Updates on Hypercholesterolaemia

Mark Abela MD MRCP Msc (Int Med) MSc (Sports Cardiology)

Clinical lead for Cardiac Rehabilitation and Cardiovascular Prevention
Special interest in Sports Cardiology, and Inherited Cardiac Conditions

Outline

- Introduction
- Risk Assessment
- Lipid Analysis Recommendations
- Targets
- Available therapies
- Novel approaches

Introduction

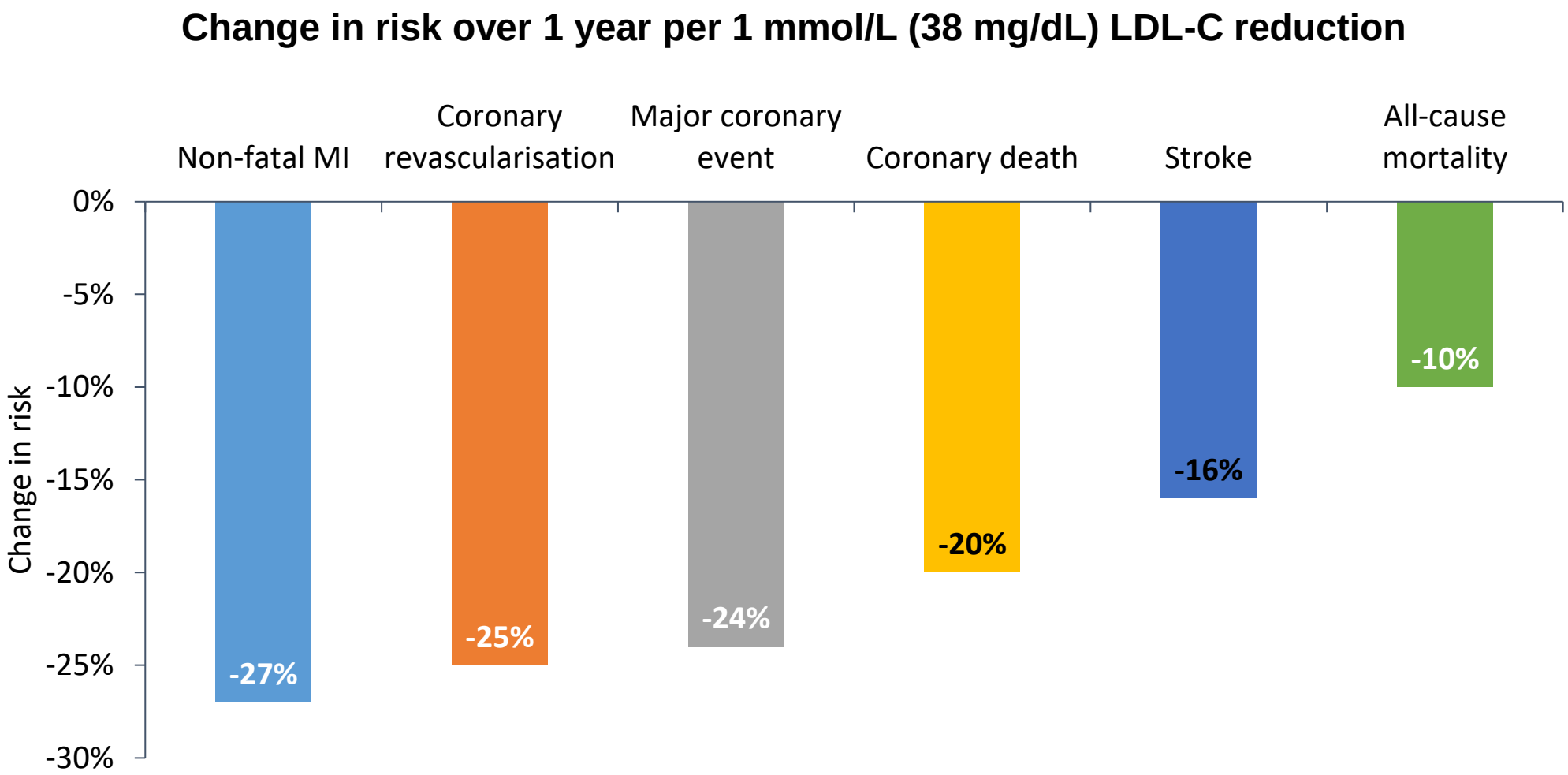
Introduction

- Cardiovascular disease (CVD) accounts for >4 million deaths / year in Europe
- Importance of ASCVD prevention remains undisputed
- More patients are surviving their first CVD event and are at high-risk of recurrences
- Hypercholesterolaemia is an important CV risk factor that plays a key role in ASCVD

The key question

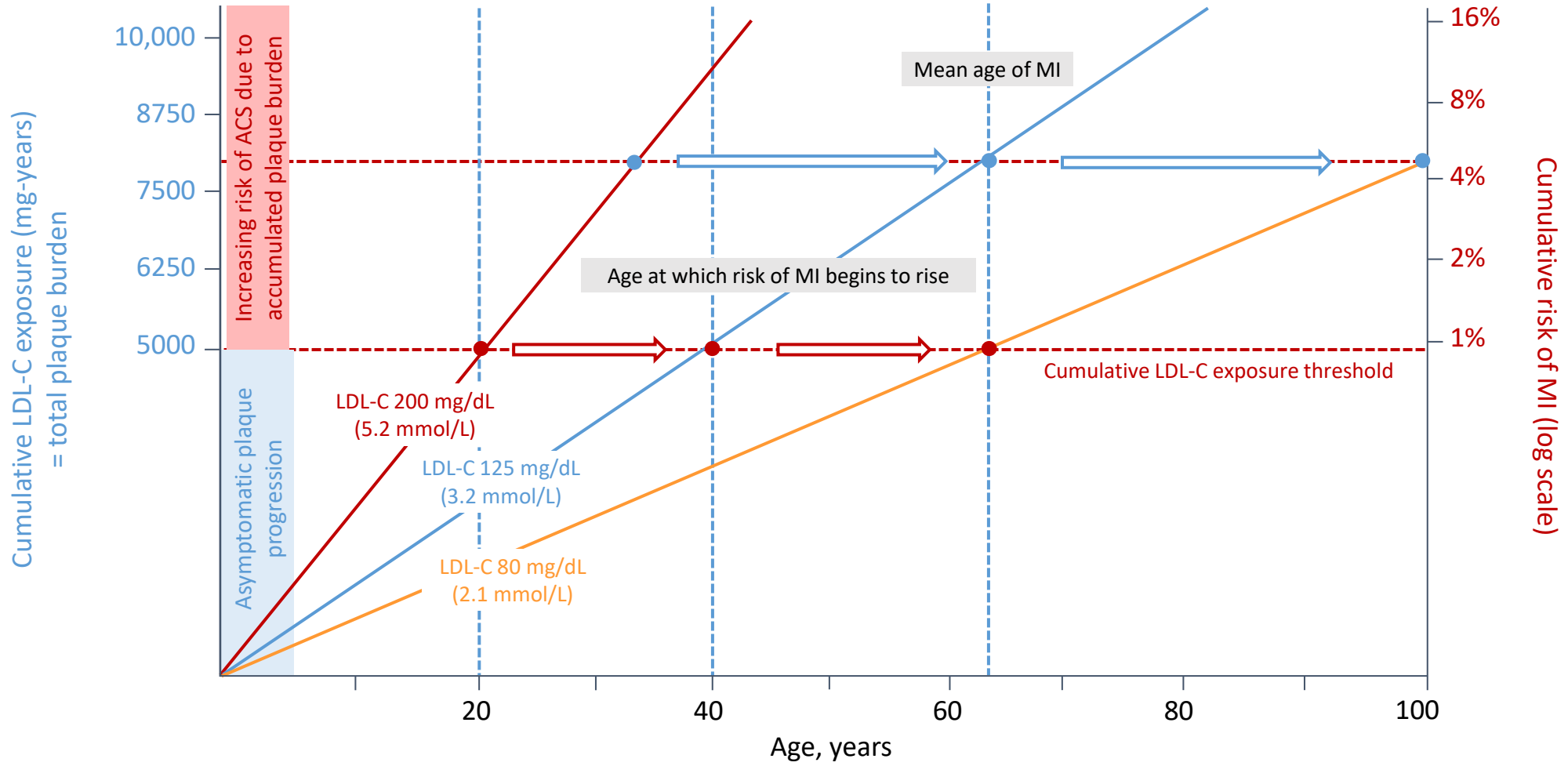
- Should every patient with hypercholesterolaemia get medical therapy?

