The Dyslipidaemia Guidelines

Alberico L. Catapano

alberico.catapano@unimi.it

Milano Oct 2019

ESC Classes of recommendations

EAS ESC European Society of Cardiology

	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

ESC Levels of evidence

EAS ESC European Society of Cardiology

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Role of LDL in atherogenesis

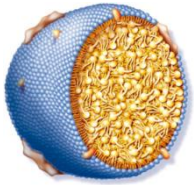
Pathological plausibility

Cellular remodelling

Release of bio-active lipids

Extracellular pathology

Lipoprotein retention
Deposits early micro- and later macro-cholesterol crystals.



Innate immunity

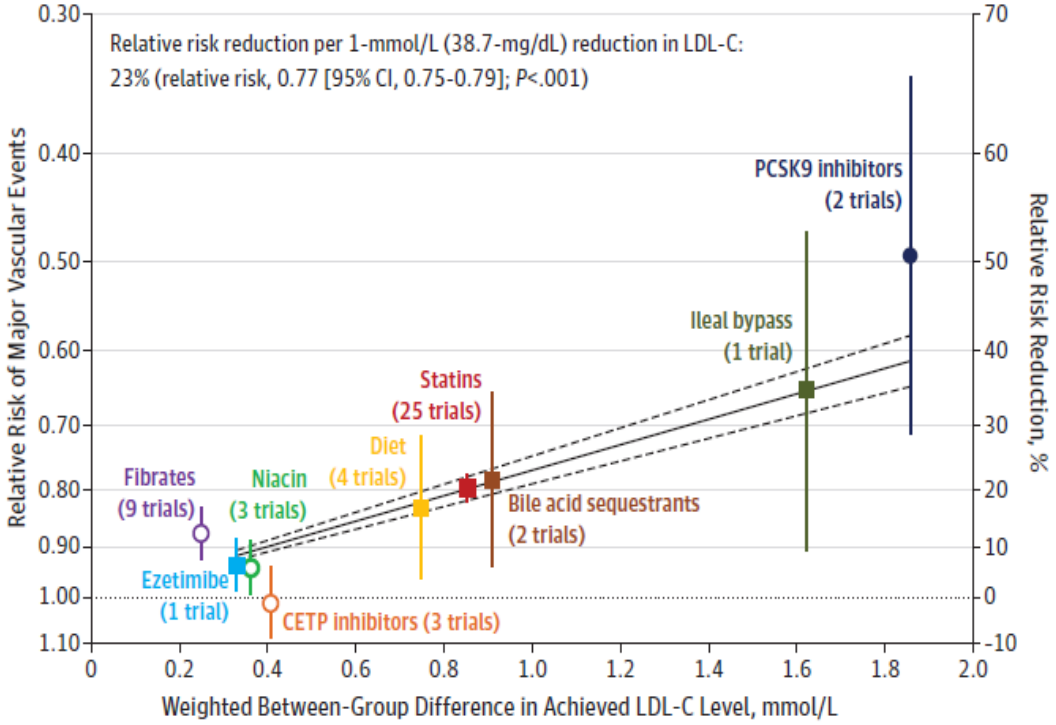
Initiates localised inflammation.
Macrophage recruitment.
Intracellular cholesterol accumulation.
Necrosis

Auto-immunity (apoB)

Adaptive immunity

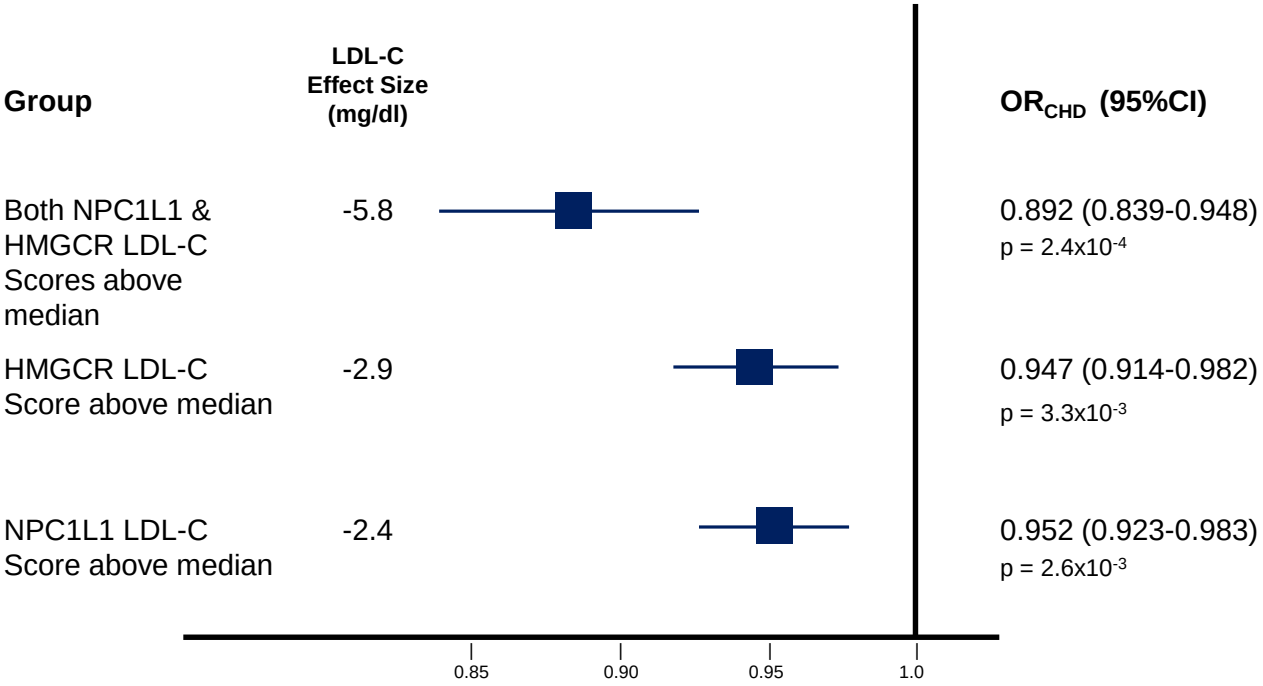
Libby P, *et al.* Nature. 2011;473(7347):317-25.
Prassl R and Laggner P. Biochemistry, Genetics and Molecular Biology; chapter 1; book edited by S. Frank and G. Kostner, Published: October 3, 2012

Meta-analysis of various methods to lower LDL-C



Silverman MG, Ference BA, et al. JAMA 2016;316:1289-1297.

