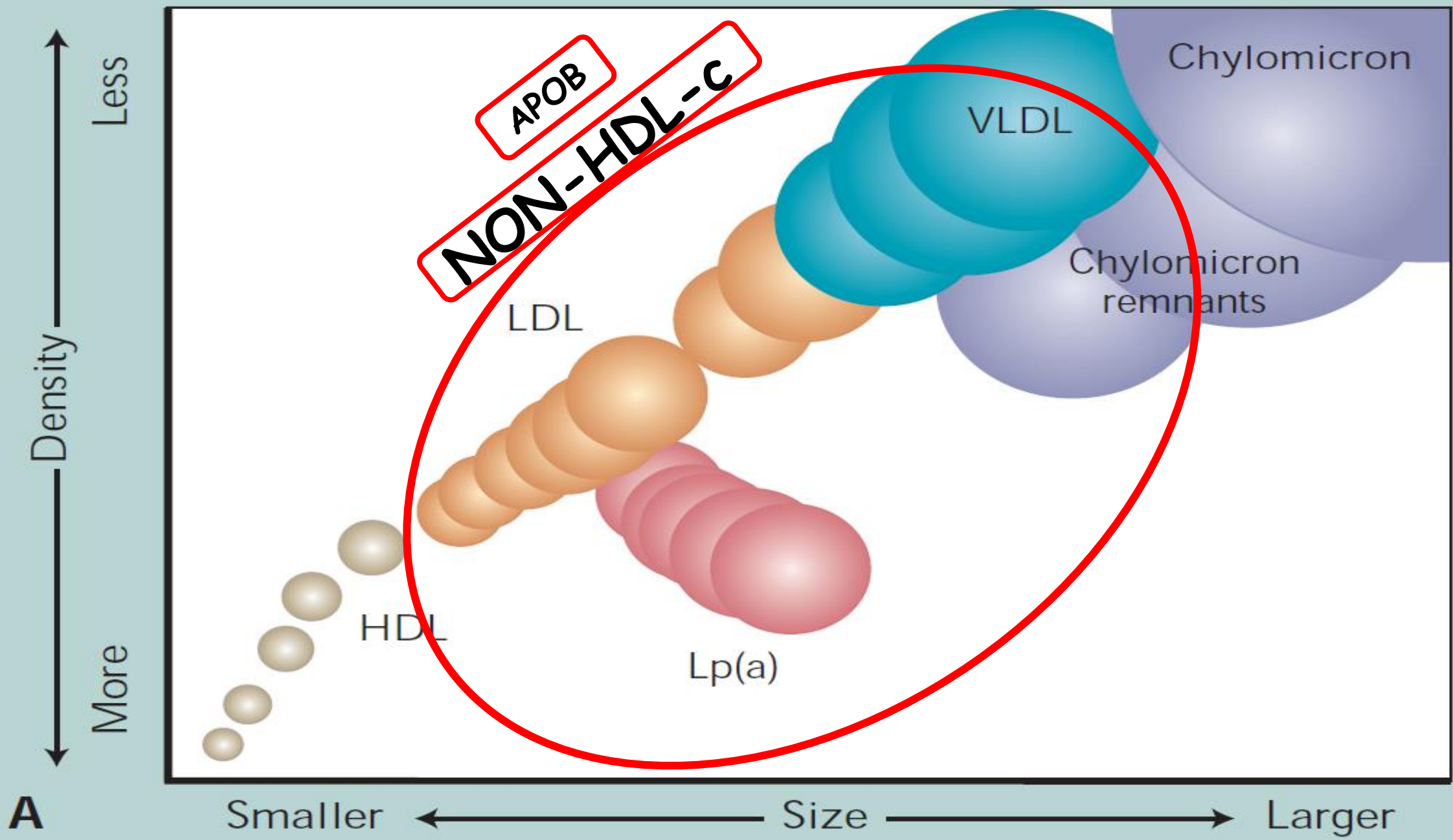
# Over a 5 year time horizon we need greater absolute LDL-C reductions to achieve greater risk reductions



CV risk reduction is associated with:

- The **magnitude** of lower LDL-C and
- The **duration** of exposure to lower LDL-C

Ference BA, et al. EAS Consensus Statement on LDL Causality. *Eur Heart J*. 2017;doi:10.1093/eurheartj/ehx144. CHD = coronary heart disease; LDL-C = low-density lipoprotein cholesterol.



A

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

# Cardiovascular risk categories (1)

## Very-high-risk

People with any of the following:

**Documented ASCVD, either clinical or unequivocal on imaging.**

Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularisation (PCI, CABG and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis) or on carotid ultrasound.

**DM with target organ damage,  $\geq 3$  major risk factors or early onset of T1DM of long duration (>20 years).**

**Severe CKD (eGFR <30 mL/min/1.73 m<sup>2</sup>).**

**A calculated SCORE  $\geq 10\%$  for 10-year risk of fatal CVD.**

**FH with ASCVD or with another major risk factor.**



# Cardiovascular risk categories (2)

<b>High-risk</b>	<p>People with:</p> <ul style="list-style-type: none"><li><b>Markedly elevated single risk factors</b>, in particular TC &gt;8 mmol/L (&gt;310 mg/dL), LDL-C &gt;4.9 mmol/L (&gt;190 mg/dL), or BP ≥180/110mmHg.</li><li><b>Patients with FH without other major risk factors.</b></li><li><b>Patients with DM without target organ damage*</b>, with DM duration ≥10 years or another additional risk factors.</li><li><b>Moderate CKD (eGFR 30–59 mL/min/1.73 m<sup>2</sup>).</b></li><li><b>A calculated SCORE ≥5% and &lt;10% for 10-year risk of fatal CVD.</b></li></ul>
<b>Moderate-risk</b>	<p><b>Young patients (T1DM &lt;35 years; T2DM &lt;50 years) with DM duration &lt;10 years, without other risk factors.</b></p> <p><b>Calculated SCORE ≥1% and &lt;5% for 10-year risk of fatal CVD.</b></p>
<b>Low-risk</b>	<p><b>Calculated SCORE &lt;1% for 10-year risk of fatal CVD.</b></p>

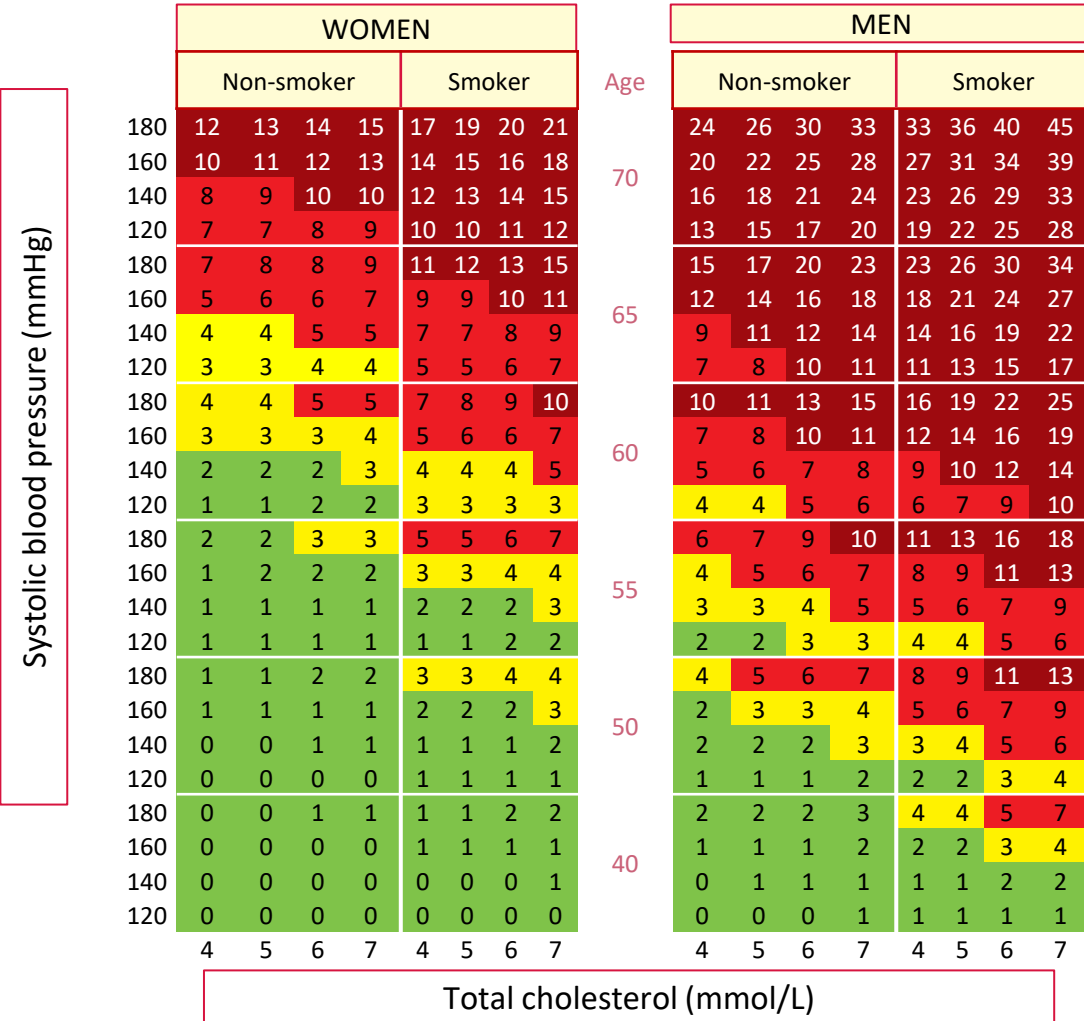
\*Target organ damage is defined as microalbuminuria, retinopathy or neuropathy

# SCORE Cardiovascular Risk Chart

## 10-year risk of fatal CVD

### High-risk regions of Europe

## SCORE chart for European populations at high cardiovascular disease risk



# Factors modifying SCORE risks (1)

**Social deprivation – the origin of many of the causes of CVD.**

**Obesity and central obesity as measured by the body mass index and waist circumference, respectively.**

**Physical inactivity.**

**Psychosocial stress including vital exhaustion.**

**Family history of premature CVD (men: <55 years; women: <60 years).**

**Chronic immune-mediated inflammatory disorder.**

# Factors modifying SCORE risks (2)

Major psychiatric disorders.

Treatment for human immunodeficiency virus (HIV) infection.

Atrial fibrillation.

Left ventricular hypertrophy.

Chronic kidney disease.

Obstructive sleep apnoea syndrome.

Non-alcoholic fatty liver disease.

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# Recommendations for cardiovascular imaging for risk assessment of atherosclerotic cardiovascular disease

Recommendations	Class	Level
<b>Arterial (carotid and/or femoral) plaque burden on ultrasonography</b> should be considered as a risk modifier in individuals at low or moderate risk.	<b>IIa</b>	<b>B</b>
<b>CAC score</b> assessment with CT should be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.	<b>IIa</b>	<b>B</b>

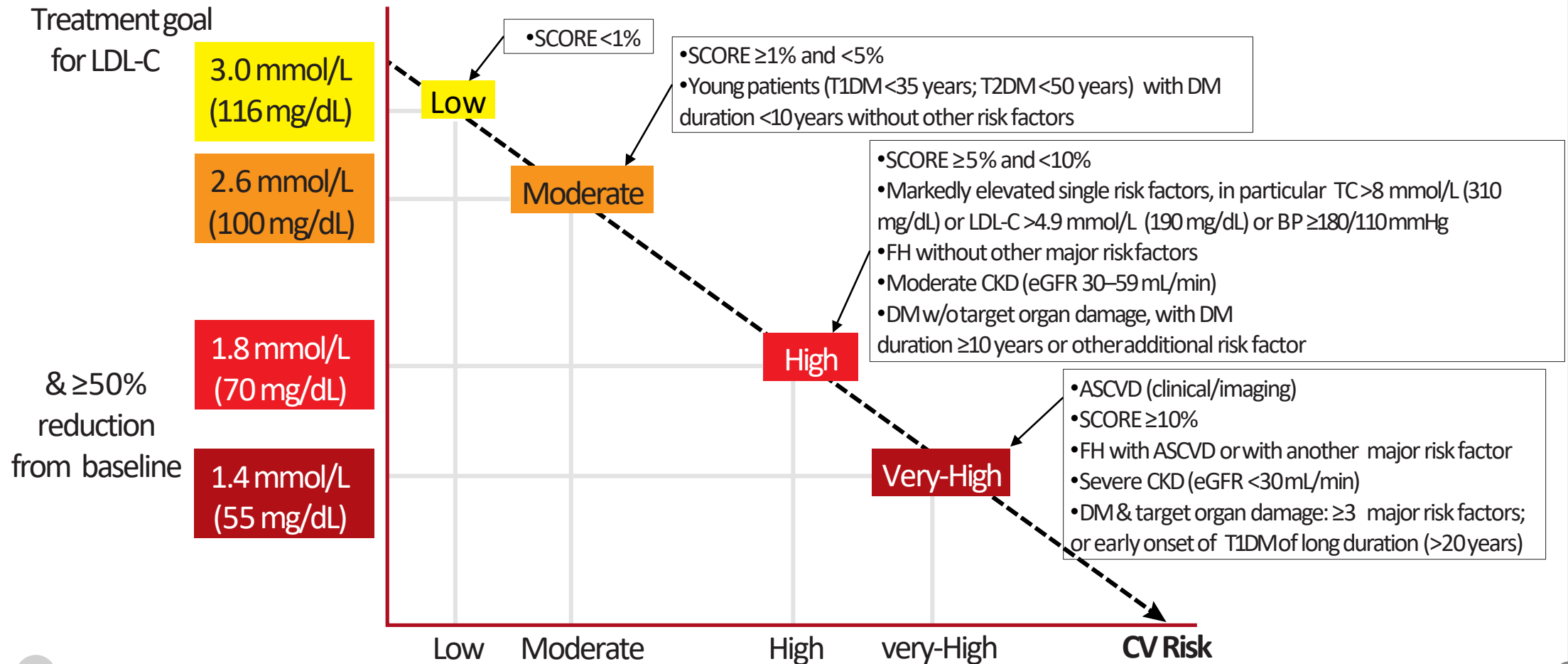
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# Recommendations for lipid analyses for cardiovascular disease risk estimation (2)

Recommendations	Class	Level
<b>Non-HDL-C evaluation</b> is recommended for risk assessment, particularly in people with high TG, diabetes, obesity or very low LDL-C.	I	C
<b>ApoB analysis is recommended for risk assessment</b> , particularly in people with high TG, diabetes, obesity or metabolic syndrome, or very low LDL-C. It can be used as an alternative to LDL-C, if available, as the primary measurement for screening, diagnosis and management, and may be preferred over non-HDL-C in people with high TG, diabetes, obesity or very low LDL-C.	I	C

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# Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk



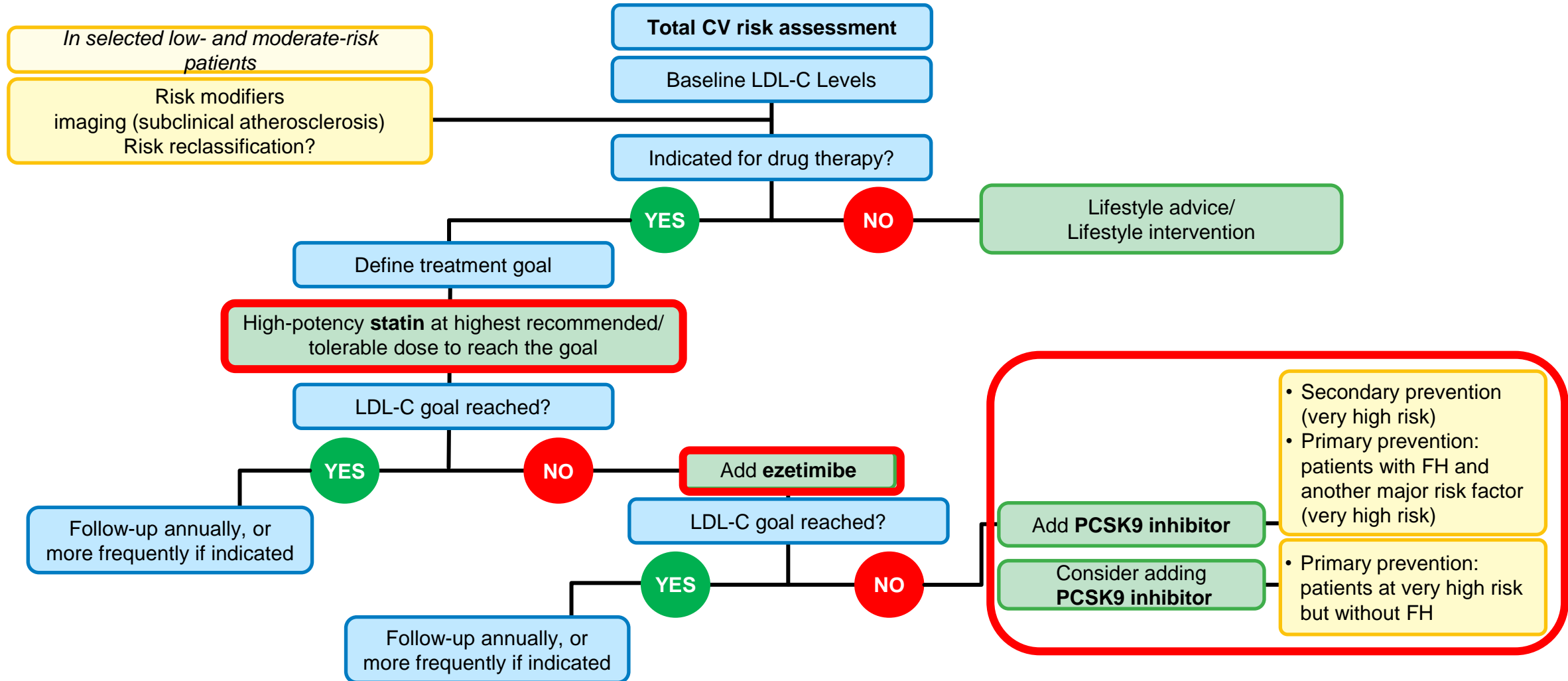
# Evidence for efficacy of LDL-lowering therapies down to below 1.4 mmol/L (55 mg/dL)

Source of evidence	Mean reduction in LDL cholesterol; mmol/L [mg/dL]	Outcome	RR (95% CI)
CTT meta-analysis <sup>1</sup> (high-intensity vs standard statin; subgroup <2.0 mmol/L)	1.71 [66] vs 1.32 [50]	MI, CHD death, stroke, coronary revasc.	0.71 (0.56-0.91) [per mmol/L]
IMPROVE-IT <sup>2</sup> (eze plus statin vs statin)	1.55 [70] vs 1.40 [54]	CV death, MI, stroke, IIA	0.94 (0.89-0.99)
FOURIER <sup>3</sup> (evolocumab plus high-dose statin ± eze vs high-dose statin ± eze)	2.37 [92] vs 0.78 [30]	CV death, MI, stroke, UA, coronary revasc	0.85 (0.79-0.92)
ODYSSEYOUTCOMES <sup>4</sup> (alirocumab plus high-dose statin ± eze vs high-dose statin ± eze)	2.37 [92] vs 1.37 [53]	MI, CHD death, stroke, UA	0.85 (0.78-0.93)

<sup>1</sup>Lancet 2010; 376: 1670-81; <sup>2</sup>NEJM 2015; 372: 2387-97; <sup>3</sup>NEJM 2017; 376: 1713-22; <sup>4</sup>NEJM 2018; 379: 2097-107



# The Guidelines Provide an Algorithm to Guide Lipid-Lowering Therapy Selection



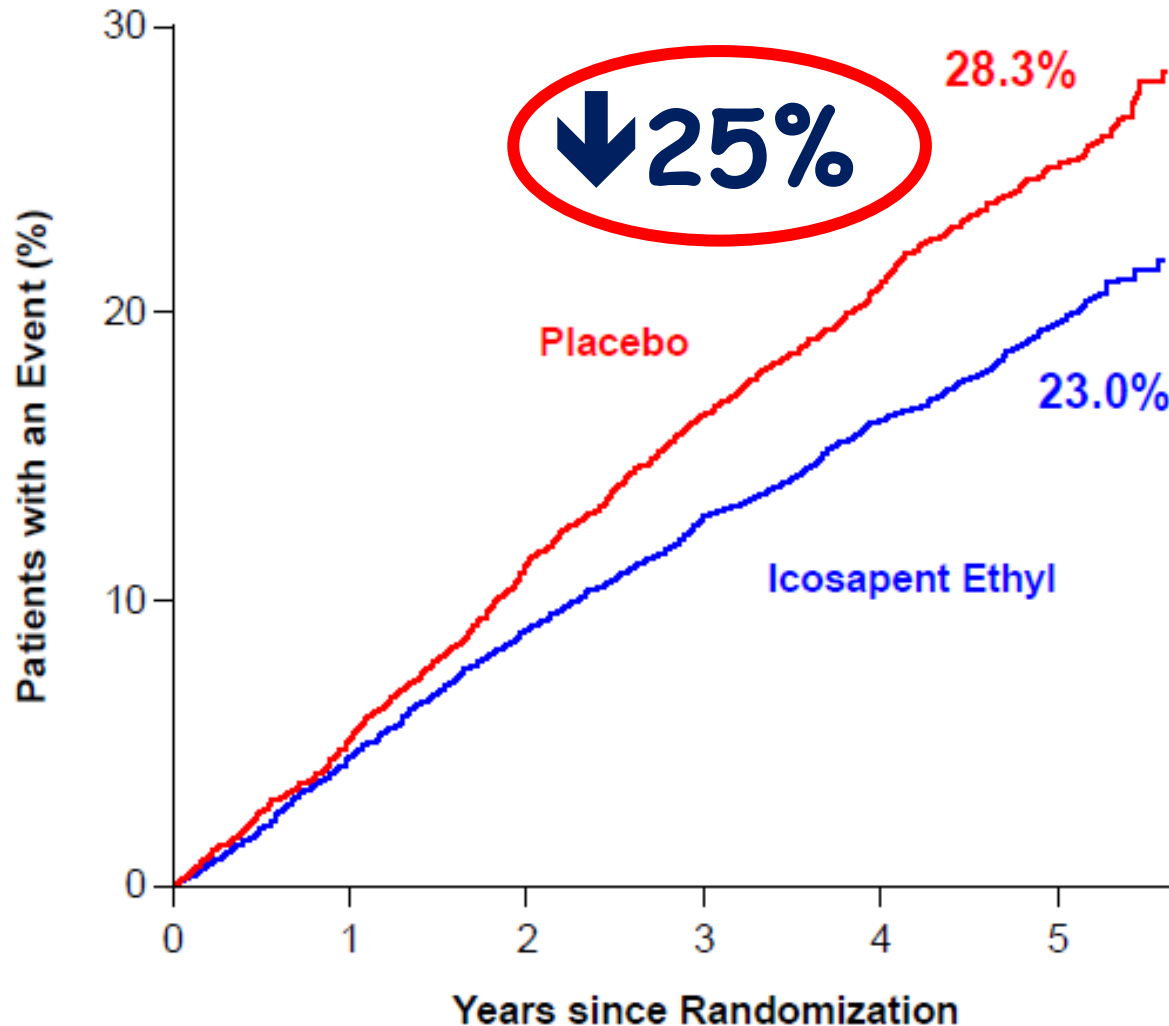
# Recommendations for drug treatments of patients with hypertriglyceridaemia (1)

Recommendations	Class	Level
<b>Statin treatment is recommended</b> as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia (TG >2.3 mmol/L (>200 mg/dL)).	I	B
<b>In high-risk (or above) patients with TG between 1.5 and 5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2 x 2 g/day) should be considered in combination with statin.</b>	Ila	B

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# Primary End Point:

CV Death, MI, Stroke, Coronary Revasc, Unstable Angina



**Hazard Ratio, 0.75**

(95% CI, 0.68–0.83)

**RRR = 24.8%**

**ARR = 4.8%**

**NNT = 21** (95% CI, 15–33)

**P=0.00000001**

# Recommendations for drug treatments of patients with hypertriglyceridaemia (2)

Recommendations	Class	Level
In primary prevention patients who are at LDL-C goal with TG >2.3 mmol/L (>200 mg/dL), <b>fenofibrate or bezafibrate</b> may be considered in combination with statins.	<b>IIb</b>	<b>B</b>
In high-risk patients who are at LDL-C goal with TG >2.3 mmol/L (>200 mg/dL), <b>fenofibrate or bezafibrate</b> may be considered in combination with statins.	<b>IIb</b>	<b>C</b>

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## PROMINENT Study Design

**MEN AND WOMEN  
WITH  
TYPE 2 DIABETES**



**10,000  
PARTICIPANTS  
24 COUNTRIES**

**TG 200-499 mg/dL (2.26-5.64 mmol/L)  
and HDL  $\leq$ 40 mg/dL (1.03 mmol/L)**

**Moderate-High Intensity Statin Therapy or LDL-C Control  
( $\leq$ 70 mg/dL or  $\leq$ 100 mg/dL if statin intolerant)  
1/3 Primary Prevention, 2/3 Secondary Prevention**

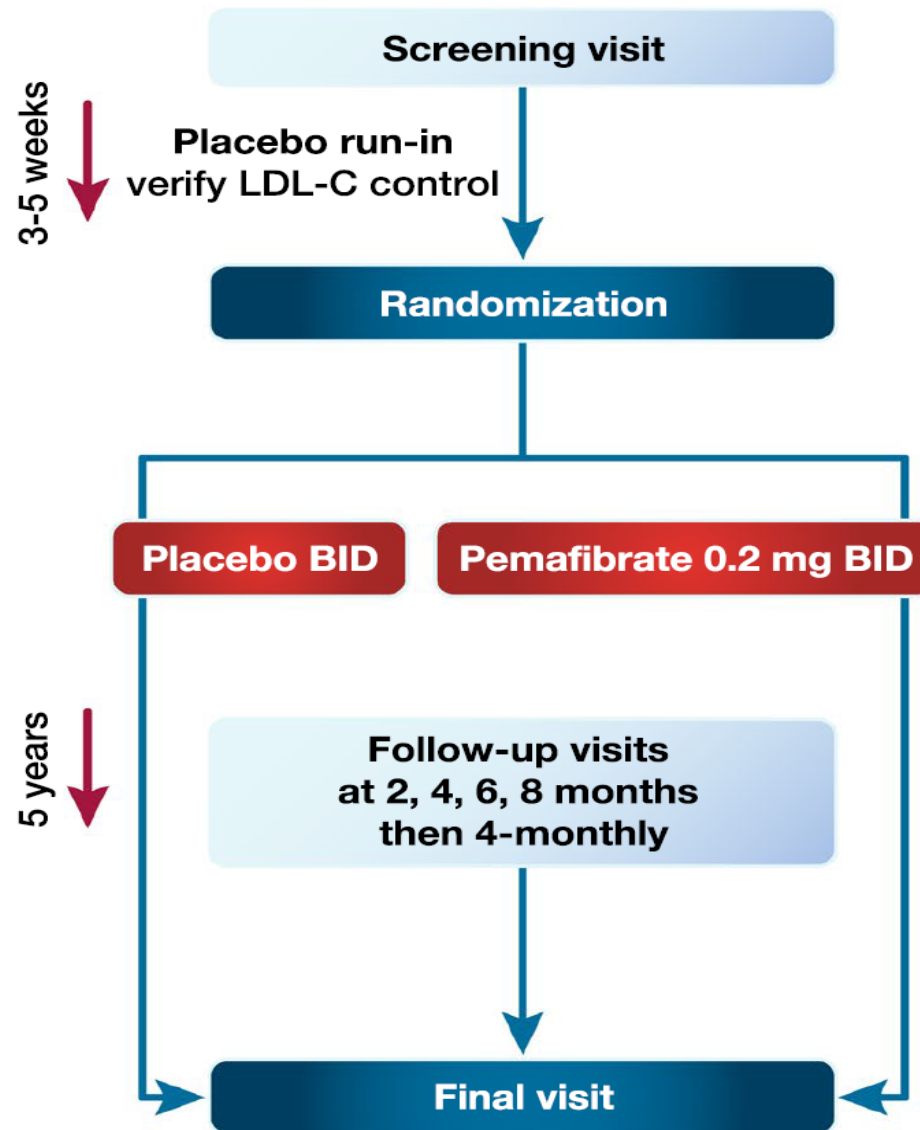
### ENDPOINTS

**Event Driven:** 1092 Primary Endpoints, 200 in women

#### PRIMARY ENDPOINT (MACE):

Myocardial infarction, ischemic stroke, or unstable angina requiring unplanned revascularization, cardiovascular death

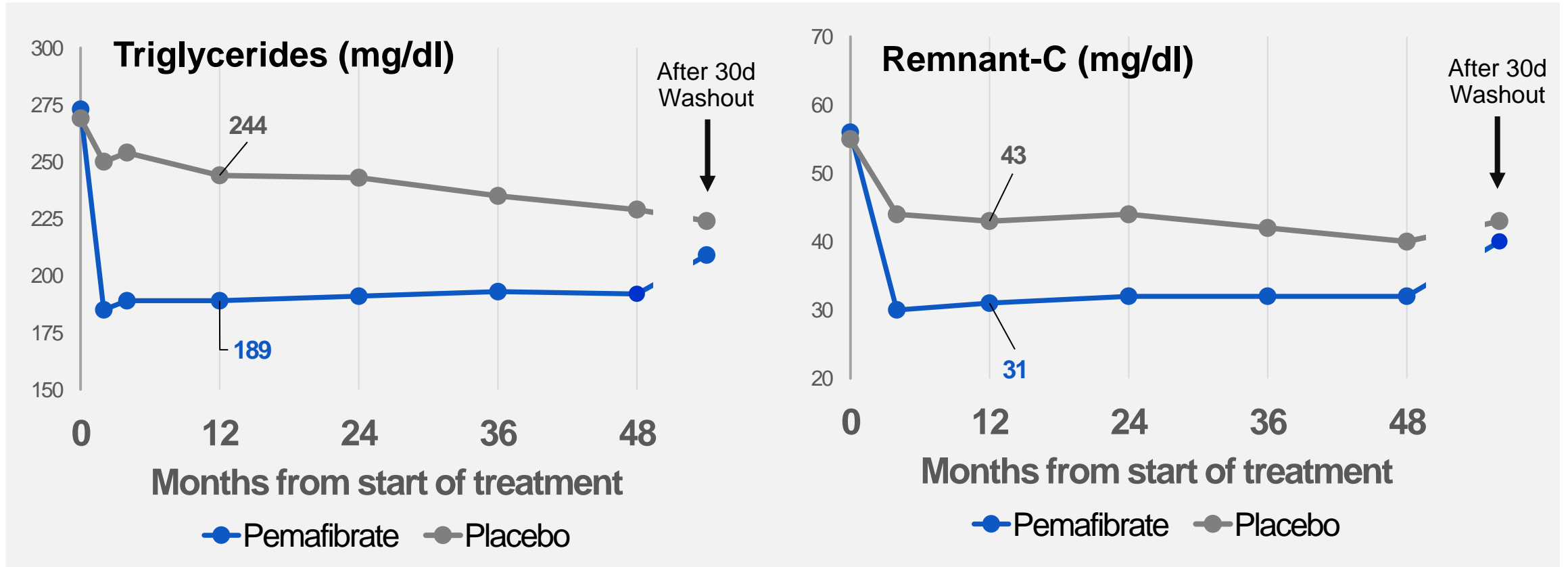
**Secondary/Tertiary Endpoints:** all-cause mortality, any coronary revascularization, heart failure, total stroke, retinopathy, nephropathy, glycemic control, PAD, biomarkers, quality of life



**F** Design of the PROMINENT study with pemafibrate. Adapted from Pradhan et al. [144] with permission. BID, twice daily; HDL, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PAD, peripheral artery disease; TG, triglycerides