Benefits of Intensive Statin Therapy are well documented



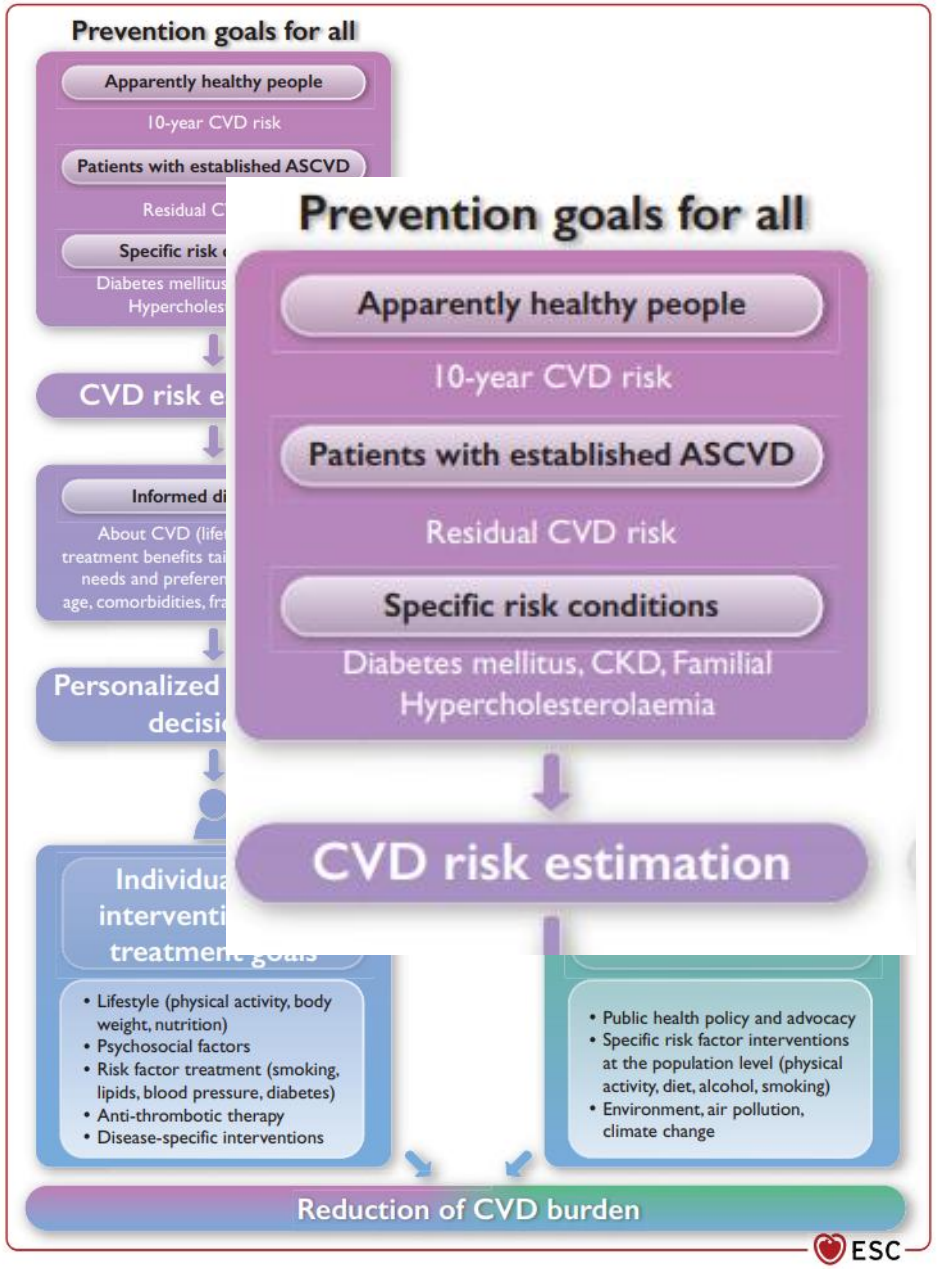
CV, cardiovascular; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction.
Adapted from Cholesterol Treatment Trialists' (CTT) Collaboration. *Lancet* 2010;376:1670-81.

Cumulative Effect of LDL on Risk of Atherosclerotic Cardiovascular Disease



ACS, acute coronary syndrome; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; MI, myocardial infarction. Adapted from Ference BA, et al. *J Am Coll Cardiol* 2018;72(10):1141-56.

Risk Assessment

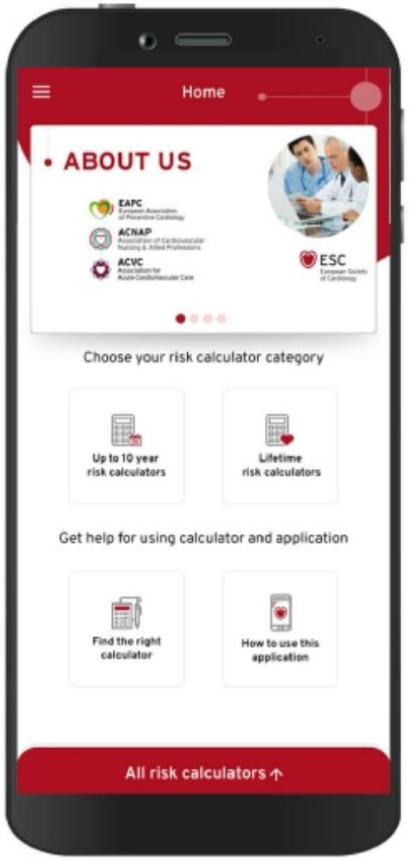


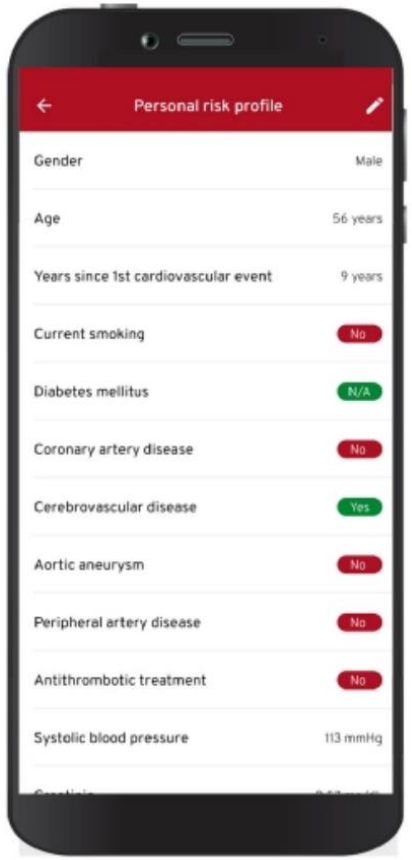
ESC European Society of Cardiology
European Heart Journal (2021) **42**, 3227–3337
doi:10.1093/eurheartj/ehab484