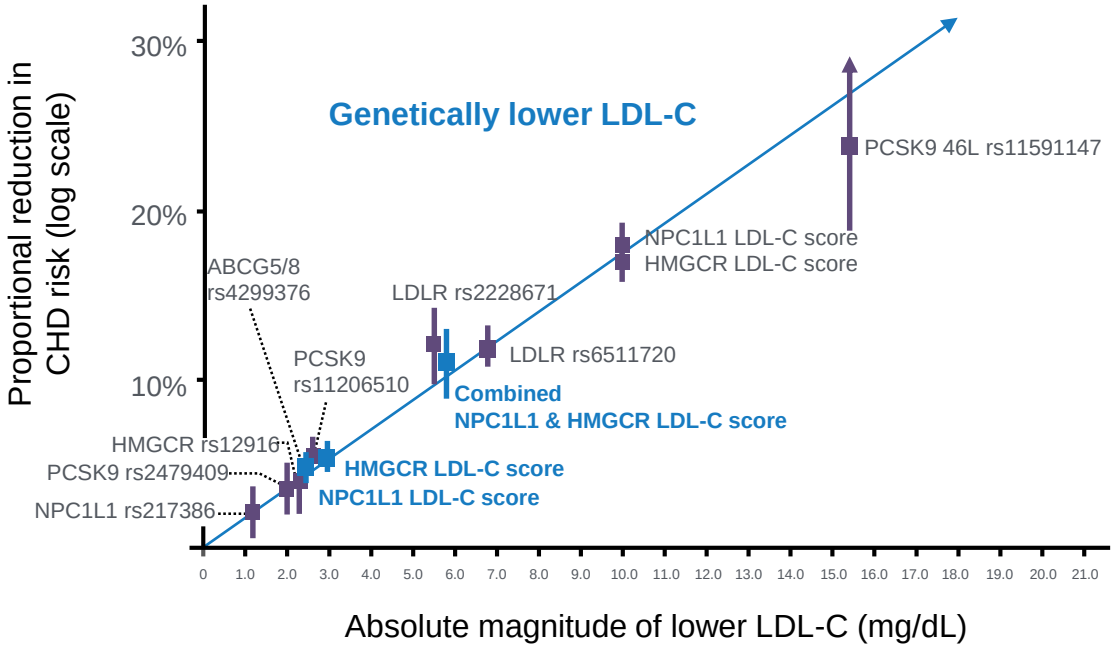
2x2 Factorial Mendelian Randomization



Ference BA et al. J Am Coll Cardiol 2015;doi:10.1016/j.jacc.2015.02.020

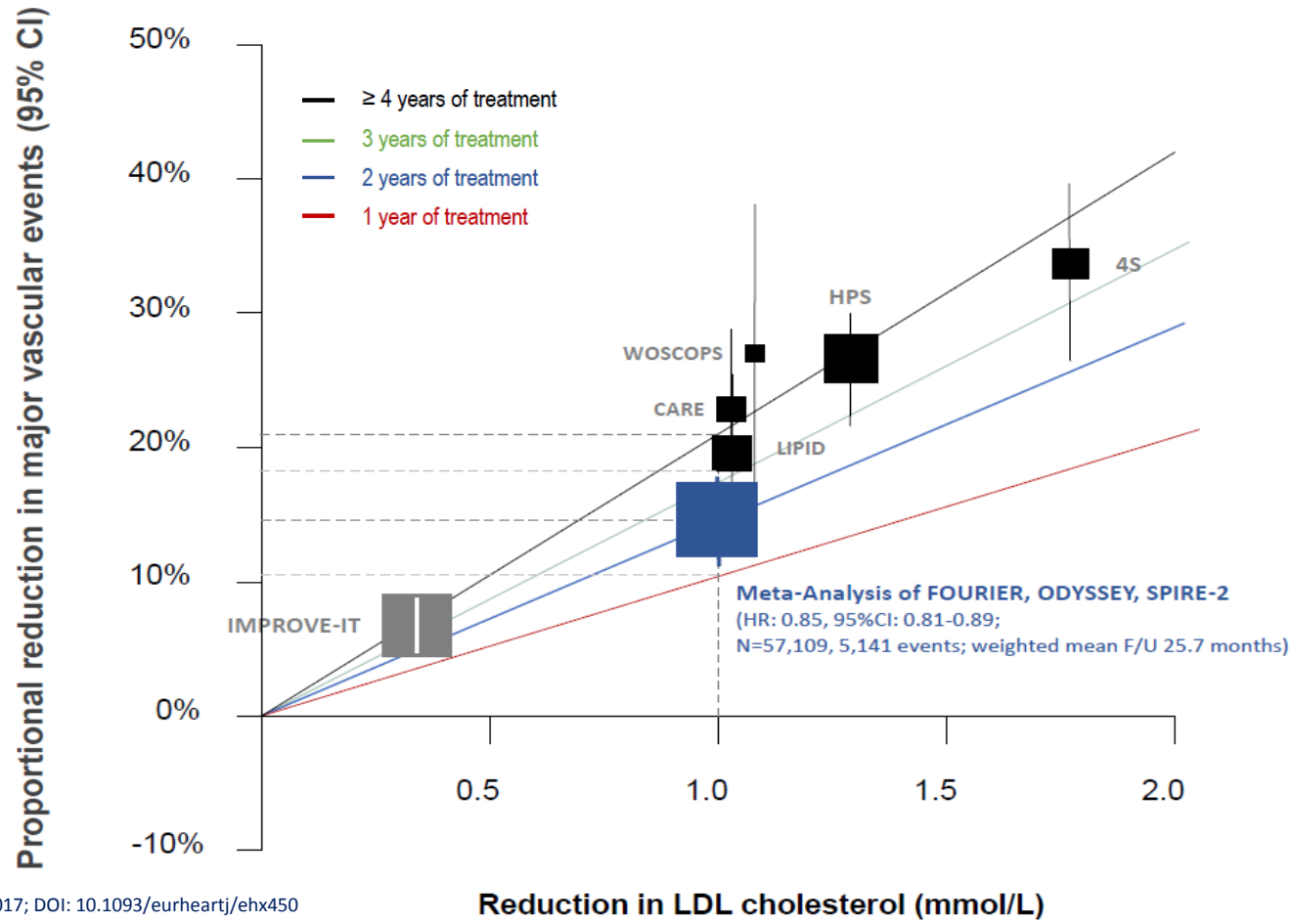
Genetic evidence supports LDL-C as a risk factor for CV events