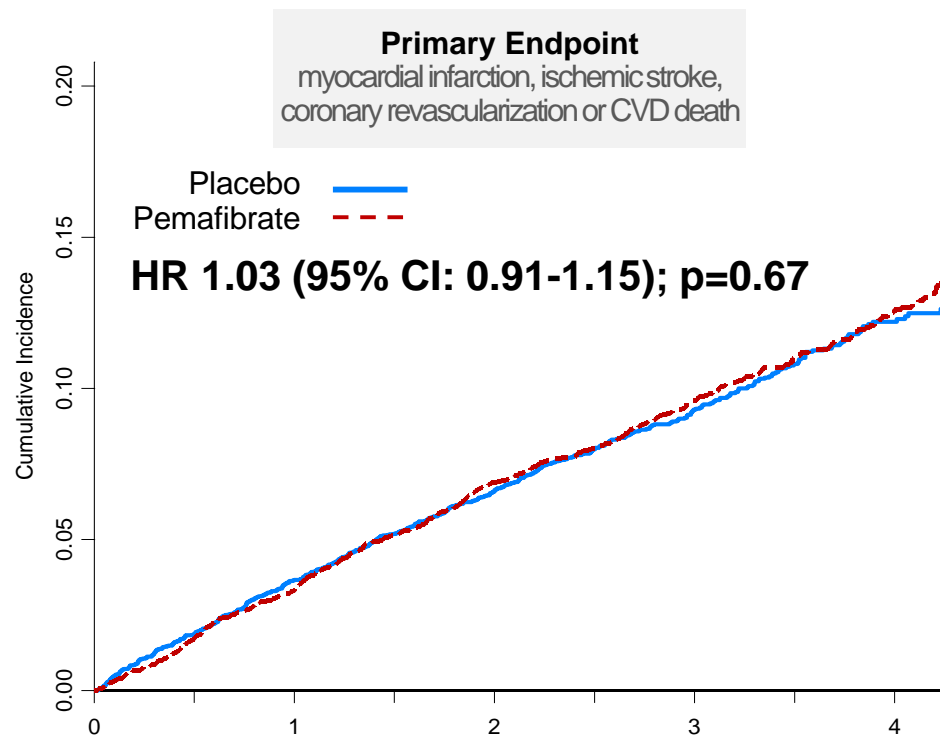
# Lipid Lowering

## Durability of biomarker changes over time

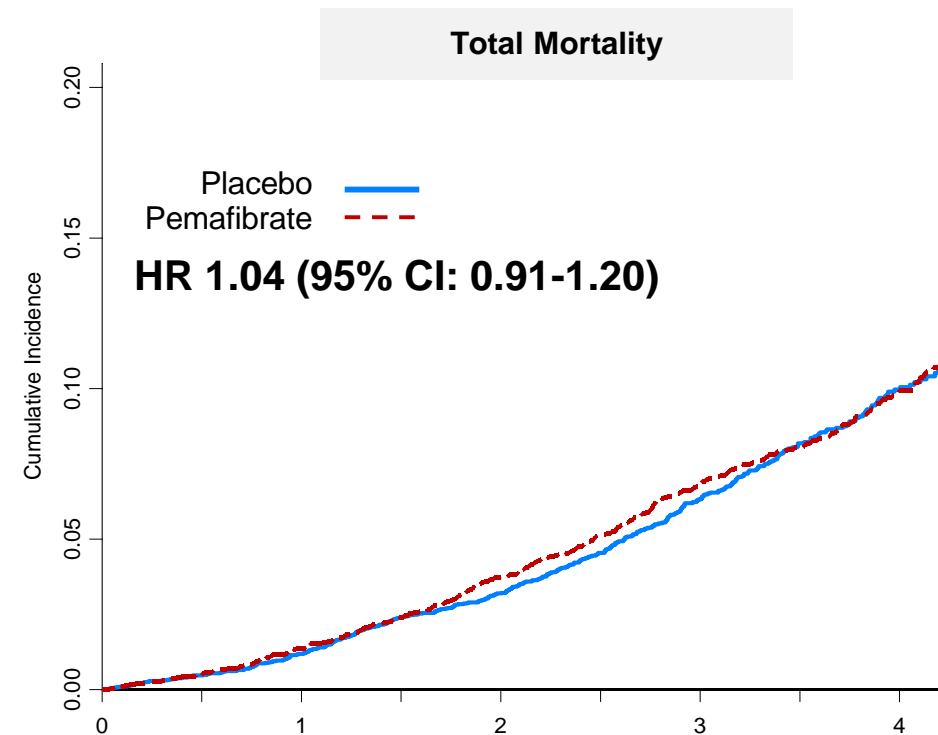


# PROMINENT Efficacy

## Primary Endpoint; Median Follow-Up 3.4 Years



No. at Risk	Follow-up (years)									
	0	1	2	3	4					
Placebo	5,257	5,083	4,926	4,764	4,597	3,652	2,839	2,064	1,131	
Pemafibrate	5,240	5,060	4,902	4,743	4,553	3,628	2,821	2,068	1,147	



No. at Risk	Follow-up (years)									
	0	1	2	3	4					
Placebo	5,257	5,206	5,148	5,058	4,966	4,004	3,144	2,313	1,310	
Pemafibrate	5,240	5,187	5,117	5,044	4,932	3,985	3,118	2,311	1,294	

Upon review of the 75% efficacy and futility analysis, the trial's DSMB recommended early termination of the study on the basis of futility.  
Final Confirmed Endpoints: 1132 primary events, 228 in women

# DYSIS II - GREECE

N=499 Chronic Coronary Syndrome

Distance to LDL-C 70 mg/dL = 27 mg/dL

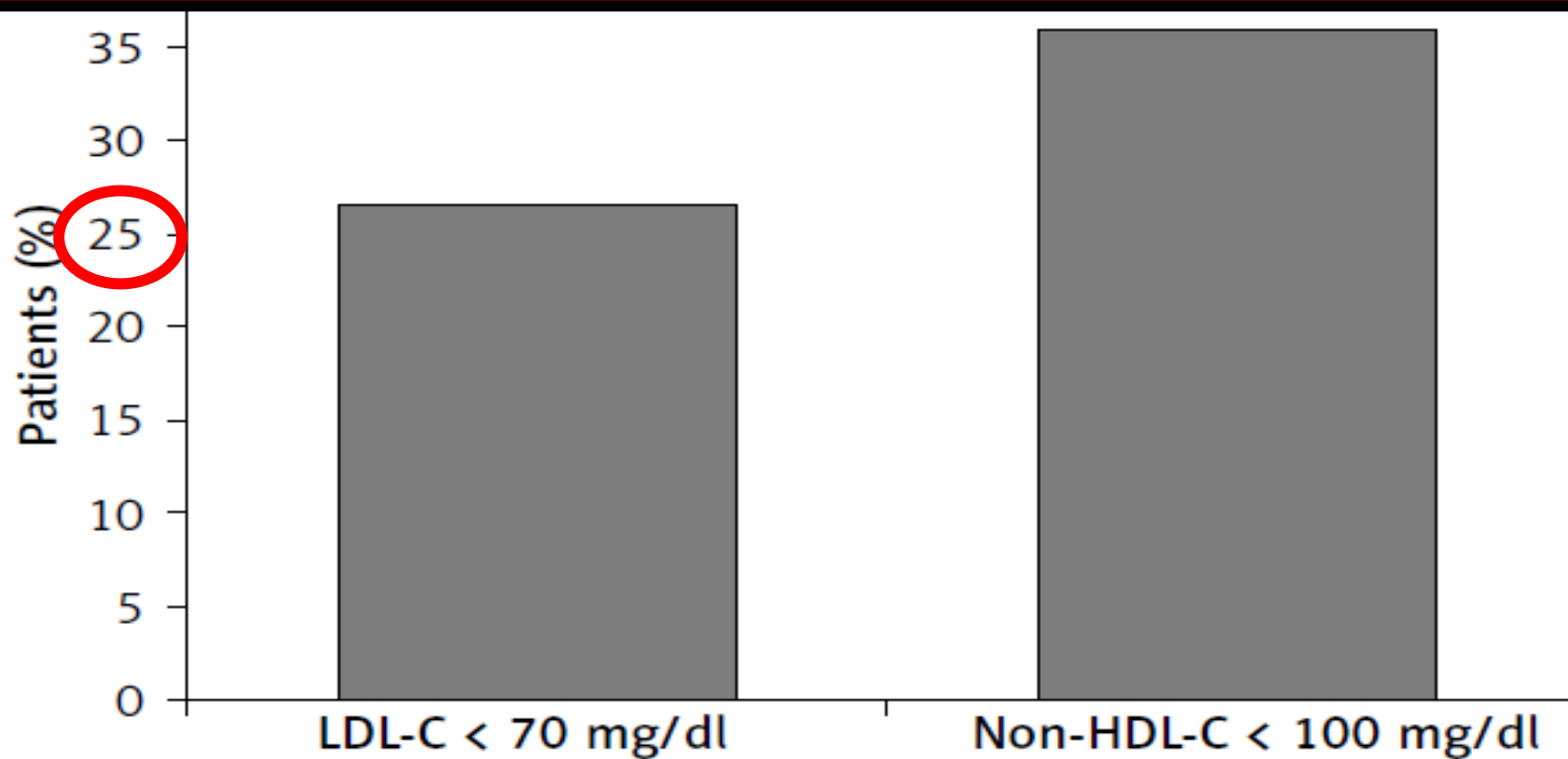
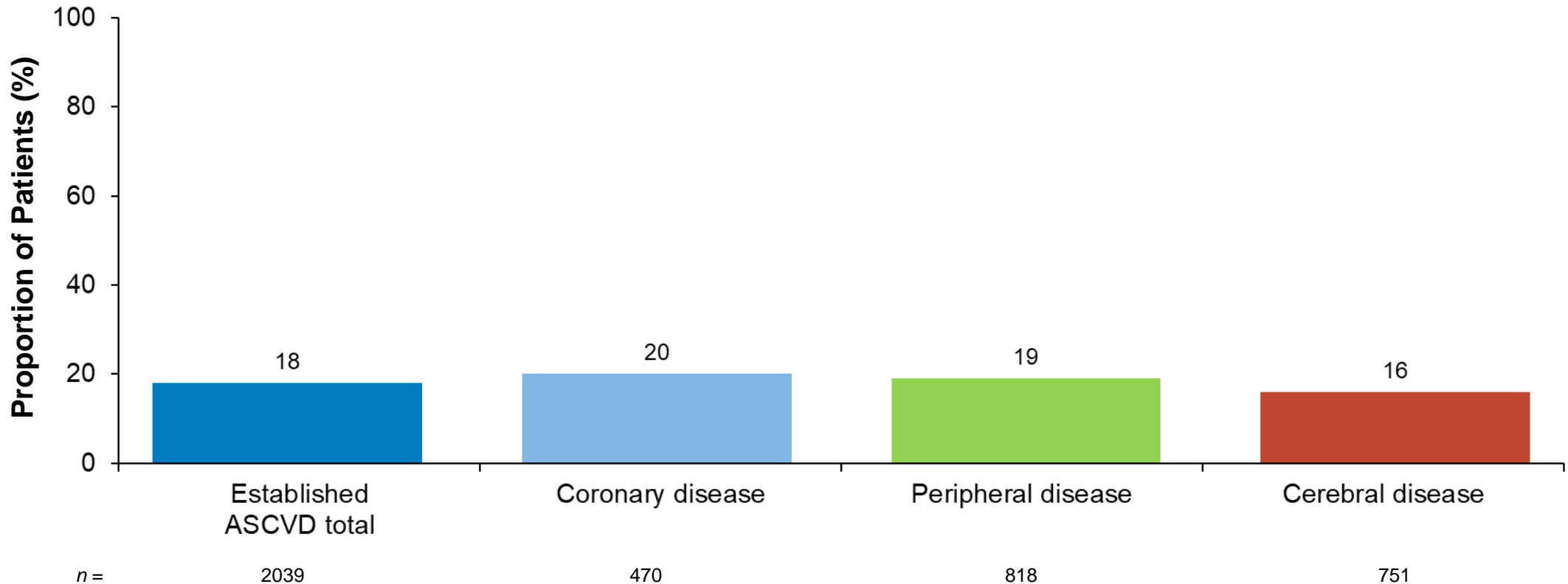


Figure 1. Lipid target value attainment in the CHD cohort

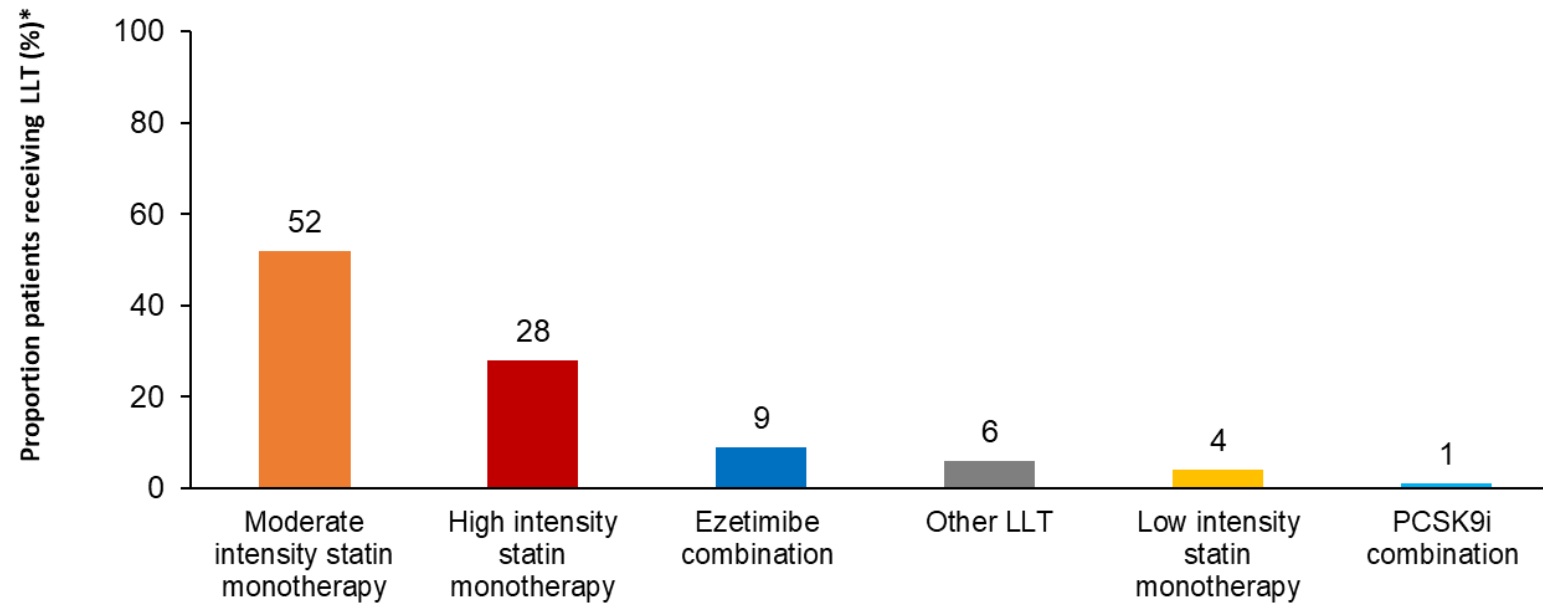


# Among Patients with Established ASCVD, 18% Achieved the 2019 ESC/EAS Very-High Risk Goal of LDL-C < 1.4 mmol/L (< 55 mg/dL)



**In very high risk patients, 2019 goal attainment was approximately half that of 2016 (18% vs 39%).**

# Overall, Moderate-Intensity Statin Monotherapy was the Most Frequently Used LLT Regimen



**Only 28% of patients were receiving high intensity statin monotherapy**  
**Few patients (9%) were receiving ezetimibe combo**  
**Even fewer patients (1%) received PCSK9i combo**

\*Stabilised LLT at time of LDL-C measurement. combo, combination

LDL-C = low-density lipoprotein cholesterol; LLT = lipid lowering therapy; PCSK9i = proprotein convertase subtilisin/kexin type 9 inhibitor.

Ray, KK, et al. *Eur J Prev Cardiol.* 2020. doi:10.1093/eurjpc/zwaa047.