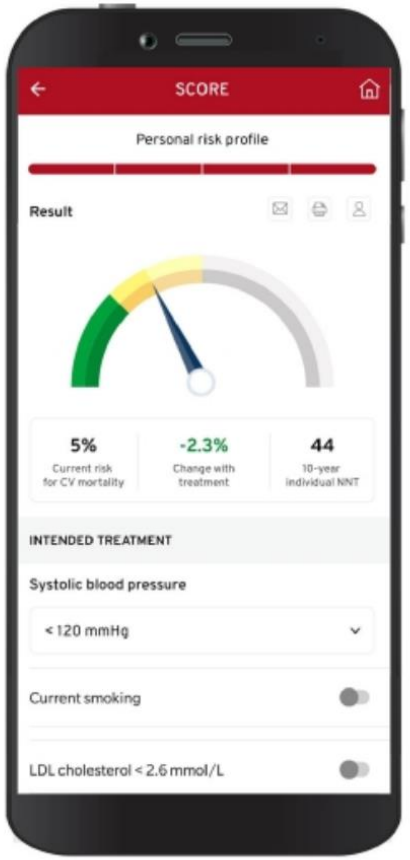
ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Risk Calculators







- SCORE2
- SCORE2-OP
- SCORE2-Diabetes
- ASCVD
- ADVANCE
- SMART
- SMART-REACH*
- DIAL*
- LIFE-CVD*

	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥190 mg/dL)
Primary prevention	**<1, low-risk**	**Lifestyle advice**	**Lifestyle advice**	**Lifestyle advice**	**Lifestyle advice**	**Lifestyle intervention, consider adding drug if uncontrolled**	**Lifestyle intervention and concomitant drug intervention**
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk (see *Table 4*)	**Lifestyle advice**	**Lifestyle advice**	**Lifestyle advice**	**Lifestyle intervention, consider adding drug if uncontrolled**	**Lifestyle intervention, consider adding drug if uncontrolled**	**Lifestyle intervention and concomitant drug intervention**
	Class[a]/Level[b]	I/C	I/C	IIa/A	IIa/A	IIa/A	IIa/A
	≥5 to <10, or high-risk (see *Table 4*)	**Lifestyle advice**	**Lifestyle advice**	**Lifestyle intervention, consider adding drug if uncontrolled**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**
	Class[a]/Level[b]	IIa/A	IIa/A	IIa/A	I/A	I/A	I/A
	≥10, or at very-high risk due to a risk condition (see *Table 4*)	**Lifestyle advice**	**Lifestyle intervention, consider adding drug if uncontrolled**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**
	Class[a]/Level[b]	IIa/B	IIa/A	I/A	I/A	I/A	I/A
Secondary prevention	**Very-high-risk**	**Lifestyle intervention, consider adding drug if uncontrolled**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**	**Lifestyle intervention and concomitant drug intervention**
	Class[a]/Level[b]	IIa/A	I/A	I/A	I/A	I/A	I/A

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

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

2019 ESC/EAS Guidelines

Very high risk	People with any of the following: • Documented ASCVD, either clinical or unequivocal on imaging • DM with target organ damage, or at least three major risk factors, or early onset of T1DM of long duration (> 20 years) • Severe CKD (eGFR < 30 mL/min/1.73 m^2) • A calculated SCORE ≥ 10% for 10-year risk of fatal CVD • FH with ASCVD or with another major risk factor
High risk	People with: • Markedly elevated single risk factors, in particular TC > 8 mmol/L (310 mg/dL), LDL-C > 4.9 mmol/L (190 mg/dL), or BP ≥ 180/110 mmHg • Patients with FH without other major risk factors • Patients with DM without target organ damage, with DM duration ≥ 10 years or another additional risk factor • Moderate CKD (eGFR 30-59 mL/min/1.73 m^2) • A calculated SCORE ≥ 5% and < 10% for 10-year risk of fatal CVD
Moderate risk	• Young patients (T1DM < 35 years; T2DM < 50 years) with DM duration < 10 years, without other risk factors • Calculated SCORE ≥ 1% and < 5% for 10-year risk of fatal CVD
Low-risk	• Calculated SCORE < 1% for 10-year risk of fatal CVD

ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FH, familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol; SCORE, Systematic Coronary Risk Estimation; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; TC, total cholesterol. Adapted from Mach F, et al. *Eur Heart J* 2020;41(1):111-88.

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

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

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

SCORE2-Diabetes

High risk / Very high-risk categories

- Established atherosclerotic cardiovascular disease (ASCVD)
- Diabetes Mellitus
- Familial Hypercholesterolaemia
- Chronic Kidney Disease

Table 11 **Dutch Lipid Clinic Network diagnostic criteria for familial hypercholesterolaemia**

Criteria (choose only one score per group, the highest applicable; diagnosis is based on the total number of points obtained)	Points
1) Family history	
First-degree relative with known premature (men aged <55 years; women <60 years) coronary or vascular disease, or first-degree relative with known LDL-C above the 95th percentile	1
First-degree relative with tendinous xanthomata and/or arcus cornealis, or children aged <18 years with LDL-C above the 95th percentile	2
2) Clinical history	
Patient with premature (men aged <55 years; women <60 years) CAD	2
Patient with premature (men aged <55 years; women <60 years) cerebral or peripheral vascular disease	1
3) Physical examination	
Tendinous xanthomata	6
Arcus cornealis before age 45 years	4
4) LDL-C levels (without treatment)	
LDL-C ≥8.5 mmol/L (326 mg/dL)	8
LDL-C 6.5–8.4 mmol/L (251–325 mg/dL)	5
LDL-C 5.0–6.4 mmol/L (191–250 mg/dL)	3
LDL-C 4.0–4.9 mmol/L (155–190 mg/dL)	1
5) DNA analysis	
Functional mutation in the *LDLR*, *apolipoprotein B*, or *PCSK9* genes	8
A 'definite' FH diagnosis requires >8 points	
A 'probable' FH diagnosis requires 6–8 points	
A 'possible' FH diagnosis requires 3–5 points	