54.5% reduction in CHD risk per 1mmol/L lower LDL-C



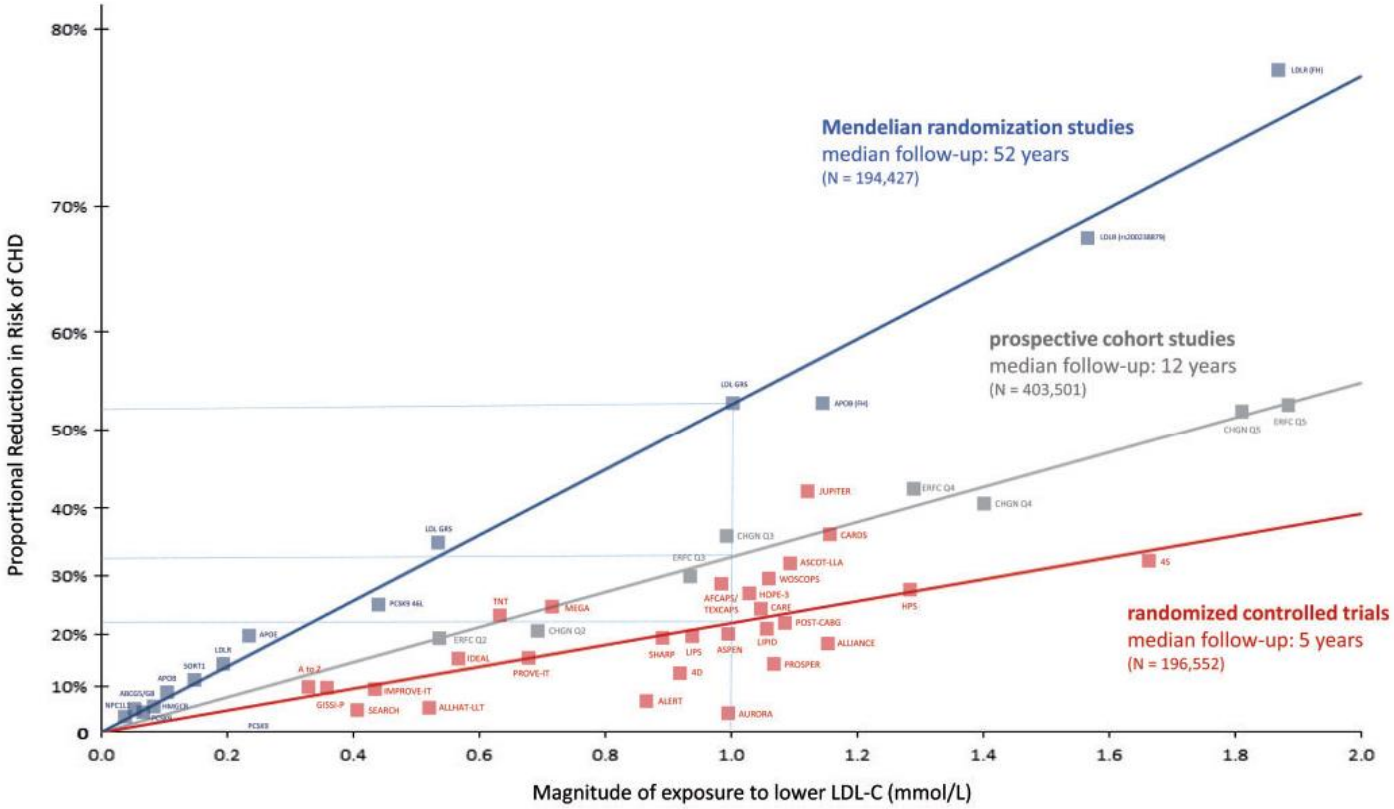
Ference et al. J Am Coll Cardiol 2012;60:2631–2639. Ference et al. J Am Coll Cardiol 2015;65:1552–1561.

Comparison of PCSK9 inhibitors and statins by duration of treatment



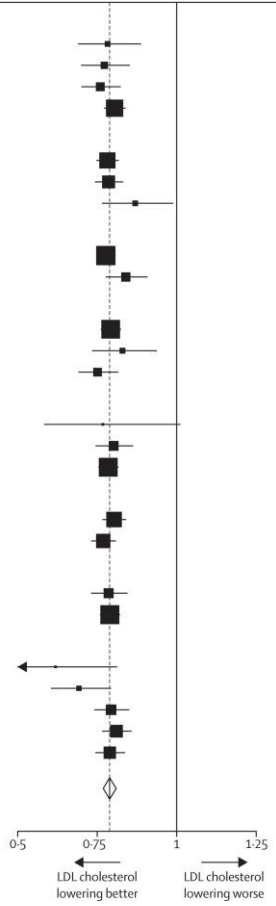
Ference BA, et al. Eur Heart J. 2017; DOI: 10.1093/eurheartj/ehx450

Effect of LDL-C by magnitude and duration of exposure



Ference BA, et al. EAS Consensus Statement on LDL Causality. Eur Heart J 2017; doi: 10.1093/eurheartj/ehx144