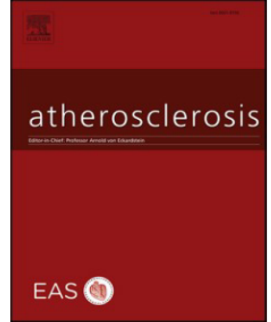


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# Atherosclerosis

journal homepage: [www.elsevier.com/locate/atherosclerosis](http://www.elsevier.com/locate/atherosclerosis)

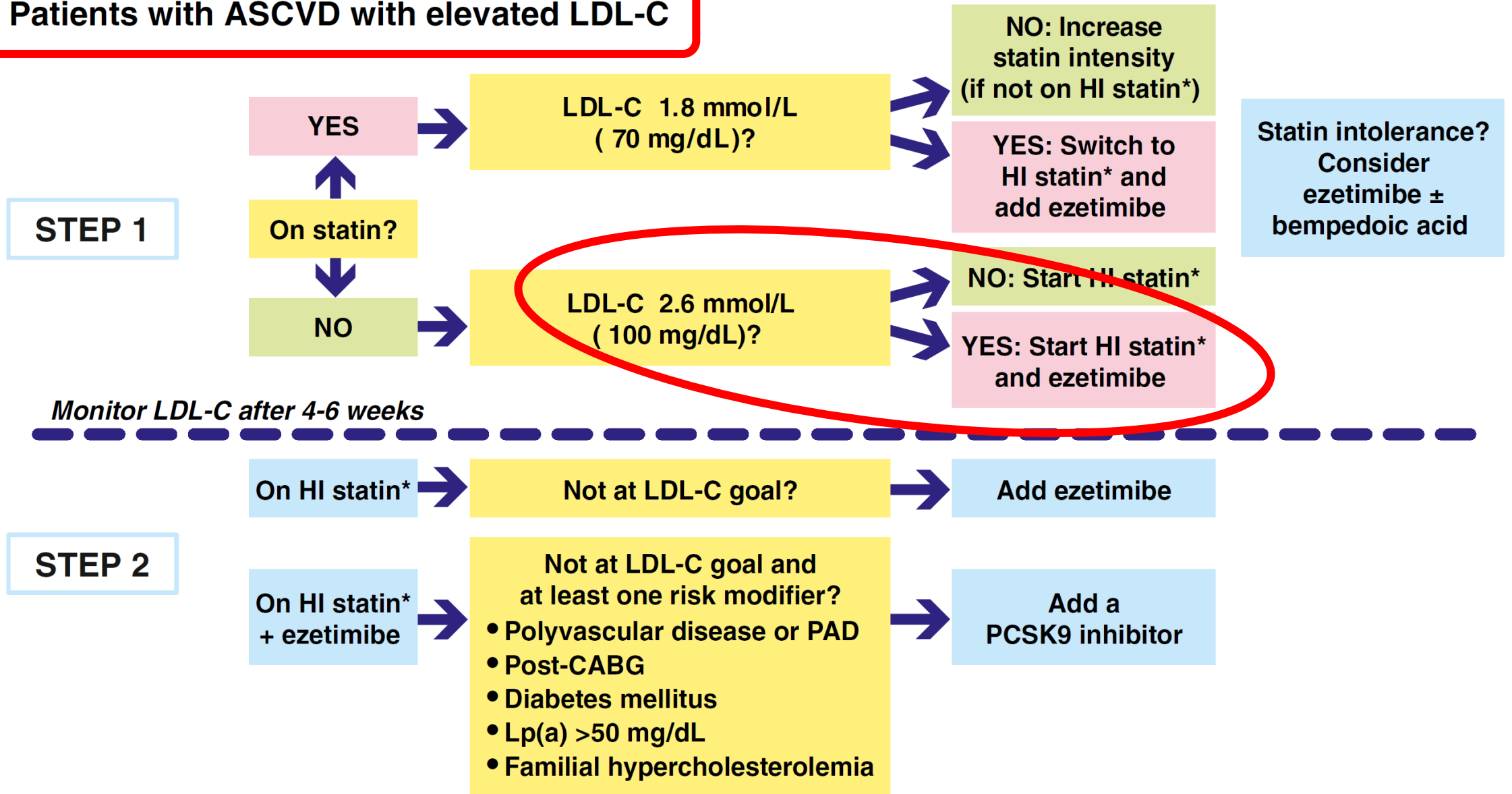


From the EAS

## Practical guidance for combination lipid-modifying therapy in high- and very-high-risk patients: A statement from a European Atherosclerosis Society Task Force

Maurizio Averna<sup>a</sup>, Maciej Banach<sup>b</sup>, Eric Bruckert<sup>c</sup>, Heinz Drexel<sup>d,e,f</sup>, Michel Farnier<sup>g</sup>, Dan Gaita<sup>h</sup>, Paolo Magni<sup>i</sup>, Winfried März<sup>j,k</sup>, Luis Masana<sup>l</sup>, Alberto Mello e Silva<sup>m</sup>, Zeljko Reiner<sup>n</sup>, Emilio Ros<sup>o,p</sup>, Michal Vrablik<sup>q</sup>, Alberto Zambon<sup>r</sup>, Jose L. Zamorano<sup>s</sup>, Jane K. Stock<sup>t</sup>, Lale S. Tokgözoğlu<sup>u</sup>, Alberico L. Catapano<sup>i,\*</sup>

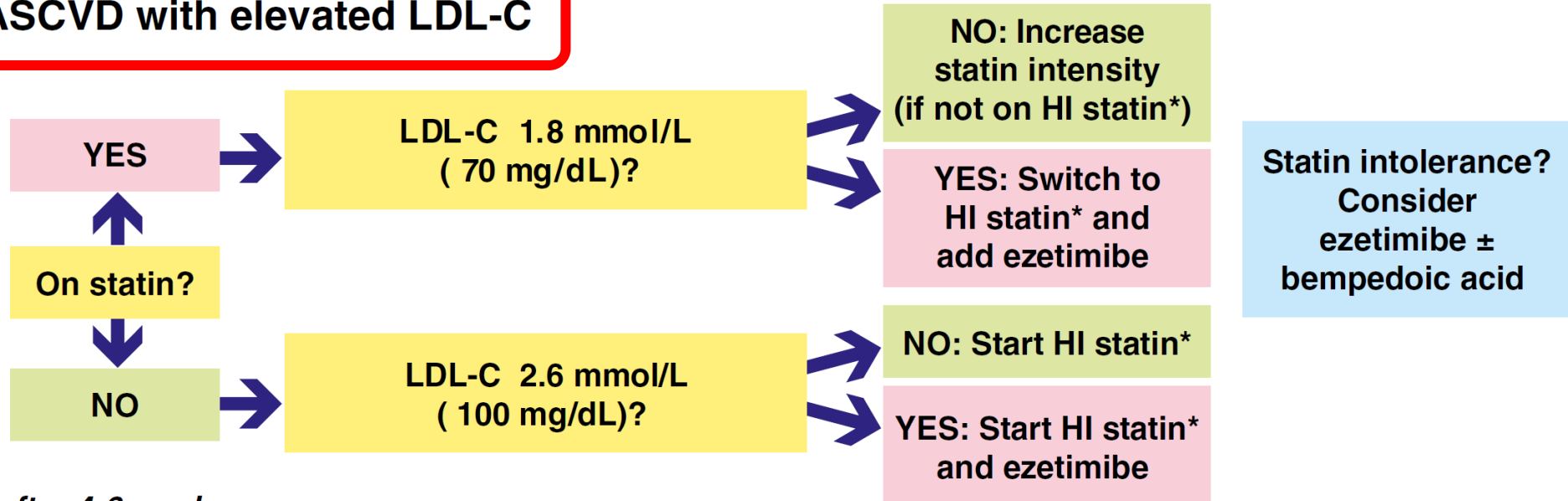
# Patients with ASCVD with elevated LDL-C



\* HI statin: high-intensity statin or maximally tolerated statin therapy

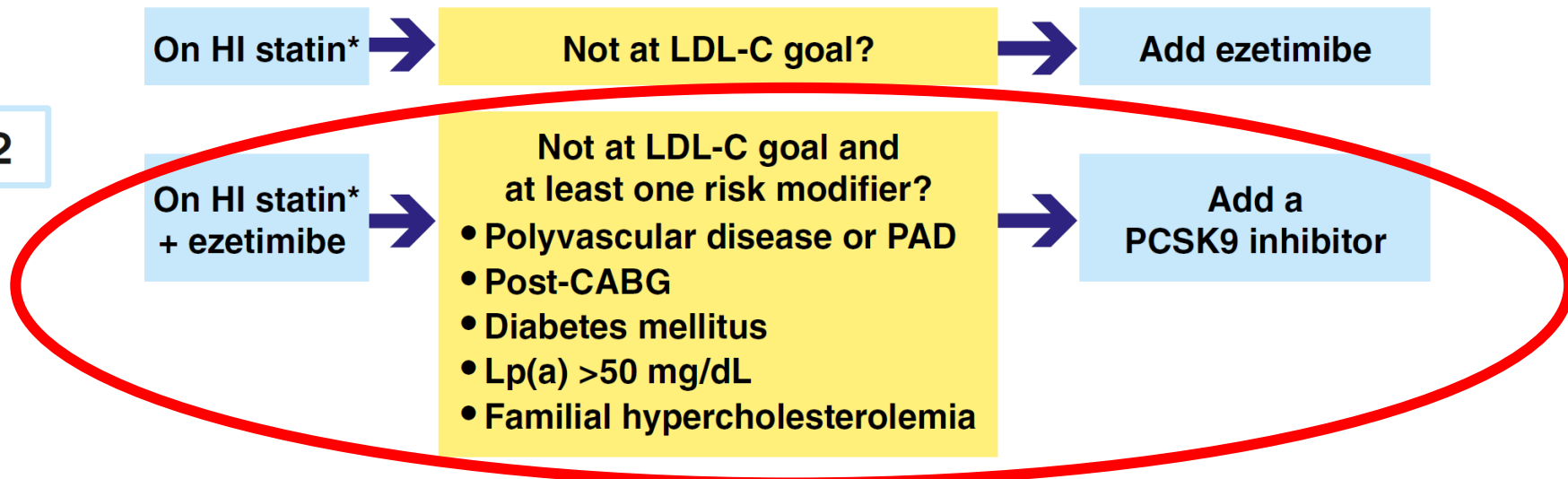
**Patients with ASCVD with elevated LDL-C**

**STEP 1**



*Monitor LDL-C after 4-6 weeks*

**STEP 2**



\* HI statin: high-intensity statin or maximally tolerated statin therapy

# 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

### SCORE2 & SCORE2-OP

10-year risk of (fatal and non-fatal) CV events in populations at moderate CVD risk



Women

Men

Non-smoking

Smoking

Non-smoking

Smoking

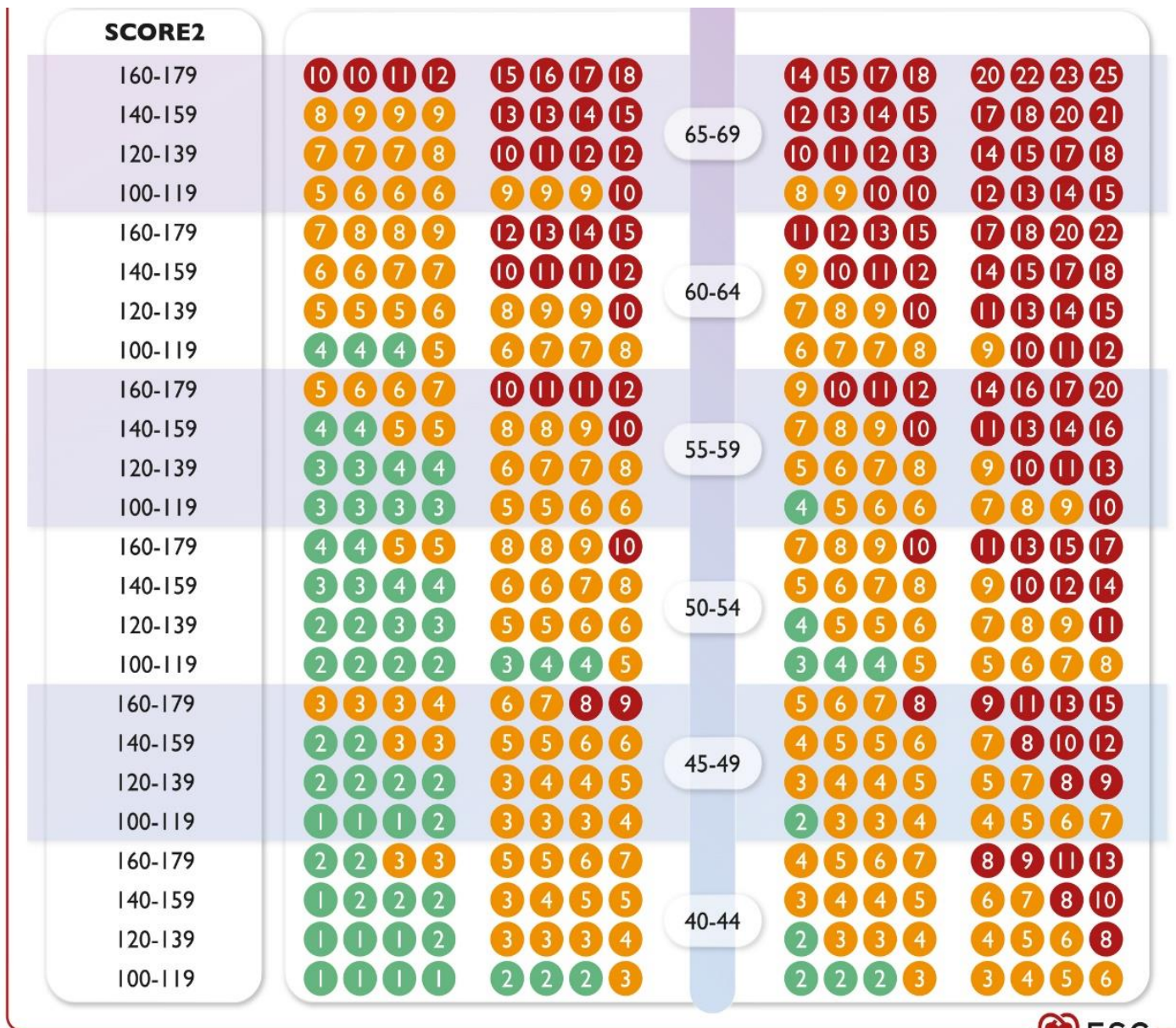
Non-HDL cholesterol

Systolic blood pressure (mmHg)  
SCORE2-OP

3.0-3.9 4.0-4.9 5.0-5.9 6.0-6.9 mmol/L mg/dL 3.0-3.9 4.0-4.9 5.0-5.9 6.0-6.9 150 200 250 150 200 250 150 200 250 150 200 250

Systolic blood pressure (mmHg)	Women Non-smoking				Women Smoking				Age (y)	Men Non-smoking				Men Smoking			
	3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9	3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9		3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9	3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9
160-179	37	39	40	42	41	43	44	46	85-89	37	45	53	62	37	45	53	61
140-159	35	36	38	39	39	40	42	43	80-84	36	43	51	59	35	43	51	59
120-139	32	34	35	37	36	38	39	41	75-79	34	41	49	57	34	41	48	57
100-119	30	32	33	34	34	35	37	38	70-74	32	39	47	55	32	39	46	55
160-179	27	28	30	31	34	35	37	39		30	35	41	47	34	40	46	53
140-159	24	25	27	28	30	32	33	35		27	32	37	43	31	36	42	48
120-139	21	22	24	25	27	28	30	31		25	29	34	40	28	33	38	44
100-119	19	20	21	22	24	25	27	28		22	26	31	36	25	30	35	40
160-179	19	20	21	23	27	29	30	32		24	27	31	35	31	35	39	44
140-159	16	17	18	19	24	25	26	28		21	23	27	30	27	30	34	38
120-139	14	15	15	16	20	21	22	24		17	20	23	26	23	26	29	33
100-119	12	12	13	14	17	18	19	20		15	17	19	22	19	22	25	29
160-179	13	14	15	16	22	23	25	26		19	21	23	25	28	31	34	36
140-159	11	11	12	13	18	19	20	22		15	17	18	20	23	25	28	30
120-139	9	9	10	11	15	16	17	18		12	13	15	16	19	20	22	24
100-119	7	7	8	8	12	13	13	14		10	11	12	13	15	16	18	20