Lipid Analysis Recommendations

Recommendations for lipid analyses for cardiovascular disease risk estimation

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

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

ESC European Society of Cardiology

European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

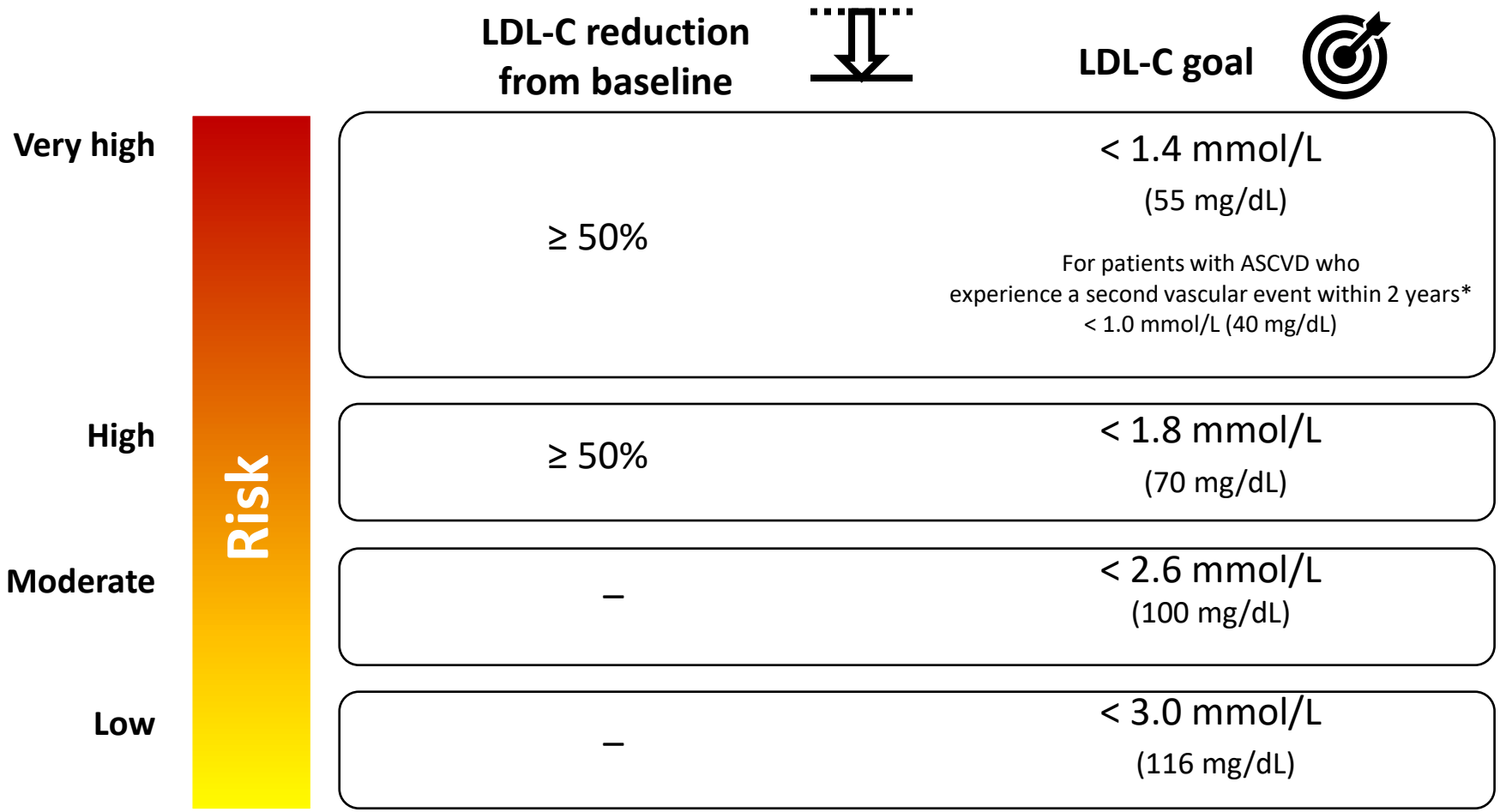
ESC/EAS GUIDELINES

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

Targets

1 mmol reduction in LDL-C, ASCVD events are reduced by 21%

Risk Stratification Dictates LDL-C Lowering Goals



*For patients[20] with **ASCVD who experience a second vascular event within 2 years** (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, **an LDL-C goal of < 1.0 mmol/L** (< 40 mg/dL) may be considered.

ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol. Adapted from Mach F, et al. *Eur Heart J* 2020;41(1):111-88.

Treatment goals for LDL-C		
In secondary prevention for patients at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.	I	A
In primary prevention for individuals at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.	I	C
In patients at high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.	I	A
Pharmacological LDL-C lowering		
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.	I	A
If the goals are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.	I	B
For secondary prevention in patients at very-high risk not achieving their goal on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.	I	A
For very-high-risk FH patients (that is, with ASCVD or with another major risk factor) who do not achieve their goal on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.	I	C

ESC European Society of Cardiology
European Heart Journal (2020) 41, 111–188
doi:10.1093/eurheartj/ehz455
ESC/EAS GUIDELINES

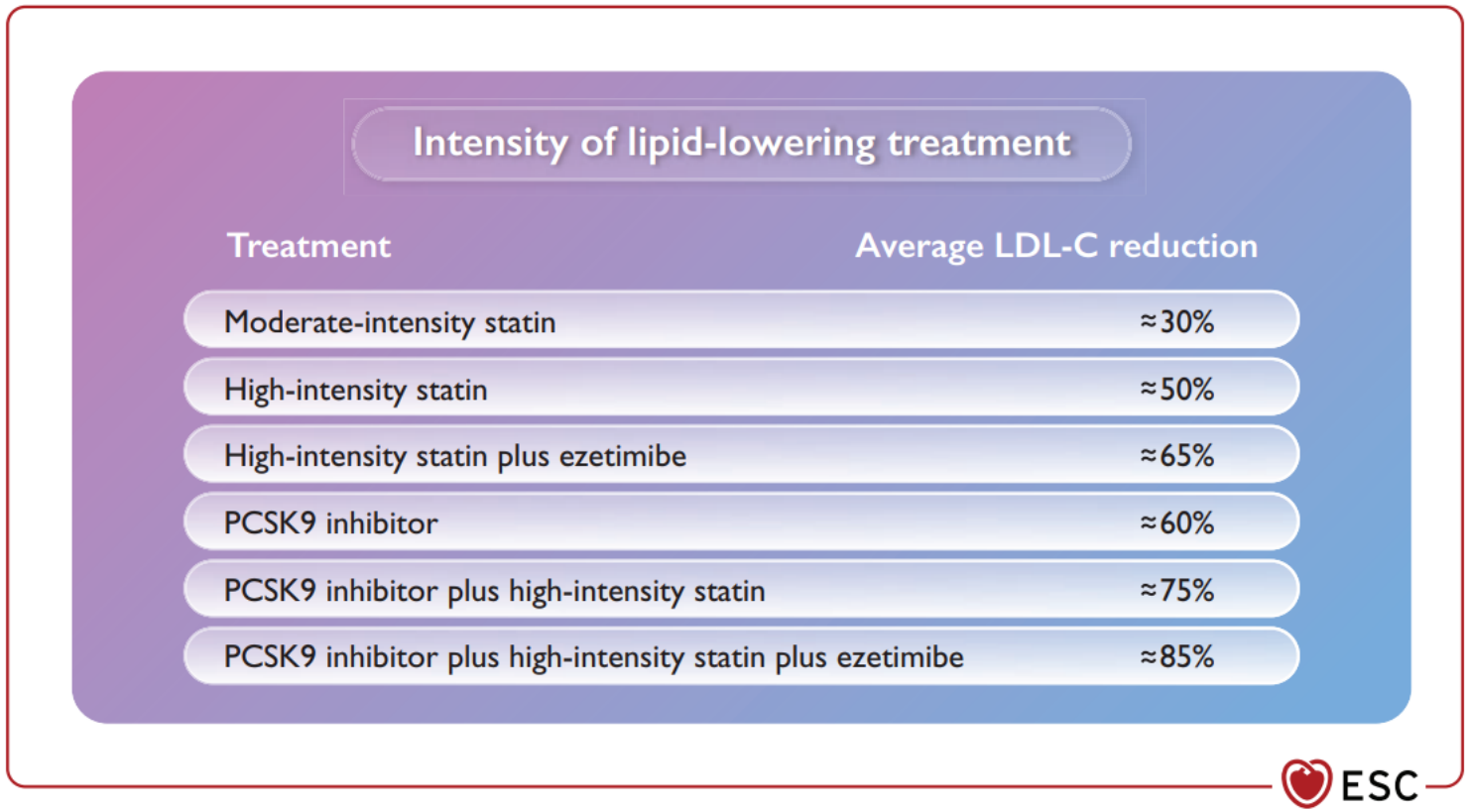
2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*

Treatment of dyslipidaemias in DM		
In patients with T2DM at very-high risk,[c] an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) is recommended.	I	A
In patients with T2DM at high risk,[c] an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) is recommended.	I	A
Statins are recommended in patients with T1DM who are at high or very-high risk.[c]	I	A
Statin therapy is not recommended in pre-menopausal patients with or without DM who are considering pregnancy, or not using adequate contraception.	III	C
Management of patients with ACS		
In all ACS patients without any contraindication or definite history of intolerance, it is recommended that high-dose statin therapy is initiated or continued as early as possible, regardless of initial LDL-C values.	I	A
If the LDL-C goal is not achieved after 4–6 weeks with the maximally tolerated statin dose, combination with ezetimibe is recommended.	I	B
If the LDL-C goal is not achieved after 4–6 weeks despite maximal tolerated statin therapy and ezetimibe, adding a PCSK9 inhibitor is recommended.	I	B