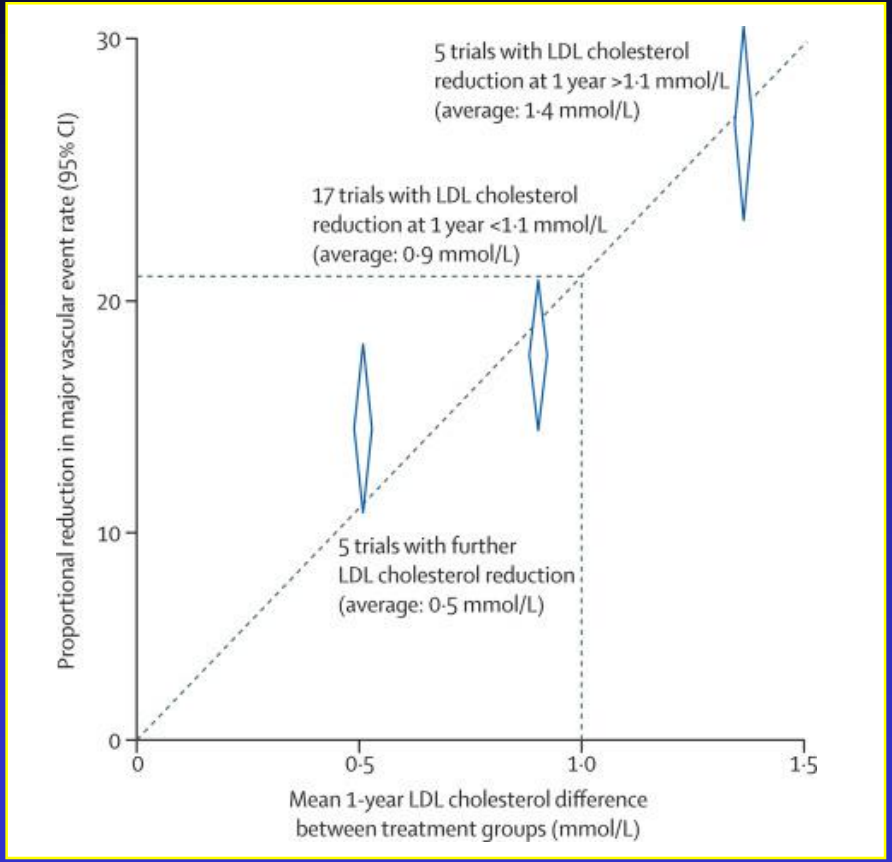
Presenting characteristics	Total number of MVEs	Annual event rate in control arm (% per year)	RR (CI) per 1 mmol/L reduction in LDL cholesterol	p value for heterogeneity or trend
Pre-treatment LDL cholesterol (mmol/L)				p=0·22
<2·5	5256	4·3	0·78 (0·69–0·89)	
≥2·5 to <3·0	4182	4·0	0·77 (0·70–0·85)	
≥3·0 to <3·5	4604	4·1	0·76 (0·70–0·82)	
≥3·5	10563	3·9	0·80 (0·77–0·84)	
Age (years)				p=0·14
≤65	13623	3·6	0·78 (0·75–0·82)	
>65 to ≤75	9211	4·6	0·79 (0·74–0·83)	
>75	2123	5·5	0·87 (0·76–0·99)	
Sex				p=0·02
Male	19922	4·4	0·78 (0·75–0·81)	
Female	5035	3·0	0·84 (0·78–0·91)	
History of vascular disease				p=0·18
CHD	19097	5·6	0·79 (0·76–0·82)	
Non-CHD vascular	1529	3·7	0·83 (0·73–0·94)	
None	4331	1·8	0·75 (0·69–0·82)	
Diabetes				p=0·78
Type 1 diabetes	337	6·0	0·77 (0·58–1·01)	
Type 2 diabetes	5621	5·1	0·80 (0·74–0·86)	
No diabetes	18862	4·0	0·78 (0·76–0·82)	
Treated hypertension				p=0·11
Yes	13939	4·5	0·80 (0·77–0·84)	
No	10471	3·5	0·77 (0·73–0·81)	
Smoking status				p=0·88
Current smokers	5225	4·7	0·79 (0·73–0·85)	
Non-smokers	19728	3·9	0·79 (0·76–0·82)	
5-year MVE risk				p=0·04
<5%	421	0·6	0·62 (0·47–0·81)	
≥5 to <10%	1453	1·6	0·69 (0·60–0·79)	
≥10 to <20%	7810	3·5	0·79 (0·74–0·85)	
≥20 to <30%	9028	5·8	0·81 (0·77–0·86)	
≥30%	6245	9·8	0·79 (0·74–0·84)	
All patients	**24957**	**4·0**	**0·79 (0·77–0·81)**	



Similar proportional reductions in risks of major vascular events per mmol/L LDL cholesterol reduction in randomised trials of statin therapy among people with different presenting characteristics

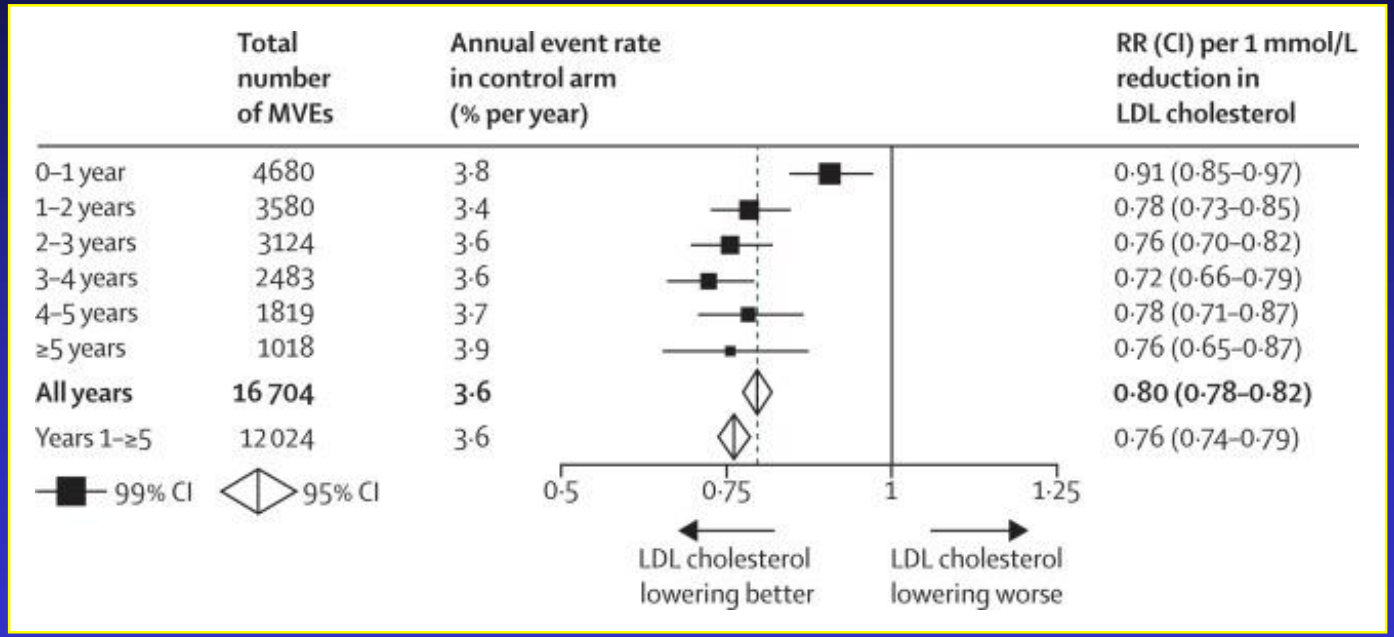
Collins R. et al.
Lancet 2016 Epub Sep 6

Proportional major vascular event reductions versus absolute LDL cholesterol reductions in randomised trials of routine statin therapy versus no routine statin use and of more intensive versus less intensive regimens