**SCORE2 and SCORE2-OP risk chart for fatal and non-fatal (MI, stroke) ASCVD Moderate CVD Risk (1)**



**SCORE2 and SCORE2-OP  
risk chart for fatal and  
non-fatal (MI, stroke)  
ASCVD  
Moderate CVD Risk (2)**



## New calculators based on European populations

### Apparently healthy < 70 years

No previous cardiovascular disease or type 2 diabetes mellitus



SCORE2

### Apparently healthy ≥ 70 years

Elderly without previous cardiovascular disease or type 2 diabetes mellitus



SCORE2-OP


# Select a calculator

I would like assistance with selecting a calculator

Patient group

10-years cardiovascular risk

Lifetime risk & treatment effect

Previous cardiovascular disease 



SMART risk score



SMART-REACH model

Type 2 Diabetes Mellitus



ADVANCE risk score



DIAL model

Apparently healthy

No previous cardiovascular disease or type 2 diabetes mellitus



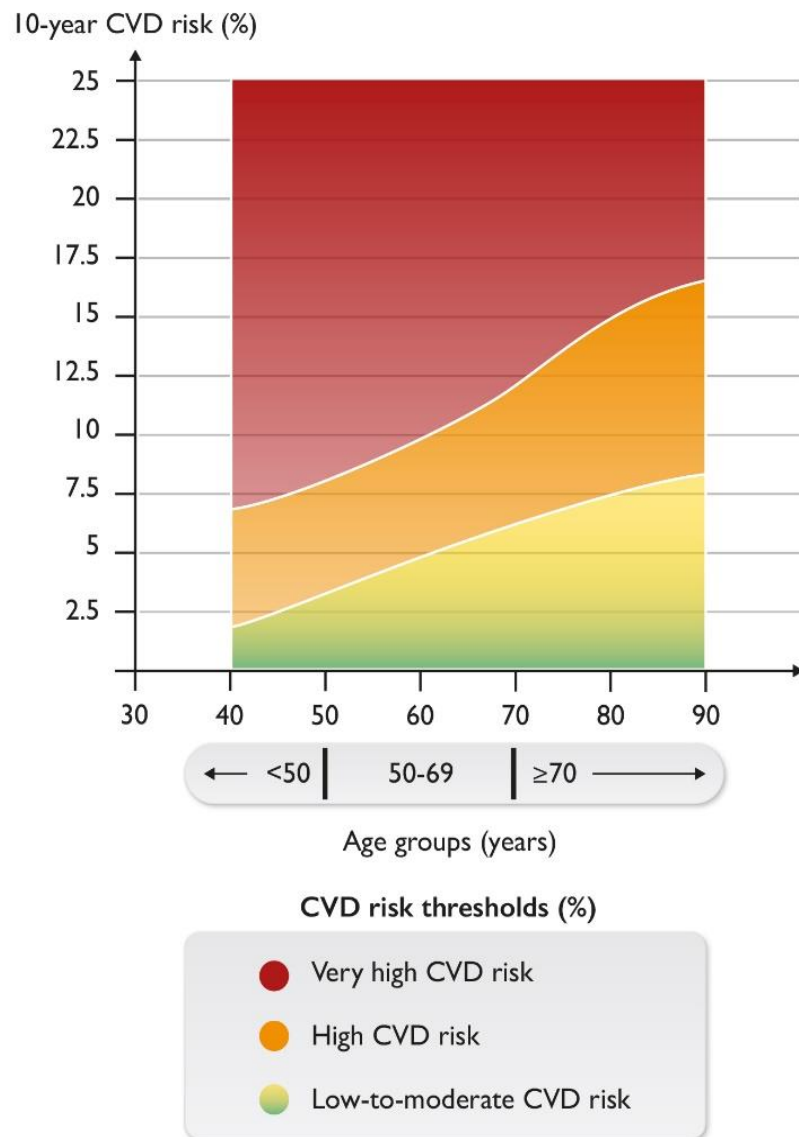
SCORE or ASCVD



LIFE-CVD model

## Cardiovascular disease risk categories based on SCORE2 and SCORE2-OP in apparently healthy people according to age

	<50 years	50-69 years	≥70 years <sup>a</sup>
<b>Low-to-moderate CVD risk:</b> risk factor treatment generally not recommended	<2.5%	<5%	<7.5%
<b>High CVD risk:</b> risk factor treatment should be considered	2.5 to <7.5%	5 to <10%	7.5 to <15%
<b>Very high CVD risk:</b> risk factor treatment generally recommended <sup>a</sup>	≥7.5%	≥10%	≥15%



**Schematic representation of increasing 10-year CVD risk thresholds across age groups**

Apparently healthy persons<sup>a</sup>

**STEP 1**

Stop smoking, lifestyle recommendations and SBP <160 mmHg (Class I)

Age < 50 years

Age 50 – 69 years

Age ≥ 70 years<sup>b</sup>

Estimate 10-year CVD risk (SCORE2)

Estimate 10-year CVD risk (SCORE2)

Estimate 10-year CVD risk (SCORE2-OP)

<2.5%    2.5 to <7.5%    ≥7.5%

<5%    5 to <10%    ≥10%

<7.5%    7.5 to <15%    ≥15%

Consider risk modifiers, lifetime CVD risk and treatment benefit<sup>b</sup>, patient preferences

Consider risk modifiers, lifetime CVD risk and treatment benefit<sup>b</sup>, patient preferences

Consider risk modifiers, lifetime treatment benefit<sup>b</sup>, comorbidities, frailty, polypharmacy, patient preferences

No additional prevention goals

No additional prevention goals

No additional prevention goals

No additional prevention goals

SBP <140 to 130 mmHg if tolerated (Class I)

AND

LDL-C <2.6 mmol/L (<100 mg/dL) (Class IIa)

SBP <140 to 130 mmHg if tolerated (Class I)

AND

LDL-C <2.6 mmol/L (<100 mg/dL) (Class IIb)

**STEP 2**

Intensified treatment based on:

- 10-year CVD risk (SCORE2)
- Lifetime CVD risk and treatment benefit<sup>b</sup>
- Comorbidities, frailty
- Patient preferences

SBP <130 mmHg if tolerated (Class I)

AND

LDL-C (Class IIa)  
 High risk <1.8 mmol/L (<70 mg/dL)    Very high risk <1.4 mmol/L (<55 mg/dL)

**STEP 2**

For specific risk factor management in patients ≥70 years, please see Section 4

**Primary Prevention:  
Assess ASCVD Risk in Each Age Group  
Emphasize Adherence to Healthy Lifestyle**

**Age 0-19 y**  
Lifestyle to prevent or reduce ASCVD risk  
Diagnosis of Familial Hypercholesterolemia → statin

**Age 20-39 y**  
Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk  
Consider statin if family history premature ASCVD and LDL-C  $\geq 160$  mg/dL ( $\geq 4.1$  mmol/L)

**Age 40-75 y and LDL-C  $\geq 70$ - $<190$  mg/dL ( $\geq 1.8$ - $<4.9$  mmol/L) without diabetes mellitus**  
10-year ASCVD risk percent begins risk discussion

LDL-C  $\geq 190$  mg/dL ( $\geq 4.9$  mmol/L)  
No risk assessment; High-intensity statin (Class I)

Diabetes mellitus and age 40-75 y  
Moderate-intensity statin (Class I)

Diabetes mellitus and age 40-75 y  
Risk assessment to consider high-intensity statin (Class IIa)

Age  $>75$  y  
Clinical assessment, Risk discussion

**ASCVD Risk Enhancers:**

- Family history of premature ASCVD
- Persistently elevated LDL-C  $\geq 160$  mg/dL ( $\geq 4.1$  mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

**Lipid/Biomarkers:**

- Persistently elevated triglycerides ( $\geq 175$  mg/dL, ( $\geq 2.0$  mmol/L))

**In selected individuals if measured:**

- hs-CRP  $\geq 2.0$  mg/L
- Lp(a) levels  $>50$  mg/dL or  $>125$  nmol/L
- apoB  $\geq 130$  mg/dL
- Ankle-brachial index (ABI)  $<0.9$



**Risk discussion:**  
Emphasize lifestyle to reduce risk factors (Class I)

**Risk discussion:**  
If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)

**Risk discussion:**  
If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)

**Risk discussion:**  
Initiate statin to reduce LDL-C  $\geq 50\%$  (Class I)

**If risk decision is uncertain:**  
Consider measuring CAC in selected adults:  
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)  
CAC = 1-99 favors statin (especially after age 55)  
CAC = 100+ and/or  $\geq 75$ th percentile, initiate statin therapy

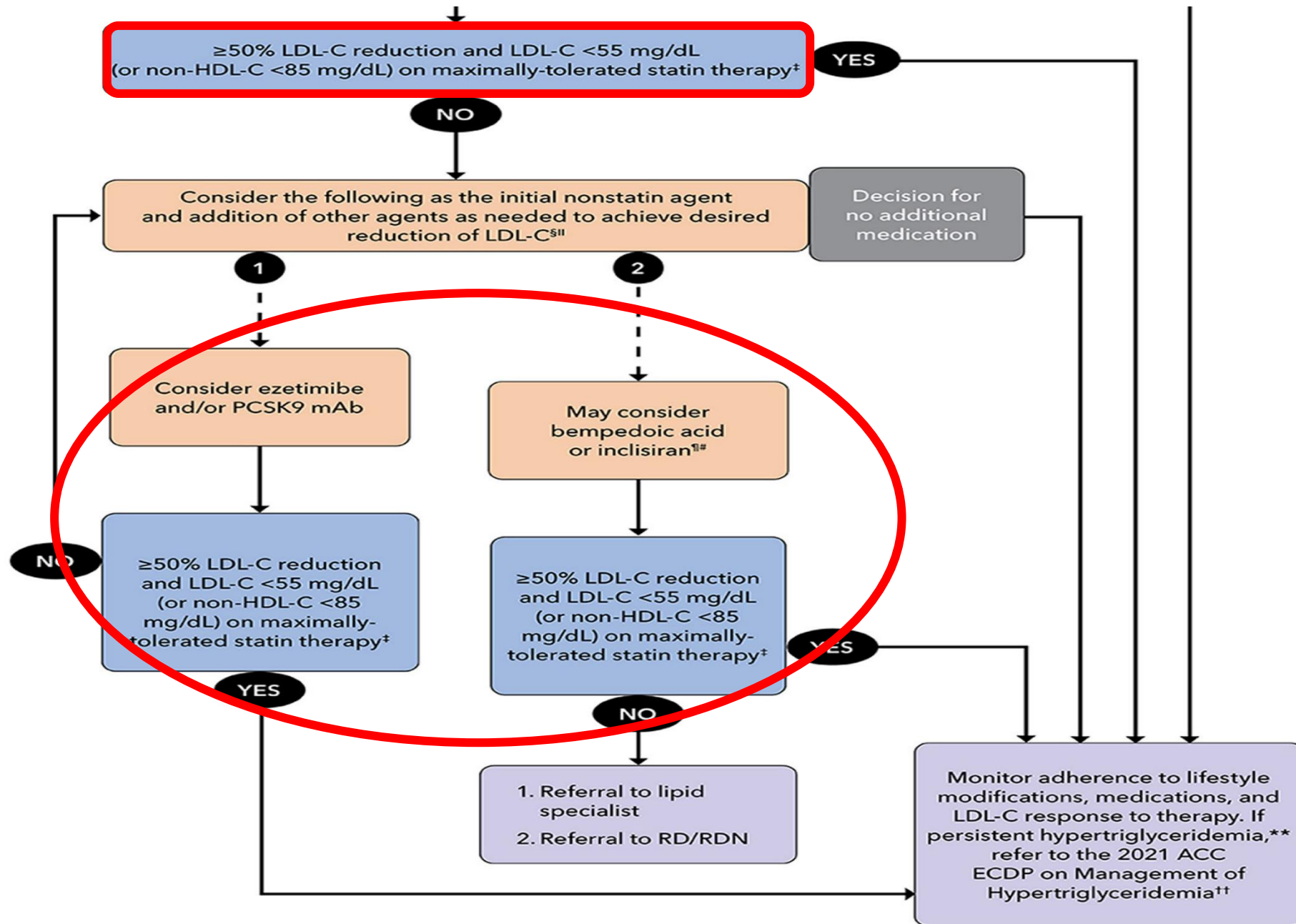
**EXPERT CONSENSUS DECISION PATHWAY**

# **2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk**

A Report of the American College of Cardiology Solution Set Oversight Committee

Endorsed by the National Lipid Association

**FIGURE 2A** Adults With Clinical ASCVD at Very High Risk on Statin Therapy for Secondary Prevention







Hellenic Atherosclerosis Society

• GUIDELINES •

# Hellenic Atherosclerosis Society Guidelines for the Diagnosis and Treatment of Dyslipidemias - 2023

Katsiki N\*, Filippatos TD\*, Vlachopoulos C, Panagiotakos D, Milionis H, Tselepis A,  
Garoufi A, Rallidis L, Richter D, Nomikos T, Kolovou G, Kypreos K, Chrysohoou C,  
Tziomalos K, Skoumas I, Koutagiar I, Attilakos A, Papagianni M, Boutari C,  
Kotsis V, Pitsavos C, Elisaf M, Tsioufis K, Liberopoulos E

*\*Equal contribution*

# LDL-C TARGETS 2023

## CVD RISK

### VERY HIGH RISK

- ESTABLISHED ASCVD
- DIABETES WITH TARGET ORGAN DAMAGE or  $\geq 3$  MAJOR RISK FACTORS
- FAMILIAL HYPERCHOLESTEROLEMIA PLUS  $\geq 1$  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  $\geq 10$  YEARS PLUS  $\geq 1$  MAJOR RISK FACTOR
- CKD 3
- AUTOIMMUNE RHEUMATIC DISEASE/HIV INFECTION
- HELLENIC SCORE II  $\geq 5$ -  
< 10%

↓ LDL-C < 70 mg/dL  
PLUS  
LDL-C ~ 50%

### MODERATE RISK

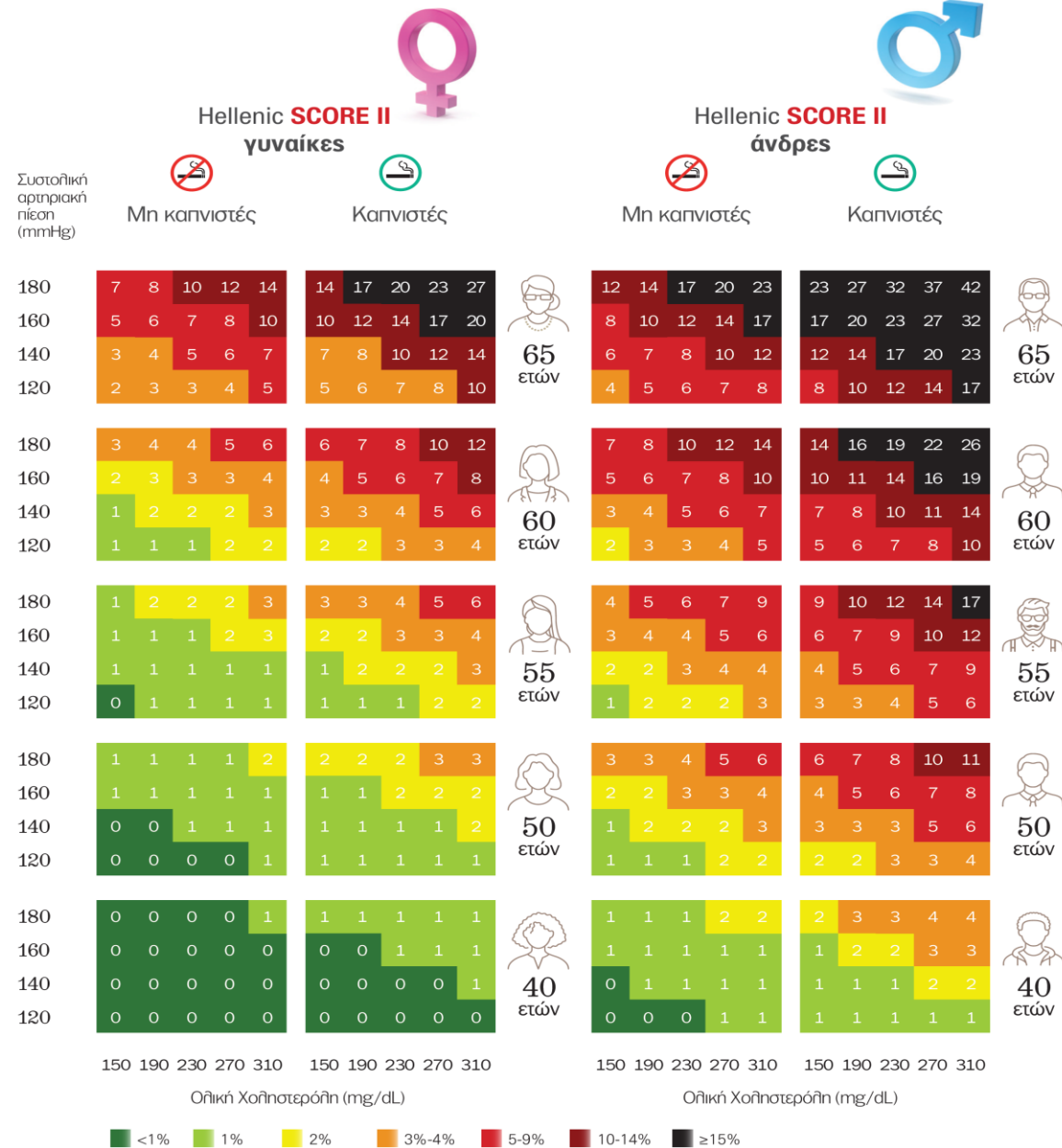
- DIABETES < 10 YEARS IN PATIENTS < 50 YEARS
- HELLENIC SCORE II  $\geq 1$ -  
< 5%

LDL-C < 100  
mg/dL

### LOW RISK

HELLENIC SCORE II  
< 1%

LDL-C < 116  
mg/dL



**TABLE 1.** Parameters that increase ASCVD risk and should be considered as risk modifiers in individuals at low or moderate risk.