ESC European Society of Cardiology
European Heart Journal (2020) **41**, 111–188
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

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



ESC European Society of Cardiology

European Heart Journal (2021) **42**, 3227–3337
doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL on average by ≥50%	Daily dose lowers LDL on average by approximately 30-49%	Daily dose lowers LDL on average by <30%
Atorvastatin 40-80 mg Rosuvastatin 20-40 mg	Atorvastatin 10-20 mg Rosuvastatin 5-10 mg Simvastatin 20-40 mg Pravastatin 40-80 mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 2-4 mg	Simvastatin 10 mg Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

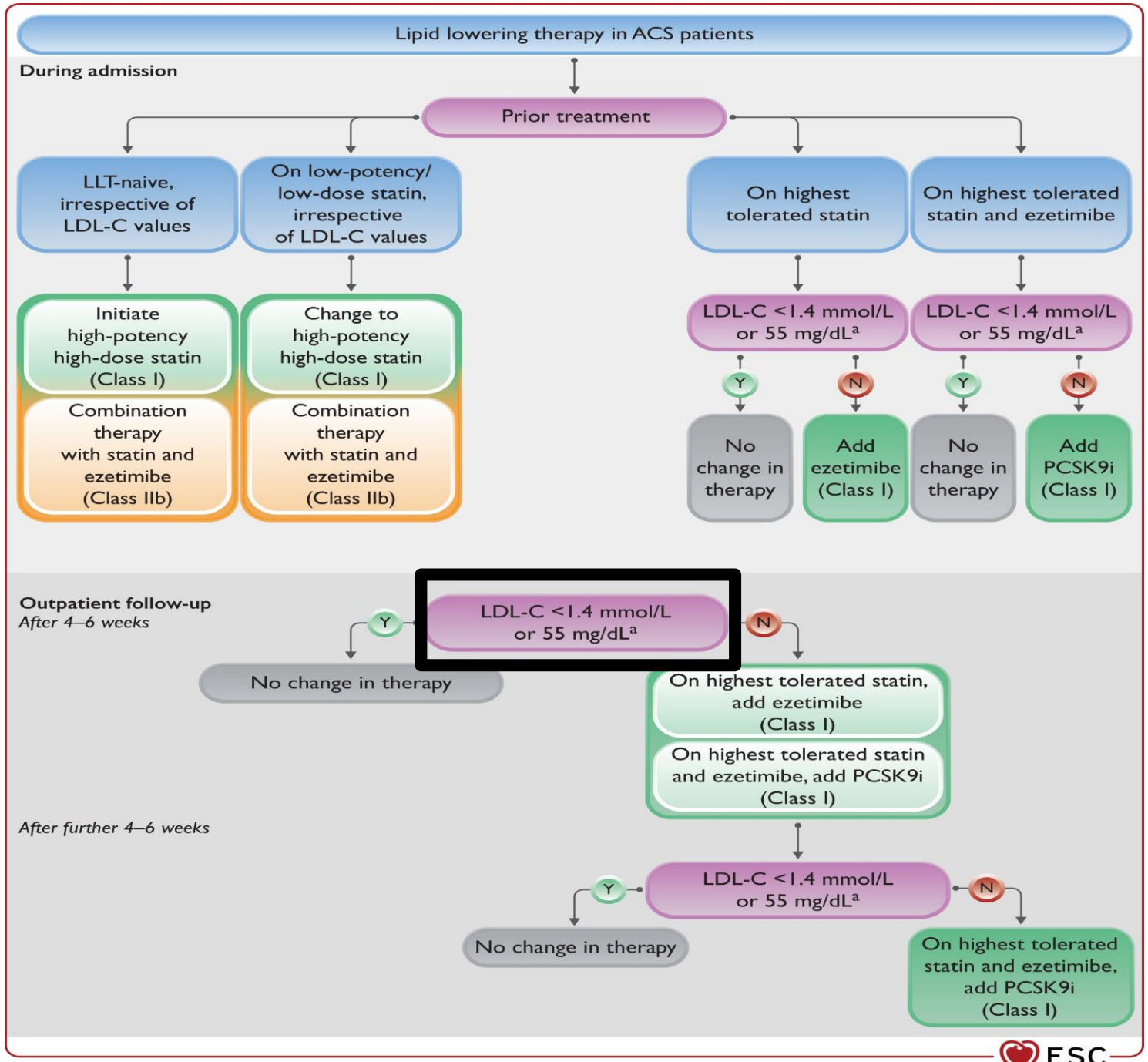
The expected LDL-C reductions in response to therapy are shown in *Figure 13*, and may vary widely among individuals. Therefore, monitoring the effect on LDL-C levels is recommended, with assessment of LDL-C levels 4-6 weeks after any treatment strategy initiation or change.

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 3227–3337
doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Therapeutic Options



JOURNAL ARTICLE GUIDELINES

2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC) FREE

Robert A Byrne ✉, Xavier Rossello, J J Coughlan, Emanuele Barbato, Colin Berry, Alaide Chieffo, Marc J Claeys, Gheorghe-Andrei Dan, Marc R Dweck, Mary Galbraith ...
Show more
Author Notes

[A] Consider LDL-C <1.0 mmol/L if recurrent event.

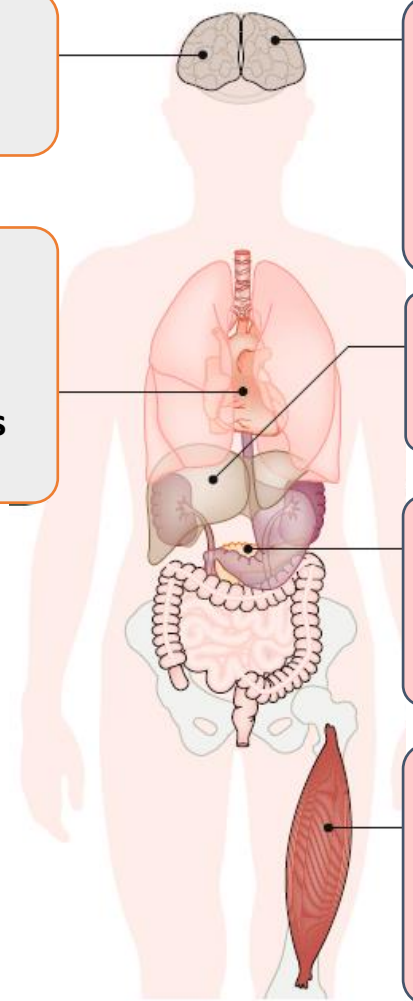
Benefits vs Risks of Statin Therapy

Benefits

Risk of stroke
- ↓ 16% for total stroke
- ↓ 21% for ischaemic stroke

Risk of major coronary events
- ↓ 27% for non-fatal MI
- ↓ 20% for CHD death

Risk of revascularisation procedures
- ↓ 25%



Adverse effects

Cognitive dysfunction
- No evidence

Risk of haemorrhagic stroke
- Small increase in individuals with prior haemorrhagic stroke in one study*

Liver symptoms/diseases
- Clinically insignificant liver enzyme elevations
- Incidence of liver failure: 1/100,000

Incidence of new-onset diabetes mellitus
- Moderate-intensity statin therapy: 0.1% per year
- High-intensity statin therapy: 0.2% per year

Incidence of muscle symptoms/diseases
- SAMS: 10-29% in observational studies and 1-2% in RCTs
- Myopathy: 1/1000
- Rhabdomyolysis: 1/10,000

*Not confirmed by any other studies. CHD, coronary heart disease; MI, myocardial infarction; RCT, randomised controlled trial; SAMS, statin-associated muscle symptoms.

Adapted from Adhyaru BB, Jacobson TA. *Nat Rev Cardiol* 2018;15(12):757-69.