Collins R. et al. Lancet 2016 Epub Sep 6

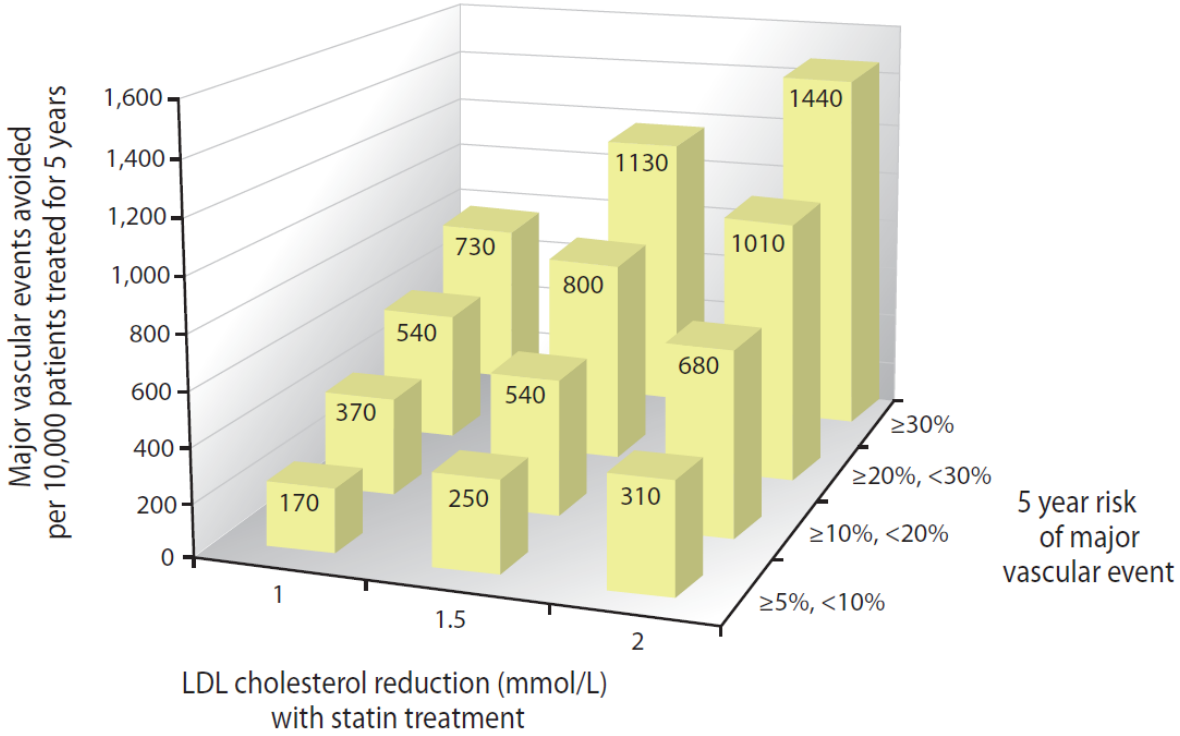
Proportional reductions in risks of major vascular events per mmol/L reduction in LDL cholesterol during each year of scheduled statin treatment, in randomised trials of routine statin therapy versus no routine statin use



Collins R. et al. Lancet 2016 Epub Sep 6

Absolute reductions in major vascular events with statin therapy

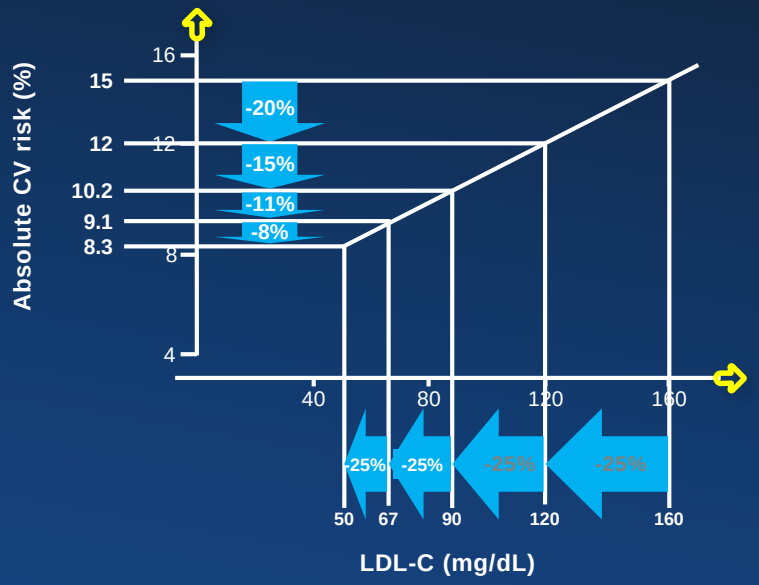
EAS ESC European Society of Cardiology



©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Relationship of LDL-C-Lowering and Risk Reduction with a Statin



– Diminishing risk reduction for the same relative LDL-C lowering

LDL-C, low-density lipoprotein cholesterol; NNT, number needed to treat.

Laufs U *et al.* Eur Heart J. 2014;35:1996-2000.

SCORE Cardiovascular Risk Chart
10-year risk of fatal CVD
High-risk regions of Europe

EAS ESC European Society of Cardiology

Systolic blood pressure (mmHg)	WOMEN Non-smoker 4	5	6	7	WOMEN Smoker 4	5	6	7	Age	MEN Non-smoker 4	5	6	7	MEN Smoker 4	5	6	7
180	12	13	14	15	17	19	20	21	70	24	26	30	33	33	36	40	45
160	10	11	12	13	14	15	16	18		20	22	25	28	27	31	34	39
140	8	9	10	10	12	13	14	15		16	18	21	24	23	26	29	33
120	7	7	8	9	10	10	11	12		13	15	17	20	19	22	25	28
180	7	8	8	9	11	12	13	15	65	15	17	20	23	23	26	30	34
160	5	6	6	7	9	9	10	11		12	14	16	18	18	21	24	27
140	4	4	5	5	7	7	8	9		9	11	12	14	14	16	19	22
120	3	3	4	4	5	5	6	7		7	8	10	11	11	13	15	17
180	4	4	5	5	7	8	9	10	60	10	11	13	15	16	19	22	25
160	3	3	3	4	5	6	6	7		7	8	10	11	12	14	16	19
140	2	2	2	3	4	4	4	5		5	6	7	8	9	10	12	14
120	1	1	2	2	3	3	3	3		4	4	5	6	6	7	9	10
180	2	2	3	3	5	5	6	7	55	6	7	9	10	11	13	16	18
160	1	2	2	2	3	3	4	4		4	5	6	7	8	9	11	13
140	1	1	1	1	2	2	2	3		3	3	4	5	5	6	7	9
120	1	1	1	1	1	1	2	2		2	2	3	3	4	4	5	6
180	1	1	2	2	3	3	4	4	50	4	5	6	7	8	9	11	13
160	1	1	1	1	2	2	2	3		2	3	3	4	5	6	7	9
140	0	0	1	1	1	1	1	2		2	2	2	3	3	4	5	6
120	0	0	0	0	1	1	1	1		1	1	1	2	2	2	3	4
180	0	0	1	1	1	1	2	2	40	2	2	2	3	4	4	5	7
160	0	0	0	0	1	1	1	1		1	1	1	2	2	2	3	4
140	0	0	0	0	0	0	0	1		0	1	1	1	1	1	2	2
120	0	0	0	0	0	0	0	0		0	0	0	1	1	1	1	1