---

Social deprivation

Obesity, especially central obesity

Physical inactivity

Family history of premature ASCVD (men: <55 years; women: <60 years)

Major psychiatric disorders

Atrial fibrillation

Left ventricular hypertrophy

Obstructive sleep apnoea syndrome

Non-alcoholic fatty liver disease

History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia

High-risk race/ethnicities (e.g., South Asian ancestry)

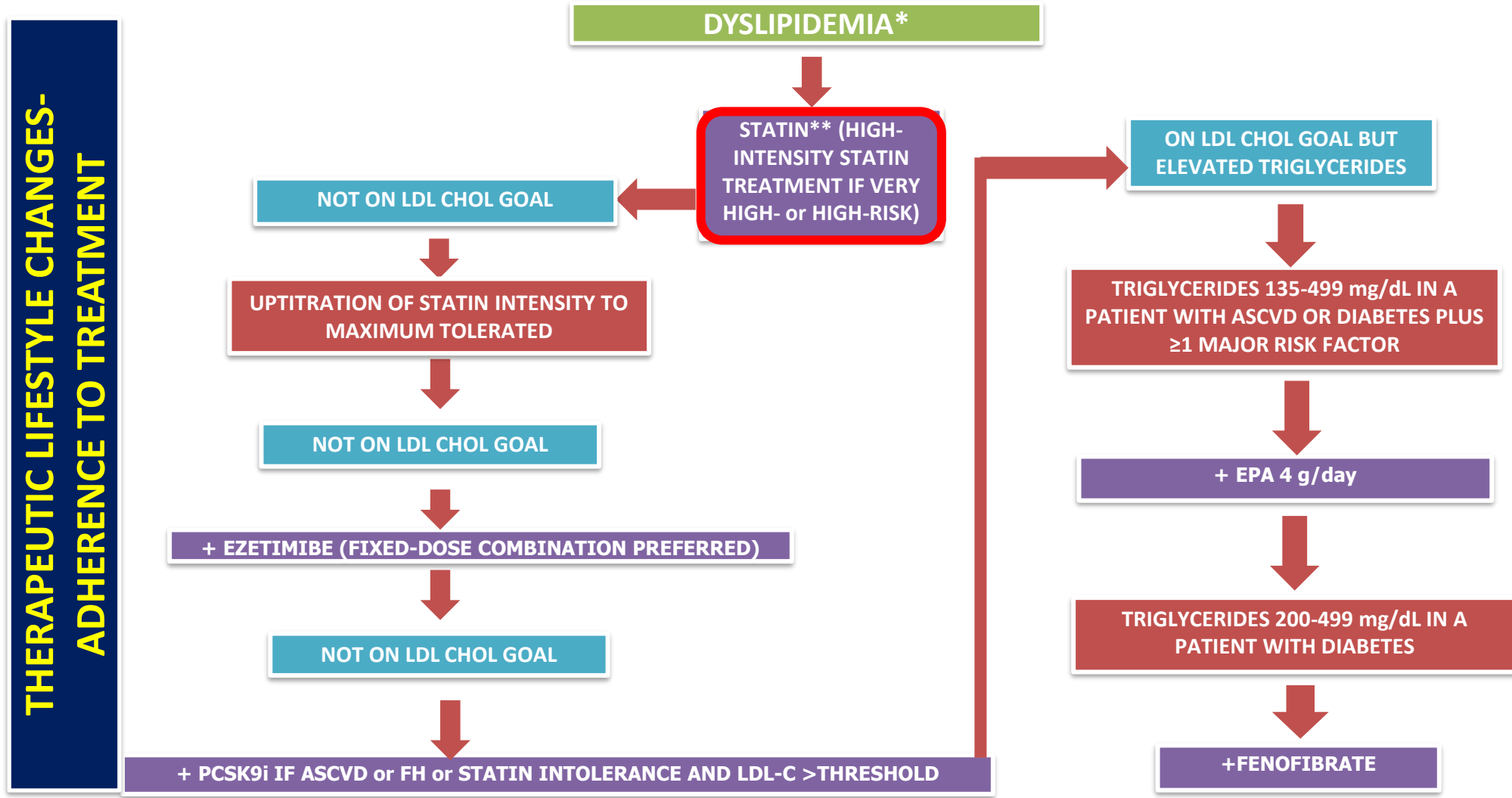
Lipid-related markers

- Persistently elevated, primary hypertriglyceridemia ( $\geq 175$  mg/dL)
- non-HDL-C  $> 190$  mg/dL
- Elevated Lp(a)  $\geq 50$  mg/dL or  $\geq 125$  nmol/L
- Elevated apoB  $\geq 130$  mg/dL (if measured)

Other biomarkers/imaging (if measured or done):

- Elevated high-sensitivity C-reactive protein ( $\geq 2.0$  mg/L)
- ABI  $< 0.9$
- Arterial (carotid and/or femoral) plaque burden on ultrasonography
- CAC score assessment with CT

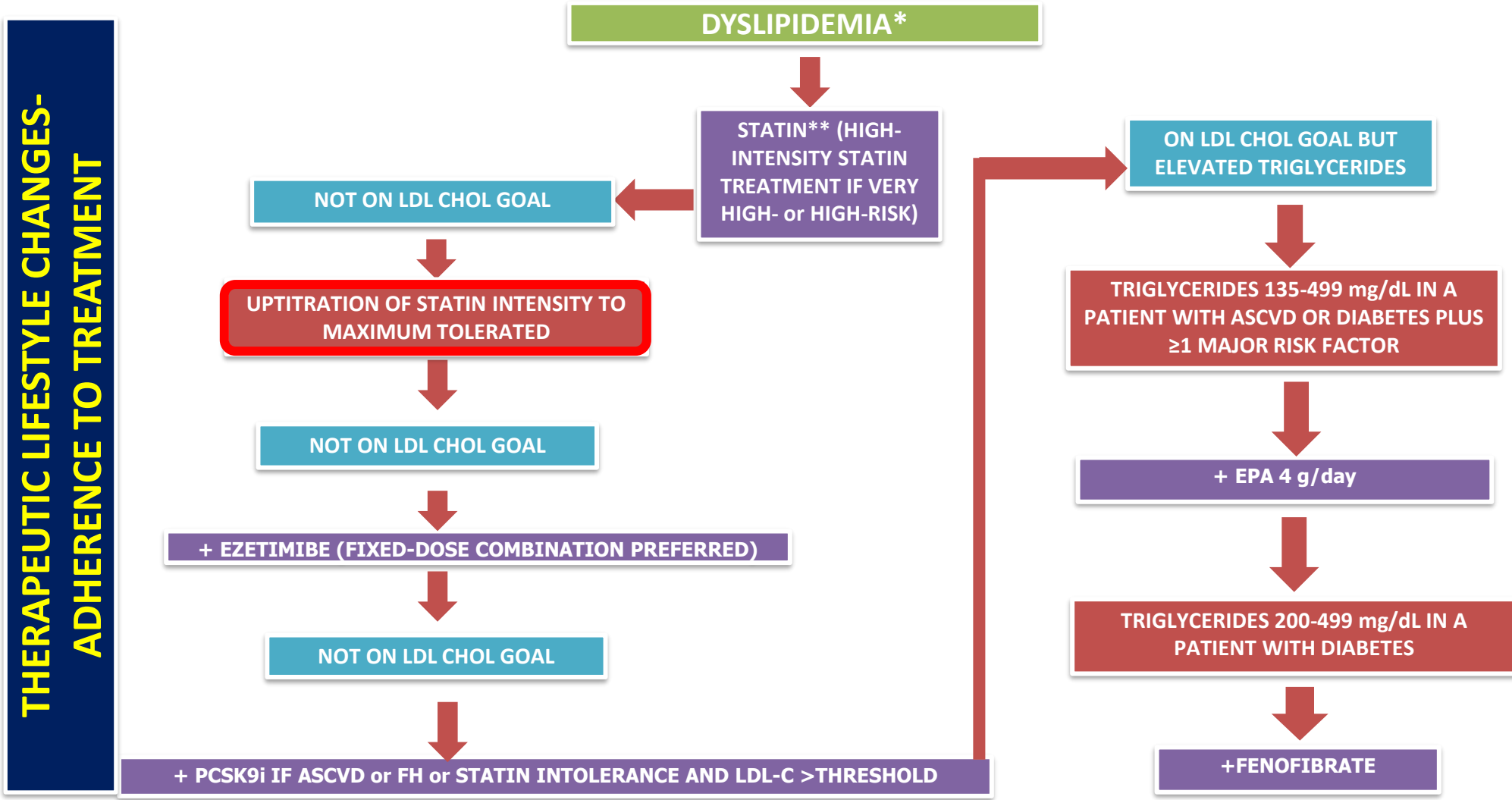
# ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023



\*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)

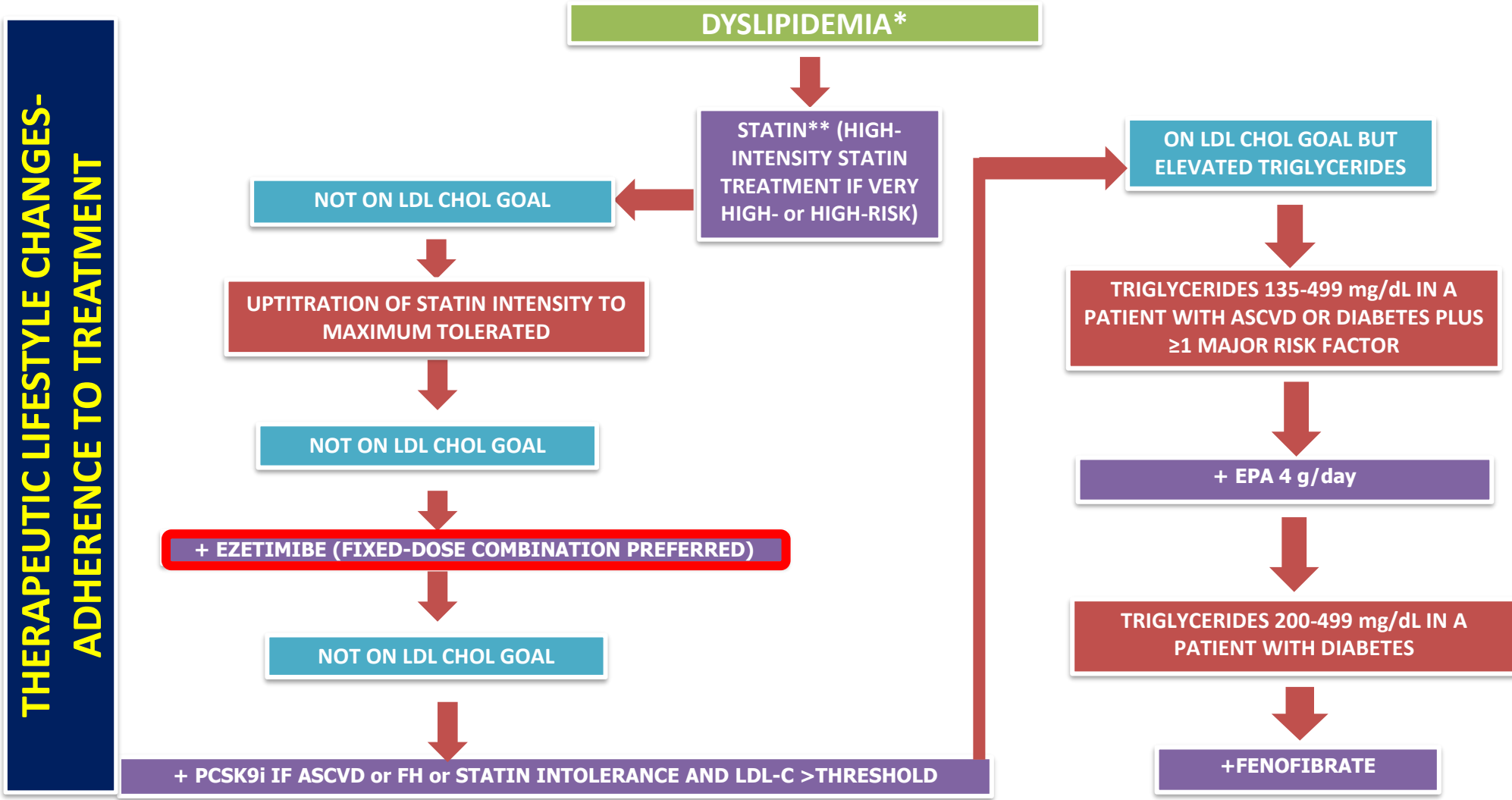
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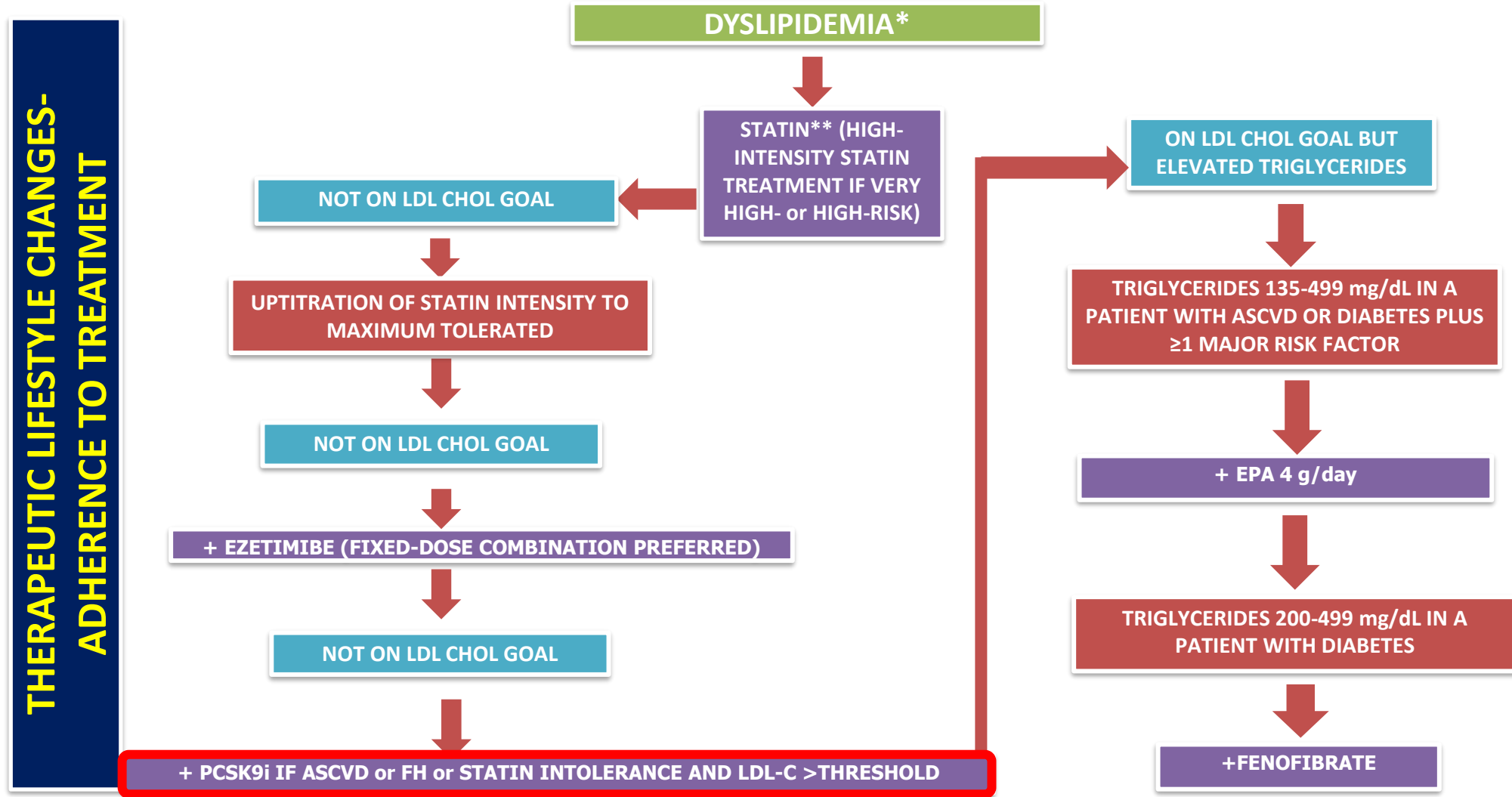