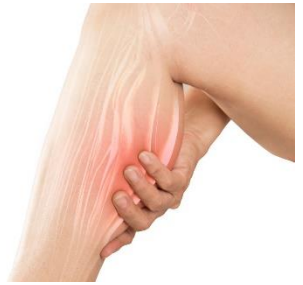
Muscle Adverse Event Terminology

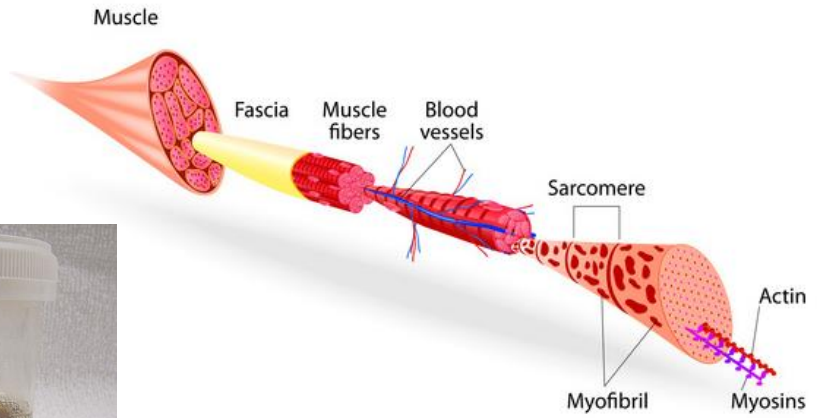
SAMS
Muscle symptoms reported during statin therapy but not necessarily caused by the statin
10-29% in observation studies. 1-2% in RCTs.

Myalgia
Muscle pain or aches

Myopathy
Unexplained muscle pain or weakness accompanied by CK concentration > 10 x ULN

Rhabdomyolysis
Severe form of myopathy, with CK typically > 40 ULN, which can cause myoglobinuria and acute renal failure





CK, creatinine kinase; SAMS, statin-associated muscle symptoms; ULN, upper limit of normal.
Newman CB, et al. *Arterioscler Thromb Vasc Biol* 2019;39:e38-e81.

PCSK9 Inhibitors

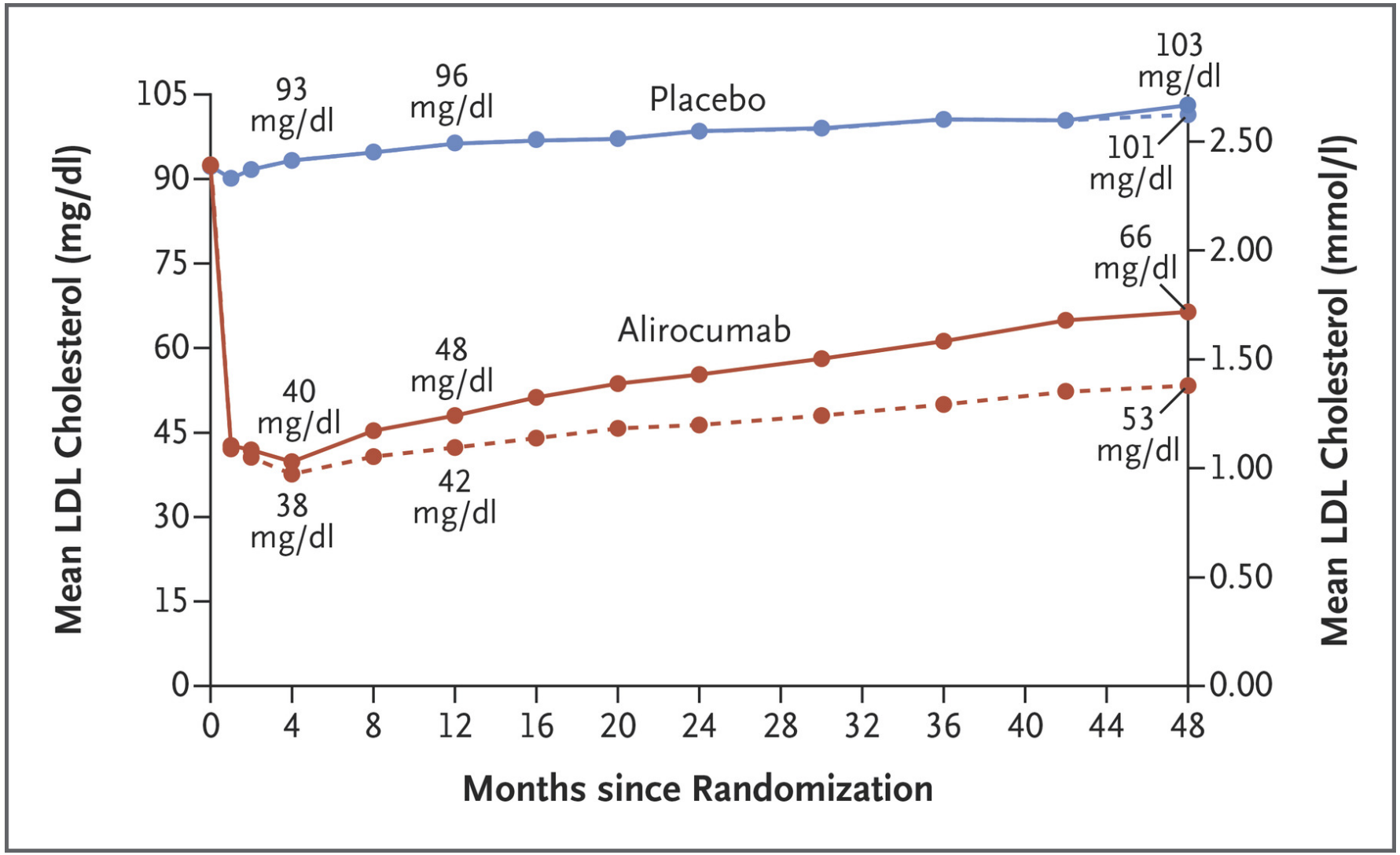
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 73, NO. 4, 2019

ORIGINAL INVESTIGATIONS

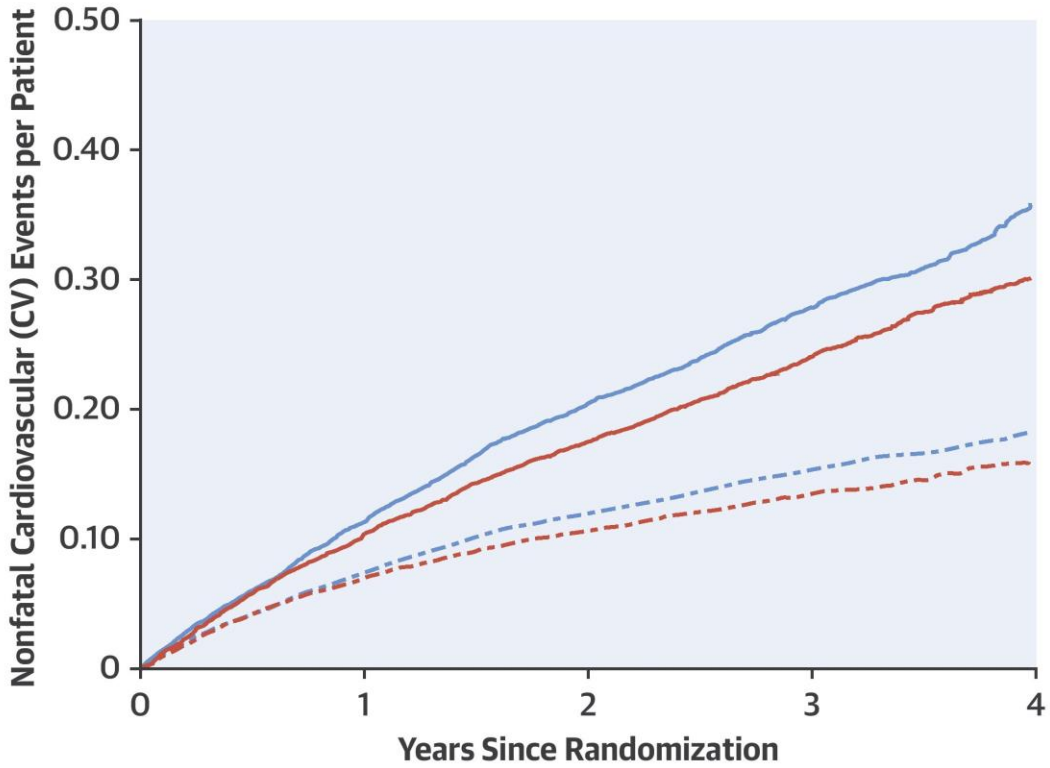
Alirocumab Reduces Total Nonfatal Cardiovascular and Fatal Events