Total cholesterol (mmol/L)

SCORE chart for European populations at high cardiovascular disease risk

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

10-year risk of fatal CVD (1)

Low-risk regions of Europe (age interactions included)

EAS ESC European Society of Cardiology

Systolic blood pressure (mmHg)	WOMEN Non-smoker				WOMEN Smoker				Age	MEN Non-smoker				MEN Smoker			
	4	5	6	7	4	5	6	7		4	5	6	7	4	5	6	7
180	7	8	8	9	11	11	12	13	70	12	14	15	17	18	20	22	24
160	6	6	7	7	9	9	10	11		10	11	13	14	15	16	18	20
140	5	5	6	6	7	8	8	9		8	9	10	12	12	13	15	17
120	4	4	5	5	6	6	7	7		7	8	9	10	10	11	12	14
180	4	4	5	5	7	7	8	9	65	8	9	10	12	12	14	16	18
160	3	3	4	4	5	6	6	7		6	7	8	9	9	11	12	14
140	2	3	3	3	4	4	5	5		5	5	6	7	7	8	9	11
120	2	2	2	2	3	3	3	4		3	4	5	5	5	6	7	8
180	2	3	3	3	4	5	5	6	60	5	6	7	8	8	10	11	13
160	2	2	2	2	3	3	4	4		4	4	5	5	6	7	8	9
140	1	1	1	2	2	2	3	3		3	3	3	4	4	5	6	7
120	1	1	1	1	2	2	2	2		2	2	2	3	3	4	4	5
180	1	1	2	2	3	3	3	4	55	3	4	4	5	6	7	8	9
160	1	1	1	1	2	2	2	3		2	2	3	3	4	4	5	6
140	1	1	1	1	1	1	1	2		1	2	2	2	3	3	3	4
120	0	0	0	1	1	1	1	1		1	1	1	2	2	2	2	3
180	1	1	1	1	2	2	2	3	50	2	2	3	3	4	5	5	6
160	0	0	1	1	1	1	1	2		1	1	2	2	2	3	3	4
140	0	0	0	0	1	1	1	1		1	1	1	1	1	2	2	3
120	0	0	0	0	0	0	0	1		0	1	1	1	1	1	1	2
180	0	0	0	0	1	1	1	1	40	1	1	1	1	2	2	3	3
160	0	0	0	0	0	0	0	1		0	0	1	1	1	1	1	2
140	0	0	0	0	0	0	0	0		0	0	0	0	1	1	1	1
120	0	0	0	0	0	0	0	0		0	0	0	0	0	0	0	1

Total cholesterol (mmol/L)

Illustration of the risk age concept

The risk of this 40 – year old male smoker with risk factors is the same (3-4%) as that of a 65 year – old man with ideal risk factor levels– therefore his risk age is 65 years.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Risk function with high-density lipoprotein cholesterol for women in populations at high cardiovascular disease risk

Age	Systolic blood pressure (mmHg)	Non-smoker: 4	5	6	7	8	Smoker: 4	5	6	7	8
65	180	7	7	8	8	9	14	14	15	16	17
	160	5	5	6	6	7	10	11	12	12	13
	140	4	4	4	5	5	8	8	9	9	10
	120	3	3	3	4	4	6	6	7	7	8
60	180	3	3	4	4	4	6	7	7	8	8
	160	2	3	3	3	3	5	5	5	6	6
	140	2	2	2	2	2	4	4	4	4	5
	120	1	1	2	2	2	3	3	3	3	4
55	180	2	2	2	2	2	4	4	4	4	5
	160	1	1	2	2	2	3	3	3	3	4
	140	1	1	1	1	1	2	2	2	2	3
	120	1	1	1	1	1	2	2	2	2	2
50	180	1	1	1	1	1	1	2	2	2	2
	160	1	1	1	1	1	1	1	1	1	2
	140	0	0	1	1	1	1	1	1	1	1
	120	0	0	0	0	0	1	1	1	1	1
40	180	0	0	0	0	0	0	0	1	1	1
	160	0	0	0	0	0	0	0	0	0	0
	140	0	0	0	0	0	0	0	0	0	0
	120	0	0	0	0	0	0	0	0	0	0

Total cholesterol (mmol/L)

Without HDL:	4.4
HDL 0.8:	8.1
HDL 1.0:	6.7
HDL 1.4:	4.5
HDL 1.8:	3.0

Without HDL:	4.2
HDL 0.8:	8.0
HDL 1.0:	6.5
HDL 1.4:	4.4
HDL 1.8:	2.9

Without HDL:	2.4
HDL 0.8:	4.6
HDL 1.0:	3.8
HDL 1.4:	2.5
HDL 1.8:	1.7

Without HDL:	5.7
HDL 0.8:	10.2
HDL 1.0:	8.5
HDL 1.4:	5.9
HDL 1.8:	4.0

Without HDL:	4.4
HDL 0.8:	8.5
HDL 1.0:	7.0
HDL 1.4:	4.7
HDL 1.8:	3.2

Without HDL:	4.5
HDL 0.8:	8.3
HDL 1.0:	6.9
HDL 1.4:	4.7
HDL 1.8:	3.2

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for cardiovascular disease risk estimation

EAS ESC European Society of Cardiology

Recommendations	Class	Level
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

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

How to use the risk estimation charts

EAS ESC European Society of Cardiology

To estimate a person's 10-year risk of cardiovascular disease (CVD) death, find the table for his/her gender, smoking status, and age. Within the table find the cell nearest to the person's blood pressure (BP) and total cholesterol (TC). Risk estimates will need to be adjusted upwards as the person approaches the next age category.

Risk is initially assessed on the level of TC and systolic BP before treatment, if known. The longer the treatment and the more effective it is, the greater the reduction in risk, but in general it will not be more than about one-third of the baseline risk. For example, for a person on antihypertensive drug treatment in whom the pre-treatment BP is not known, if the total cardiovascular (CV) SCORE risk is 6%, then the pre-treatment total CV risk may have been 9%.

Low-risk persons should be offered advice to maintain their low-risk status. While no threshold is universally applicable, the intensity of advice should increase with increasing risk.

The charts may be used to give some indication of the effects of reducing risk factors, given that there is apparently a time lag before the risk reduces. In general, people who stop smoking halve their cumulative risk over a relatively short period of time.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Risk estimation: key messages (1)

EAS ESC European Society of Cardiology

In apparently healthy persons, CVD risk is most frequently the result of multiple, interacting risk factors. This is the basis for total CV risk estimation and management.