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## **ELIGIBLE PATIENTS FOR PCSK9 INHIBITORS**

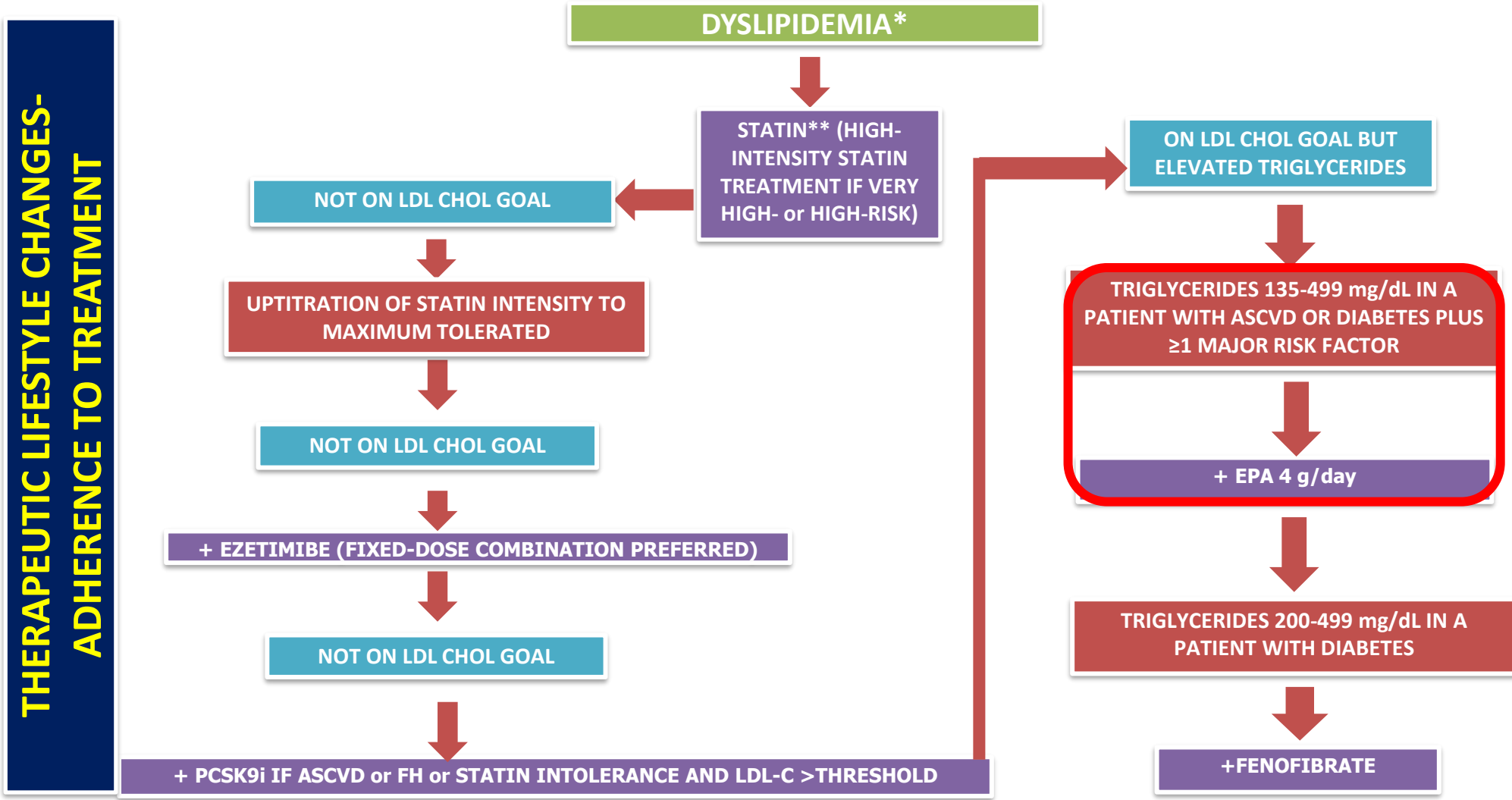
**1. ASCVD PLUS FH OR RECURRENT/PROGRESSIVE DISEASE DURING THE LAST 2 YEARS OR PREMATURE ASCVD (MEN <45/WOMEN <55 YEARS ) WITH LDL-C  $\geq$ 70 mg/dL**

**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**

# ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023

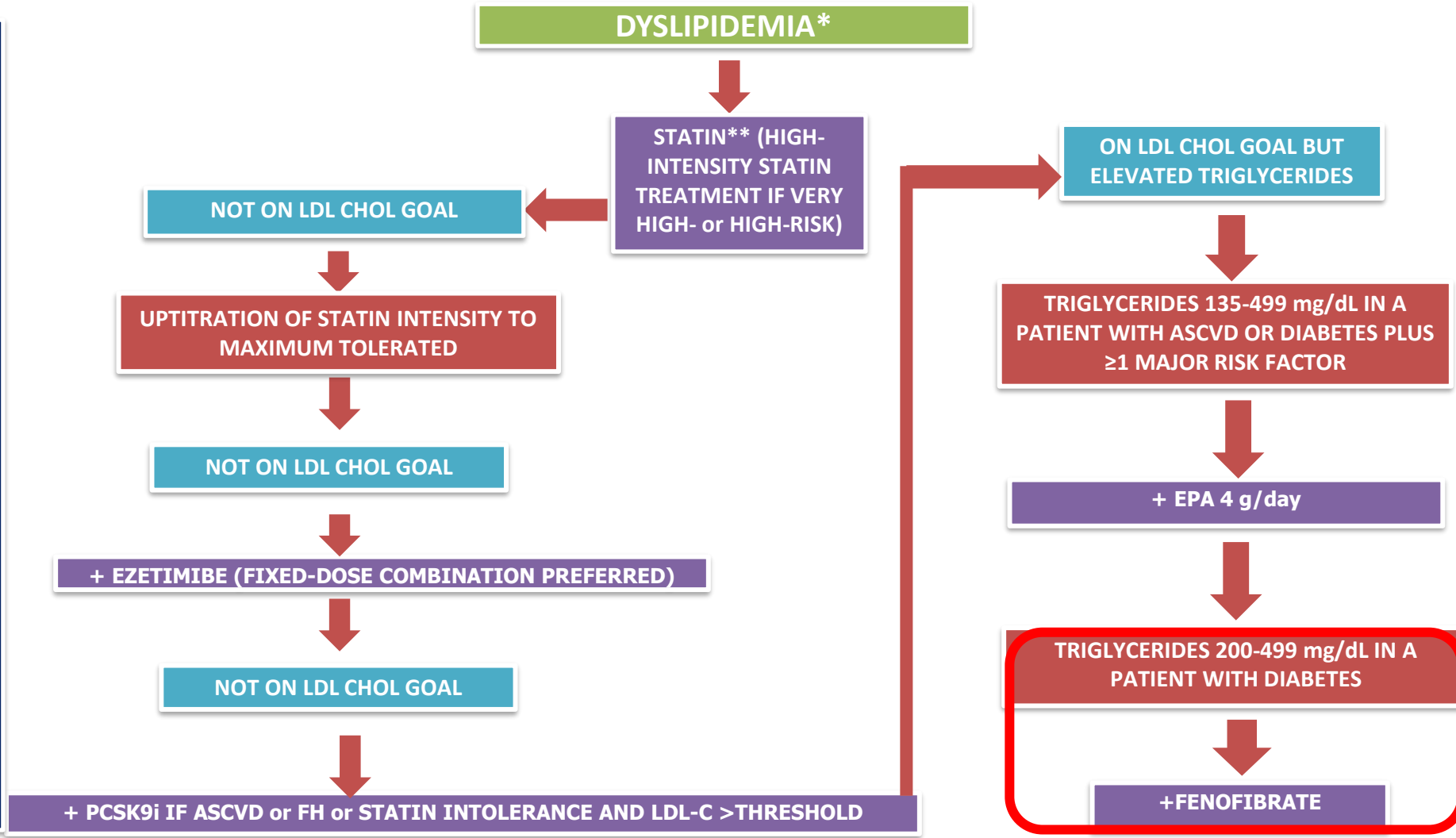


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# ALGORITHM FOR THE THERAPEUTIC MANAGEMENT OF PATIENTS WITH DYSLIPIDEMIA 2023

**THERAPEUTIC LIFESTYLE CHANGES-  
ADHERENCE TO TREATMENT**



**\*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)**

**TABLE 56.** Laboratory follow-up in patients on hypolipidemic drug treatment.

**At diagnosis:** TC, TGs, HDL-C, LDL-C, Lp(a), glucose, eGFR, AST, ALT, CK, TSH



**8 ± 4 weeks following treatment initiation or intensification:** TC, TGs, HDL-C, LDL-C, glucose, eGFR, ALT, CK (if myalgias are reported)



**Every 12 months when on treatment target:** TC, TGs, HDL-C, LDL-C, glucose, eGFR, ALT (if evidence of liver injury), CK (if myalgias are reported)

LDL-C: low-density lipoprotein cholesterol

LIPID PARAMETER	RESULT	TARGET VALUES*
TOTAL CHOLESTEROL (mg/dL)		<170 (DEPENDING ON LDL-C TARGET)
LDL CHOLESTEROL (mg/dL)**		<55 FOR VERY HIGH-RISK PATIENTS <70 FOR HIGH-RISK PATIENTS <100 FOR MODERATE RISK PATIENTS <116 FOR LOW-RISK PATIENTS
TRIGLYCERIDES (mg/dL)		<150
HDL CHOLESTEROL (mg/dL)		>40 FOR MEN >50 FOR WOMEN
NON-HDL CHOLESTEROL (mg/dL)		<85 FOR VERY HIGH-RISK PATIENTS <100 FOR HIGH-RISK PATIENTS <130 FOR MODERATE RISK PATIENTS
ApoB (mg/dL)		<65 FOR VERY HIGH-RISK PATIENTS <80 FOR HIGH-RISK PATIENTS <100 FOR MODERATE RISK PATIENTS
Lp(a) (mg/dL)***		<30

\*TARGET VALUE IS DEFINED BY THE PHYCISIAN BASED ON CVD RISK

\*\*IF LDL-C>190 mg/dL, FH SHOULD BE EXCLUDED

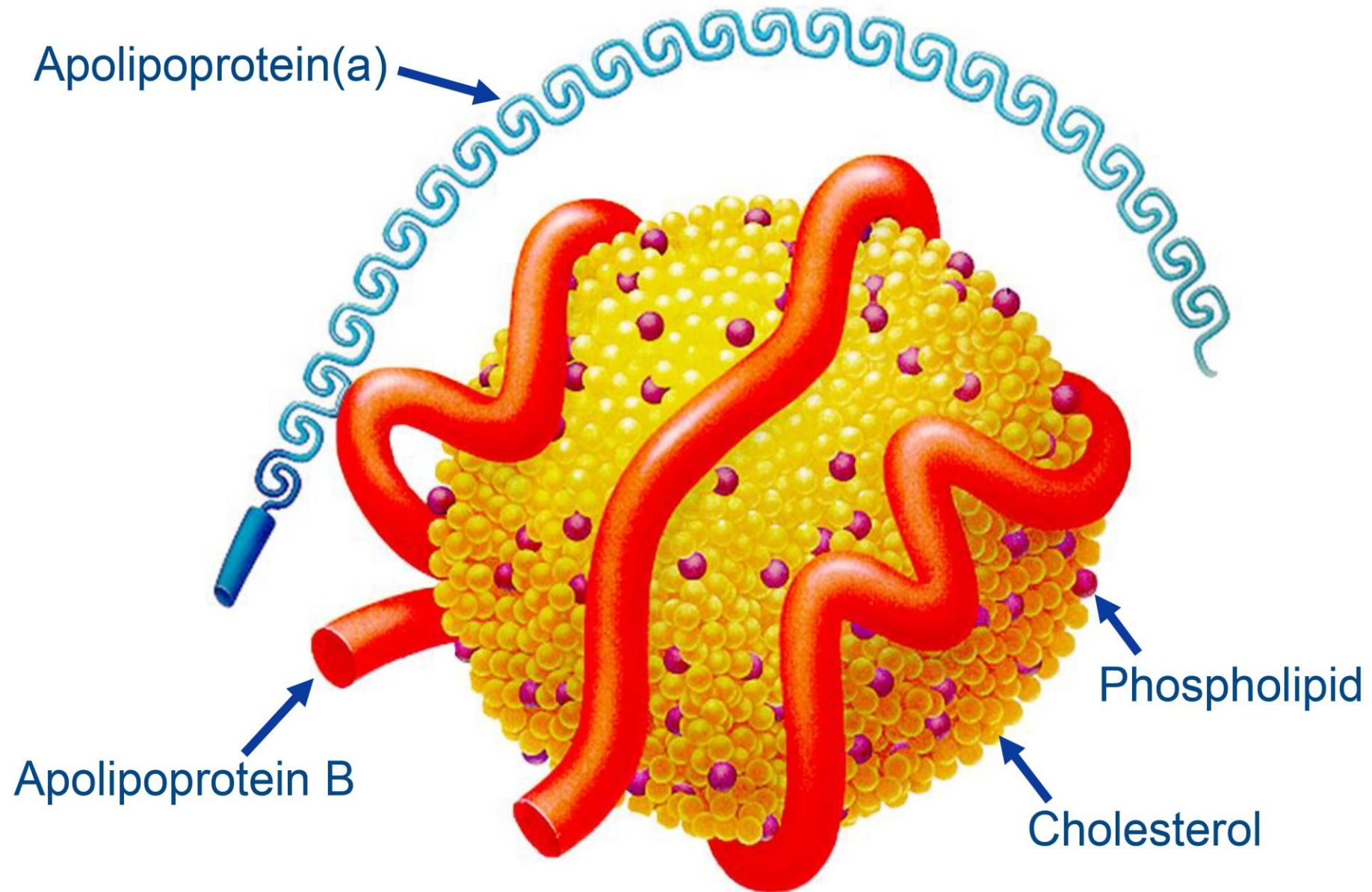
\*\*Lp(a) >180 mg/dL IS ASSOCIATED WITH VERY HIGH CVD RISK

# LIPID VALUES IN CHILDREN AND ADOLESCENTS

	ACCEPTABLE, mg/dL	BORDELINE, mg/dL	ABNORMAL, mg/dL
<b>TOTAL CHOLESTEROL</b>	<170	170-199	≥200
<b>TRIGLYCERIDES (0-9 years)</b>	<75	75-99	≥100
<b>TRIGLYCERIDES (10-19 years)</b>	<90	90-129	≥130
<b>HDL CHOLESTEROL</b>	>45	40-45	<40
<b>LDL CHOLESTEROL*</b>	<110	110-129	≥130
<b>Non-HDL CHOLESTEROL</b>	<120	120-144	≥145

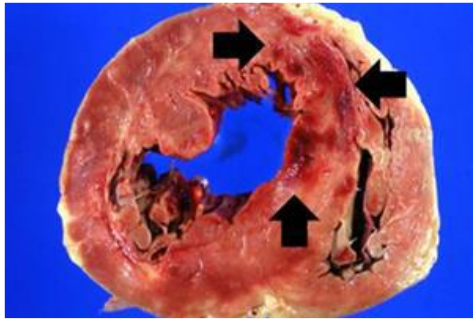
**\*IF LDL CHOLESTEROL >160 mg/dL, FH SHOULD BE EXCLUDED**