The ODYSSEY OUTCOMES Trial

>50% reduction in LDL-C within first 3 months



CENTRAL ILLUSTRATION: Mean Cumulative Functions and Kaplan-Meier Curves for Nonfatal Cardiovascular Events



Number at Risk					
Placebo	9,462	9,219	8,888	3,898	737
Alirocumab	9,462	9,217	8,919	3,946	746

Placebo: Total Nonfatal CV
Alirocumab: Total Nonfatal CV
Placebo: First Nonfatal CV
Alirocumab: First Nonfatal CV

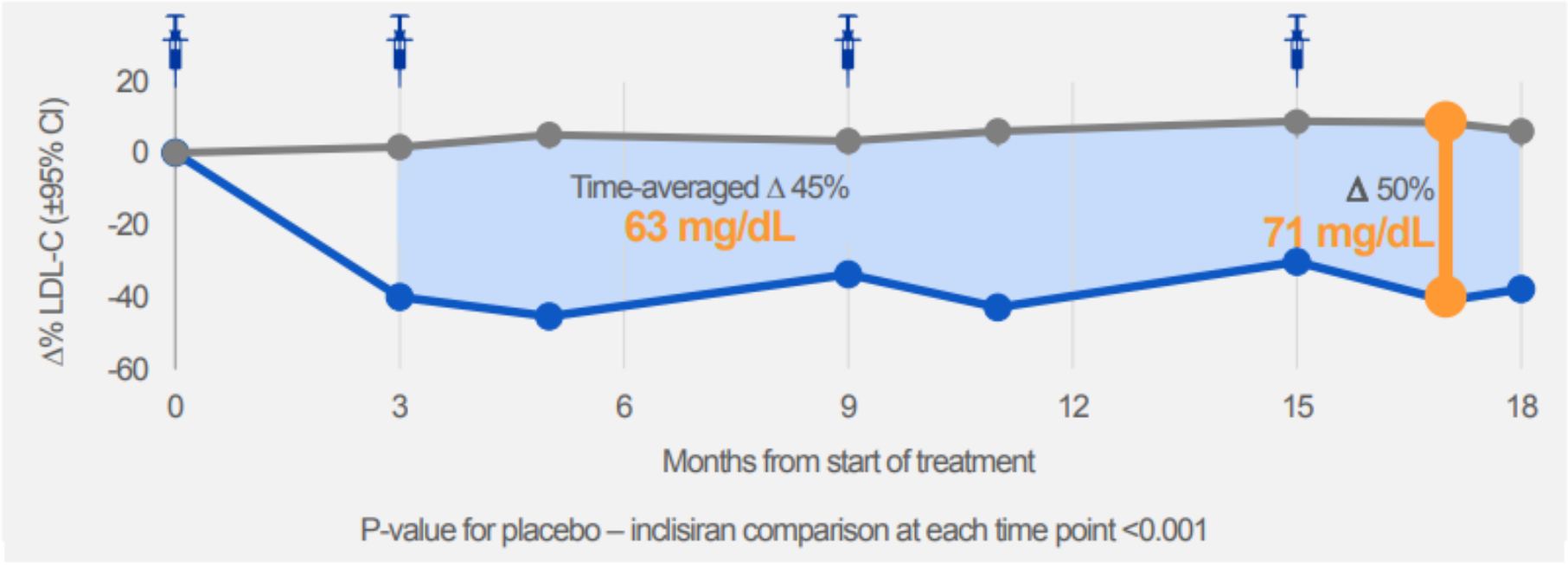
Szarek, M. et al. J Am Coll Cardiol. 2019;73(4):387-96.

Reduction in LDL-C within first 3 months

ORION-9: Efficacy

Durable and potent effect over 18 months

Percent and absolute change in LDL-C over time – observed values in ITT patients



1. All 95% confidence intervals are less than ±2% and therefore are not visible outside data points

Recommendations	Class[a]	Level[b]
Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia [triglycerides >2.3 mmol/L (200 mg/dL)].[533]	I	A
In patients taking statins who are at LDL-C goal with triglycerides >2.3 mmol/L (200 mg/dL), fenofibrate or bezafibrate may be considered.[534–536]	IIb	B
In high-risk (or above) patients with triglycerides >1.5 mmol/L (135 mg/dL) despite statin treatment and lifestyle measures, n-3 PUFAs (icosapent ethyl 2 × 2 g/day) may be considered in combination with a statin.[84]	IIb	B

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 3227–3337
doi:10.1093/eurheartj/ehab484

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Future Directions

JOURNAL ARTICLE

Inclisiran and cardiovascular events: a patient–level analysis of phase III trials

Kausik K Ray ✉, Frederick J Raal, David G Kallend, Mark J Jaros, Wolfgang Koenig, Lawrence A Leiter, Ulf Landmesser, Gregory G Schwartz, David Lawrence, Andrew Friedman ... Show more

Author Notes

European Heart Journal, Volume 44, Issue 2, 7 January 2023, Pages 129–138,
https://doi.org/10.1093/eurheartj/ehac594