Risk factor screening including the lipid profile should be considered in men >40 years old and in women >50 years of age or post-menopausal.

A risk estimation system such as SCORE can assist in making logical management decisions, and may help to avoid both under- and over-treatment.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Risk estimation: key messages (2)

EAS ESC European Society of Cardiology

Certain individuals declare themselves to be at high or very-high CVD risk without needing risk scoring and require immediate attention to all risk factors. This is true for patients with documented CVD, diabetes, familial hypercholesterolaemia, chronic kidney disease, carotid or femoral plaques, coronary artery calcium (CAC) score >100, or extreme Lp(a) elevation.

All risk estimation systems are relatively crude and require attention to qualifying statements.

Additional factors affecting risk can be accommodated in electronic risk estimation systems such as HeartScore (www.heartscore.org).

The total risk approach allows flexibility – if optimal control cannot be achieved with one risk factor, trying harder with the other factors can still reduce risk.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Cardiovascular risk categories (1)

EAS ESC European Society of Cardiology

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, ≥3 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.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Cardiovascular risk categories (2)

EAS ESC European Society of Cardiology

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 factors. 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.

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

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for lipid analyses for cardiovascular disease risk estimation (1)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
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 for screening, diagnosis and management.	I	C
TG analysis is recommended as a part of the routine lipid analysis.	I	C

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

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

EAS ESC European Society of Cardiology

Recommendations	Class	Level
Non-HDL-C evaluation is recommended for risk assessment, particularly in people with high TG, diabetes, obesity or very low LDL-C.	I	C
ApoB analysis is recommended for risk assessment, 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

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for lipid analyses for cardiovascular disease risk estimation (3)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
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

© ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for cardiovascular imaging for risk assessment of atherosclerotic cardiovascular disease

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

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Intervention strategies as a function of total cardiovascular risk and untreated low-density lipoprotein cholesterol levels

EAS ESC European Society of Cardiology

	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	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	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	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

www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Intervention strategies as a function of total cardiovascular risk and untreated low-density lipoprotein cholesterol levels

ESC
European Society of Cardiology
EAS

Treatment targets and goals for cardiovascular disease prevention (1)

EAS ESC European Society of Cardiology

Smoking	No exposure to tobacco in any form.
Diet	Healthy diet low in saturated fat with a focus on whole grain products, vegetables, fruit and fish.
Physical activity	3.5–7 hours moderately vigorous physical activity per week or 30–60 min most days.
Body weight	BMI 20–25 kg/m^2, waist circumference <94 cm (men) and <80 cm (women).
Blood pressure	<140/90 mmHg[a]

© ESC

[a] Lower treatment targets are recommended for most treated hypertensive patients, provided that the treatment is well tolerated.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Treatment targets and goals for cardiovascular disease prevention (3)

EAS ESC European Society of Cardiology

LDL-C	**Moderate-risk:** A goal of <2.6 mmol/L (<100 mg/dL). **Low-risk:** A goal of <3.0 mmol/L (<116 mg/dL)
Non-HDL-C	Non-HDL-C secondary goals are <2.2, 2.6 and 3.4 mmol/L (<85, 100 and 130 mg/dL) for very-high-, high- and moderate-risk people, respectively.
Apolipoprotein B	ApoB secondary goals are <65, 80 and 100 mg/dL for very-high-, high- and moderate-risk people, respectively.
Triglycerides	No goal but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
Diabetes	HbA1c: <7% (<53 mmol/mol).

© ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for treatment goals for low-density lipoprotein cholesterol (1)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
In secondary prevention patients at very-high risk[c], an LDL-C reduction of at least 50% from baseline[d] 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 but without FH[c], an LDL-C reduction of at least 50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.	I	C
In primary prevention, for individuals with FH at very-high risk, an LDL-C reduction of at least 50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C

[c]For definitions see Table 1.
[d]The term 'baseline' refers to the LDL-C level in a person not taking any LDL-C lowering medication. In people who are taking LDL-C-lowering medication(s), the projected baseline (untreated) LDL-C levels should be estimated, based on the average LDL-C-lowering efficacy of the given medication or combination of medications.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for treatment goals for low-density lipoprotein cholesterol (2)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
For patients 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 therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.	IIb	B
In patients at high-risk[c], an LDL-C reduction of at least 50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.	I	A

©ESC

[c] For definitions see Table 1.
[d] The term 'baseline' refers to the LDL-C level in a person not taking any LDL-C lowering medication. In people who are taking LDL-C-lowering medication(s), the projected baseline (untreated) LDL-C levels should be estimated, based on the average LDL-C-lowering efficacy of the given medication or combination of medications.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for treatment goals for low-density lipoprotein cholesterol (3)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
In individuals at moderate risk[c], an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.	IIa	A
In individuals at low risk[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.	IIb	A