# Lp(a) - the mysterious brother of LDL

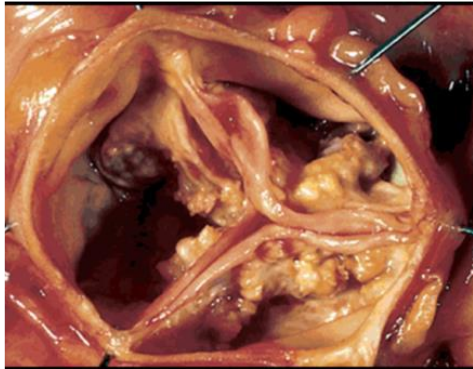




# Why worry?



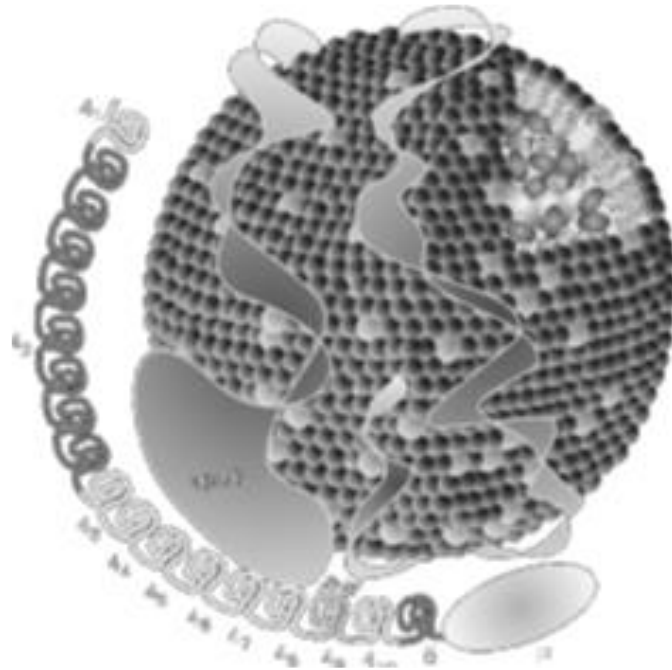
**MI**



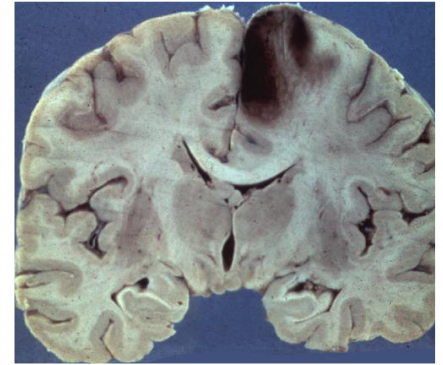
**AS**



**PAD**



**Stroke**

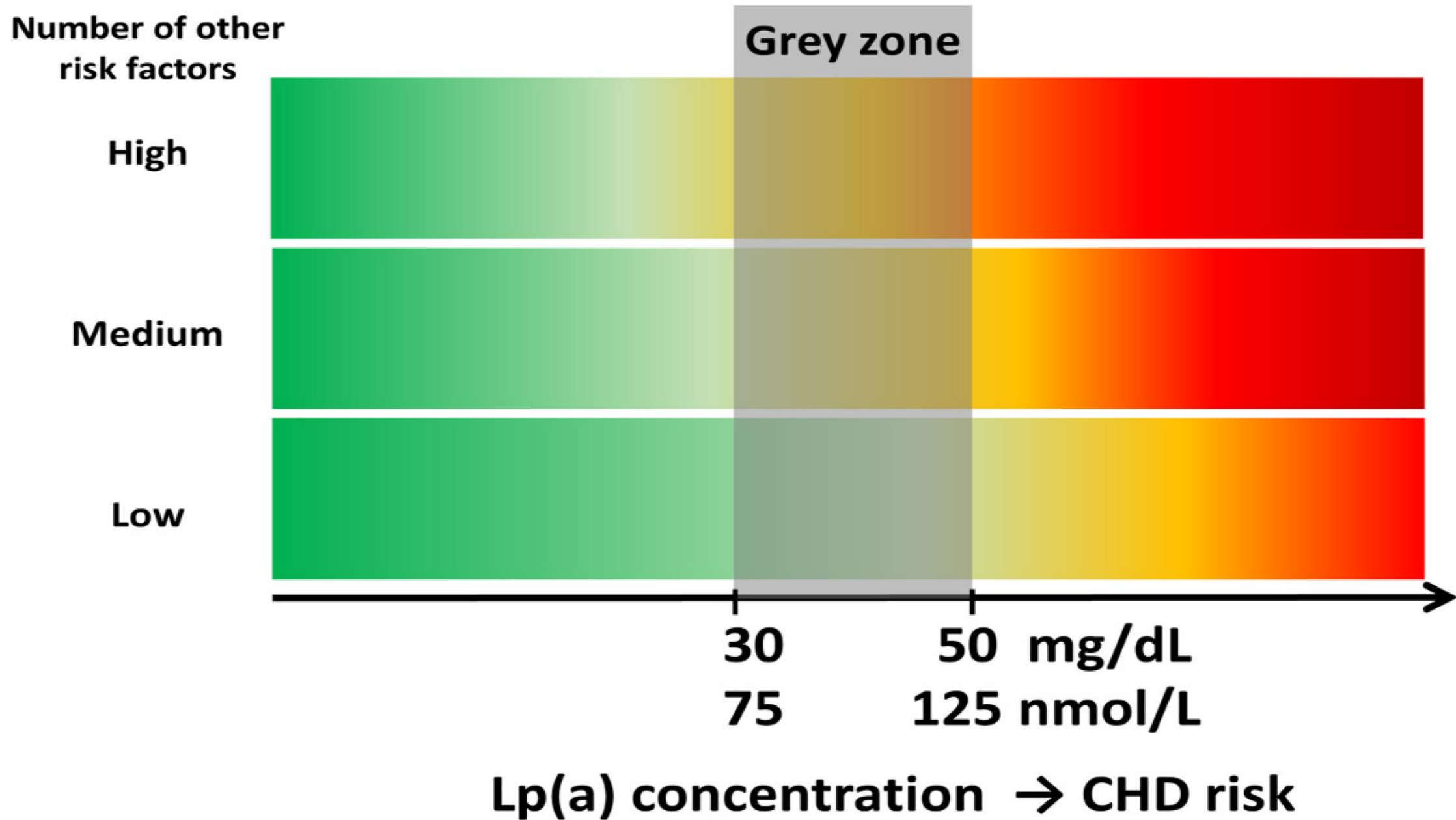


**HF**

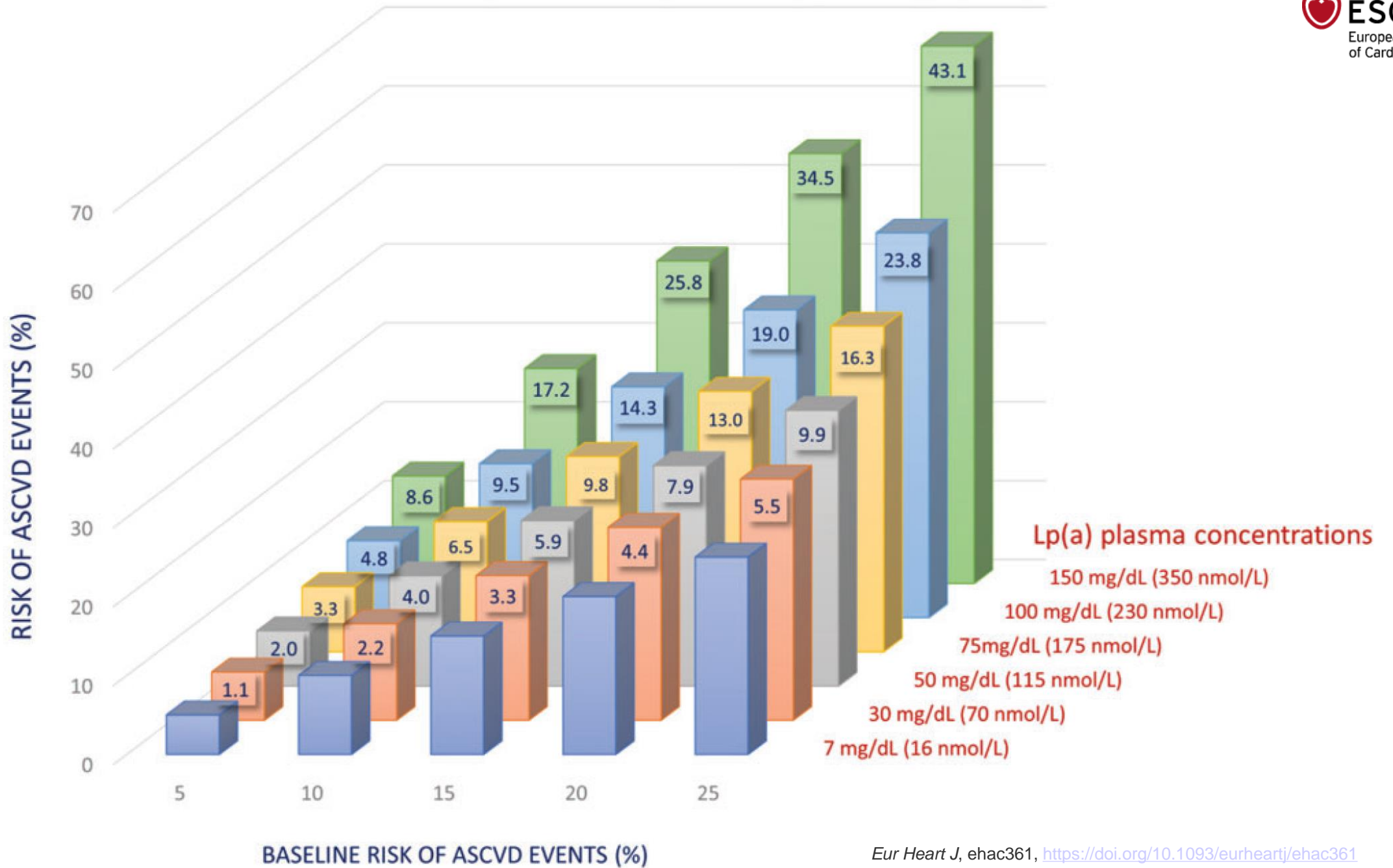


**Death**





A



# New dyslipidemia guidelines

**ESC/EAS GUIDELINES**

**2019**



**Lp(a) measurement should be considered at least once in each adult person's lifetime**

Eur.Heart J. 41:111-188, 2020



**Canadian Cardiovascular Society**

*Leadership. Knowledge. Community.*

**2021**

**We recommend measuring Lp(a) level once in a person's lifetime as a part of the initial lipid screening.**

Can.J.Cardiol (in press)

doi: 10.1016/j.cjca.2021.03.016

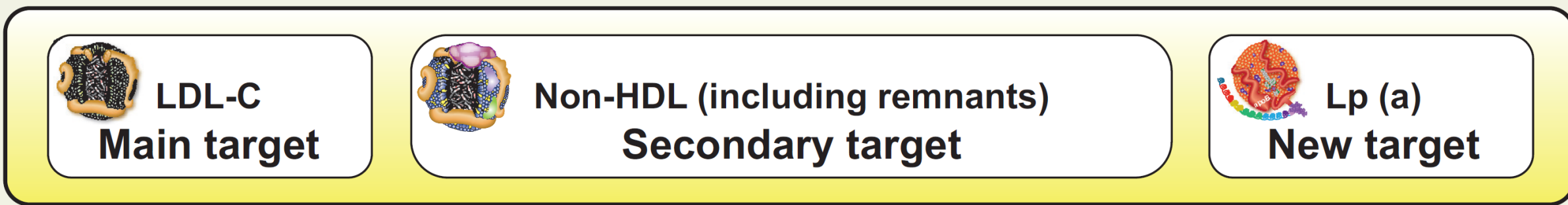
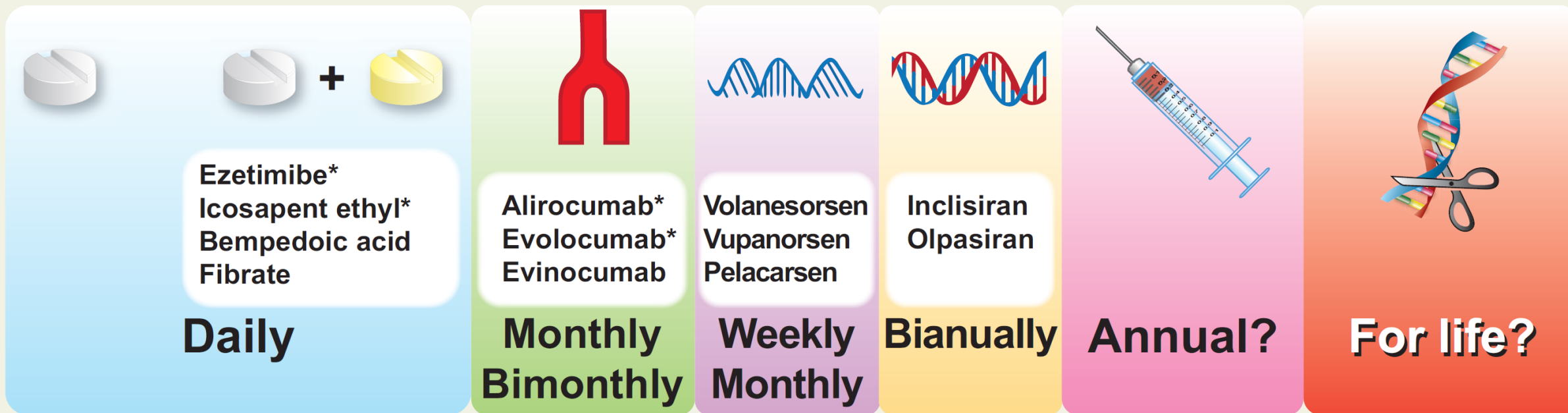
**Idea behind: don't wait until the first event occurs**

# Conclusion:

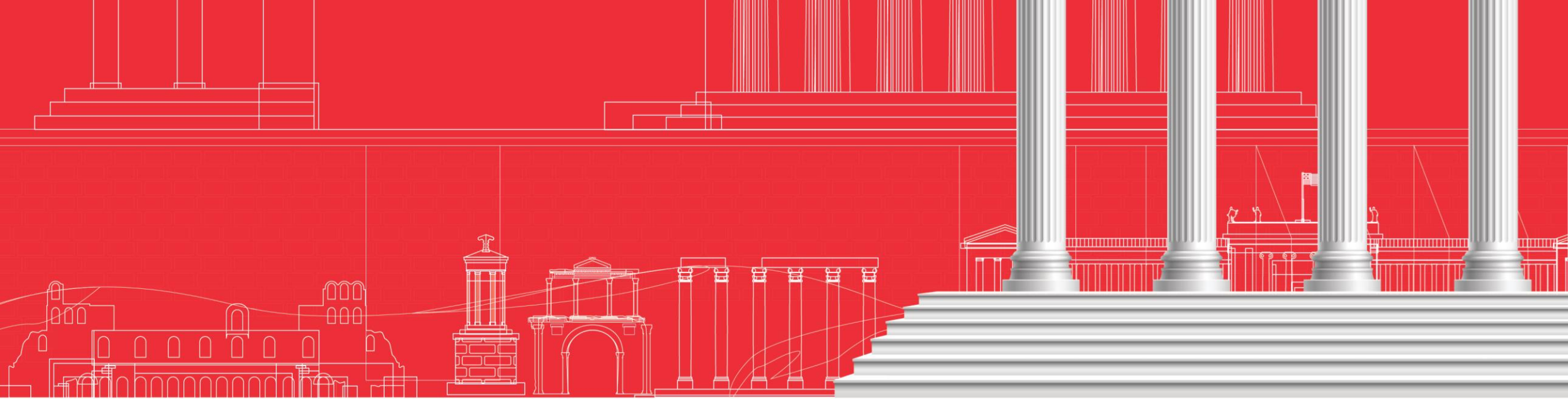
- ♥ **Starting LDL lowering with a healthy lifestyle as early as possible will provide most benefit**
- ♥ **Risk based approach will guide the extent of LDL lowering**
- ♥ **Low levels of LDL-C are well tolerated and safe and should be aimed in higher risk individuals**
- ♥ **Getting to guideline recommended goals and staying there prevents CV events**

# Evolution of Lipid Lowering Therapies:

Statins\* → Oral combination → MoAb → ASO → siRNA → Vaccination → Gene editing



\*Therapies shown to decrease CV events



# 94<sup>TH</sup> | EAS CONGRESS



ATHENS  
GREECE

**May 24-27, 2026**