Published: 04 November 2022 **Article history** ▾

ORION Trial

Key Question

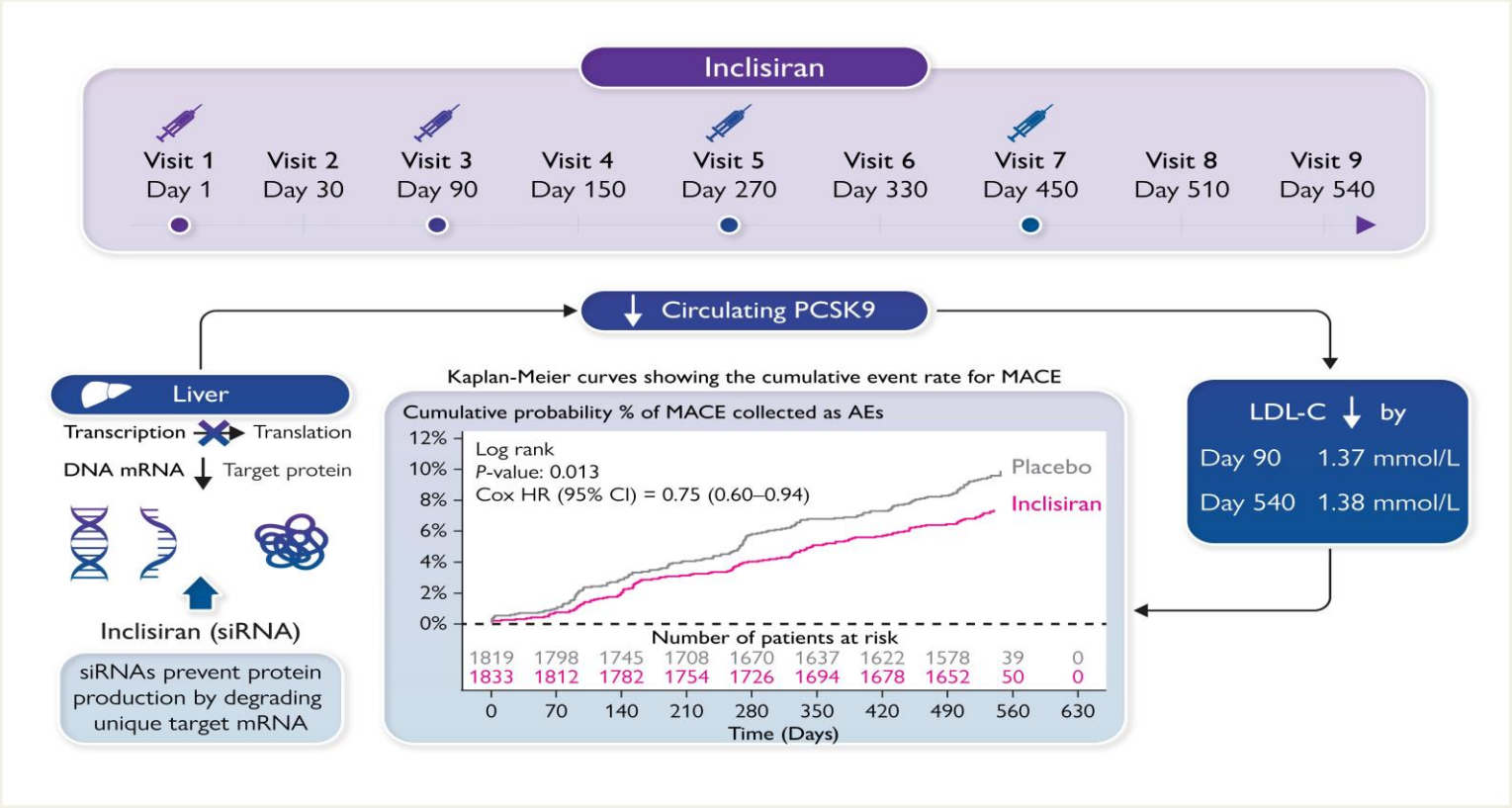
To evaluate the effect on the prespecified exploratory endpoint, cardiovascular events. This was studied in a patient-level, pooled analysis of the pivotal Phase III ORION trials (ORION-9, ORION-10 and ORION-11) over 18 months.

Key Finding

Inclisiran significantly reduced major adverse cardiovascular events (OR [95% CI] : 0.74 [0.58–0.94]), but not fatal and non-fatal myocardial infarction (OR [95% CI] : 0.80 [0.50–1.27]) and fatal and non-fatal stroke (OR [95% CI] : 0.86 [0.41–1.81]).

Take Home Message

This pooled analysis offers early insights into the potential cardiovascular benefits of lowering LDL-C with inclisiran and suggests potential benefits for major adverse cardiovascular event reduction.



Inclisiran and risk of reported MACE from the patient-level pooled ORION-9, ORION-10 and ORION-11 trials.

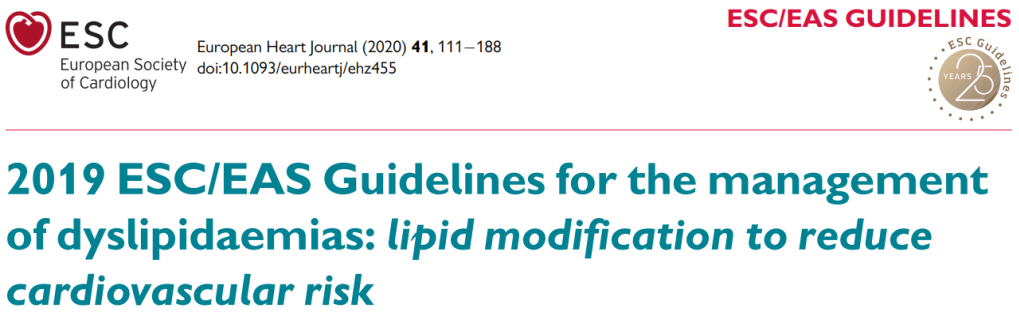
Potential outcome benefit with Incliseran

↓ Major adverse CV events

↔ Similar rates of fatal / non-fatal MI

Bempedoic Acid

- An oral cholesterol synthesis inhibitor
- Intended in combination with ezetimibe in patients with statin intolerance.
- Reduces LDL-C by 30%, up to 50% when with ezetimibe



Randomized Controlled Trial > N Engl J Med. 2023 Apr 13;388(15):1353-1364.
doi: 10.1056/NEJMoa2215024. Epub 2023 Mar 4.

Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients

Steven E Nissen [1], A Michael Lincoff [1], Danielle Brennan [1], Kausik K Ray [1], Denise Mason [1], John J P Kastelein [1], Paul D Thompson [1], Peter Libby [1], Leslie Cho [1], Jorge Plutzky [1], Harold E Bays [1], Patrick M Moriarty [1], Venu Menon [1], Diederick E Grobbee [1], Michael J Louie [1], Chien-Feng Chen [1], Na Li [1], LeAnne Bloedon [1], Paula Robinson [1], Maggie Horner [1], William J Sasiela [1], Jackie McCluskey [1], Deborah Davey [1], Pedro Fajardo-Campos [1], Predrag Petrovic [1], Jan Fedacko [1], Witold Zmuda [1], Yury Lukyanov [1], Stephen J Nicholls [1]; CLEAR Outcomes Investigators

Collaborators, Affiliations + expand

PMID: 36876740 DOI: 10.1056/NEJMoa2215024

- Primary end point was a four-component composite
  - Death from cardiovascular causes
  - Nonfatal myocardial infarction
  - Nonfatal stroke
  - Coronary revascularization

- Reduced 4-component composite end point
  - Bempedoic Acid vs Placebo
  - 819 patients (11.7% vs 13.3%)

- Bempedoic acid had no significant effects on fatal or nonfatal stroke, death from cardiovascular causes, and death from any cause

FREE ACCESS

EDITORIAL

PDF/EPUB

Tools Share

The Lower the ApoB, the Better: Now, How Does ApoB Fit in the Upcoming Era of Targeted Therapeutics?

Mohamed B. Elshazly and **Renato Quispe**

Originally published 29 Aug 2022 | https://doi.org/10.1161/CIRCULATIONAHA.122.061188 | Circulation. 2022;146:673–675

This article is a commentary on the following

ORIGINAL ARTICLE

Small Interfering RNA to Reduce Lipoprotein(a) in Cardiovascular Disease

Michelle L. O'Donoghue, M.D., M.P.H., Robert S. Rosenson, M.D., Baris Gencer, M.D., M.P.H., J. Antonio G. López, M.D., Norman E. Lepor, M.D., Seth J. Baum, M.D., Elmer Stout, M.D., Daniel Gaudet, M.D., Ph.D., Beat Knusel, Ph.D., Julia F. Kuder, M.A., Xinhui Ran, M.S., Sabina A. Murphy, M.P.H., et al., for the OCEAN(a)-DOSE Trial Investigators*

November 17, 2022
N Engl J Med 2022; 387:1855-1864
DOI: 10.1056/NEJMoa2211023
Chinese Translation 中文翻译

CONCLUSIONS

Olpasiran therapy significantly reduced lipoprotein(a) concentrations in patients with established atherosclerotic cardiovascular disease. Longer and larger trials will be necessary to determine the effect of olpasiran therapy on cardiovascular disease. (Funded by Amgen; OCEAN[a]-DOSE ClinicalTrials.gov number, NCT04270760.)

Conclusion

- Hypercholesterolaemia is an important variable in ASCVD
- Different targets for different patient populations
- Aim to change to high dose statin + ezetimibe early on
- Achievable targets with good therapy
- Doesn’t replace diet / exercise

Thank You