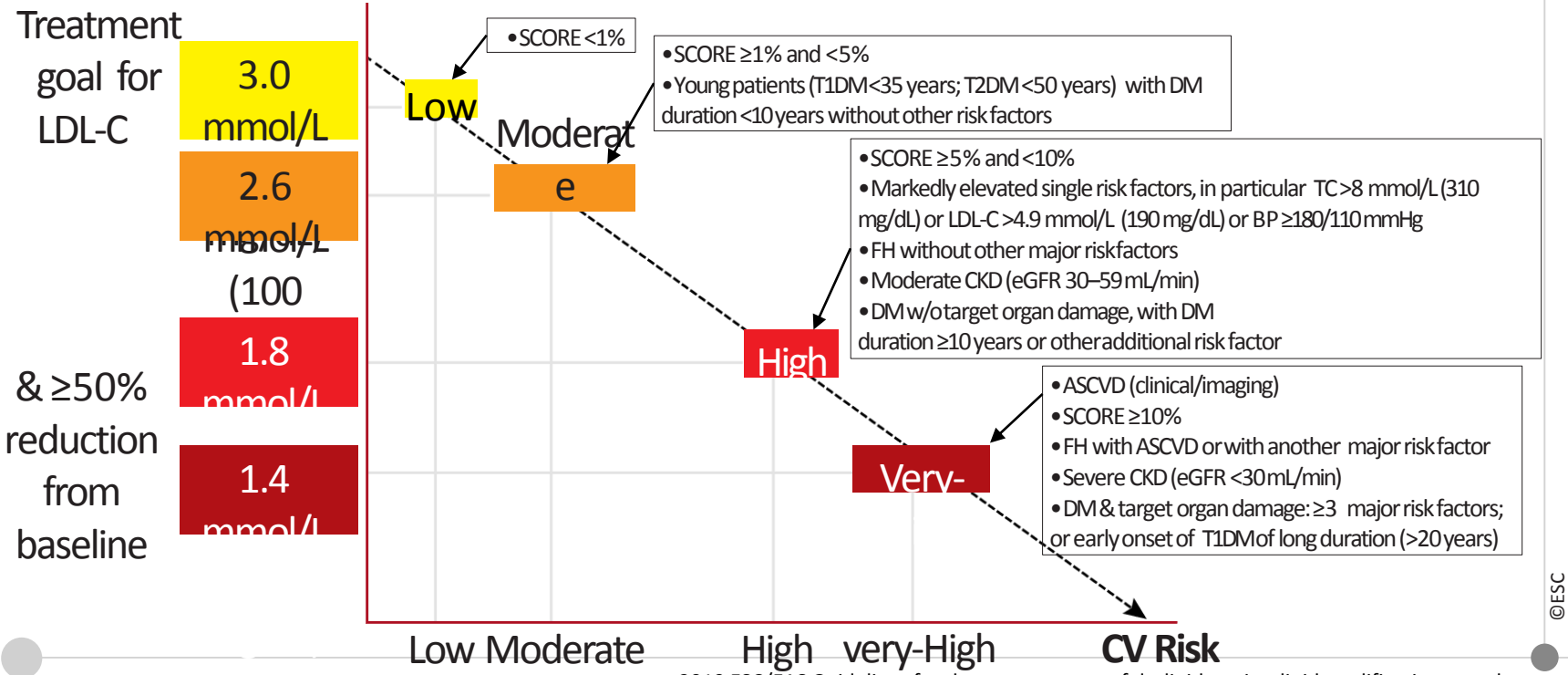
©ESC

[c] For definitions see Table 1.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

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

EAS ESC European Society of Cardiology



©ESC

www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Summary of lifestyle measures and healthy food choices for managing total cardiovascular risk (1)

EAS ESC European Society of Cardiology

Dietary recommendations should always take into account local food habits; however, interest in healthy food choices from other cultures should be promoted.

A wide variety of foods should be eaten. Energy intake should be adjusted to prevent overweight and obesity.

Consumption of fruits, vegetables, legumes, nuts, wholegrain cereal foods and fish (especially oily) should be encouraged.

Foods rich in trans fatty acids should be avoided totally; foods rich in saturated fatty acids (SFAs) (tropical oils, fatty or processed meat, sweets, cream, butter, regular cheese) should be replaced with the above foods and with monounsaturated fat (extra virgin olive oil) and polyunsaturated fat (non-tropical vegetable oils) in order to keep SFA intake <10% (<7% in the presence of high plasma cholesterol values).

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Summary of lifestyle measures and healthy food choices for managing total cardiovascular risk (2)

EAS ESC European Society of Cardiology

Salt intake should be reduced to <5 g/day by avoiding table salt and limiting salt in cooking, and by choosing fresh or frozen unsalted foods; many processed and convenience foods, including bread, are high in salt.

For those who drink alcoholic beverages, moderation should be advised (<10 g/day for women and for men) and patients with hypertriglyceridaemia should abstain.

The intake of beverages and foods with added sugars, particularly soft drinks, should be discouraged, especially for persons who are overweight, have hypertriglyceridaemia, metabolic syndrome or diabetes.

Physical activity should be encouraged, aiming at regular physical exercise for at least 30 min/day every day.

Use of and exposure to tobacco products should be avoided.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for pharmacological low-density lipoprotein cholesterol lowering (1)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
It is recommended to prescribe a high-intensity statin up to the highest tolerated dose to reach the goals[c] set for the specific level of risk.	I	A
If the goals[c] are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.	I	B
For primary prevention patients at very-high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.	IIb	C

©ESC

[c] For definitions see Full Text.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for pharmacological low-density lipoprotein cholesterol lowering (2)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
For secondary prevention, patients at very-high risk not achieving their goal[c] on a maximum tolerated dose of 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 statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.	I	C
If a statin-based regimen is not tolerated at any dosage (even after re-challenge), ezetimibe should be considered.	IIa	C

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for pharmacological low-density lipoprotein cholesterol lowering (3)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
If a statin-based regimen is not tolerated at any dosage (even after re-challenge), a PCSK9 inhibitor added to ezetimibe may also be considered.	IIb	C
If the goal[c] is not achieved, statin combination with a bile acid sequestrant may be considered.	IIb	C

[c] For definitions see Full Text.

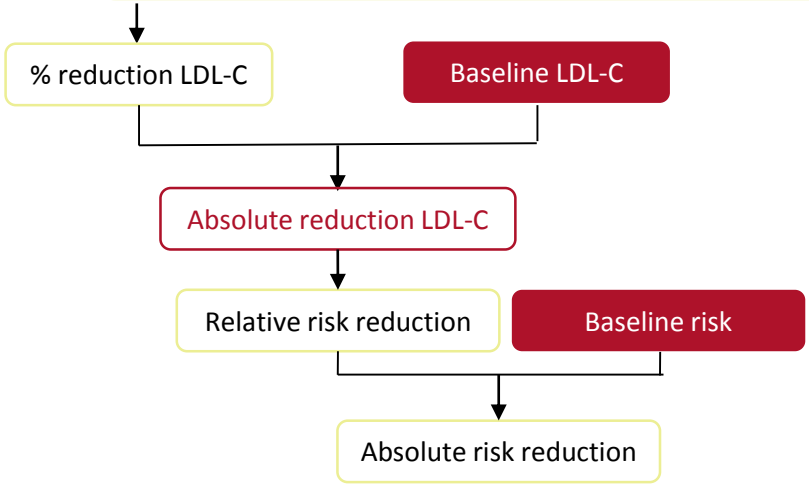
©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Expected clinical benefit of low-density lipoprotein cholesterol lowering therapies

Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%



LDL-C = low-density lipoprotein cholesterol;
PCSK9 = proprotein convertase subtilisin/kexin type 9.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Achievable reductions of low-density lipoprotein cholesterol as a function of the therapeutic approach

EAS ESC European Society of Cardiology

LDL-C, mmol/L (mg/dL)	Reduction obtainable with different therapeutic strategies				
	Moderate-intensity statins		High-intensity statins		PCSK9 inhibitor plus high-intensity statin
		Plus ezetimibe		Plus ezetimibe	
4.5	3.2	2.5	2.3	1.6	0.9
(175)	(123)	(96)	(88)	(61)	(35)
4.3	3.0	2.4	2.2	1.5	0.9
(165)	(116)	(91)	(83)	(58)	(33)
4.0	2.8	2.2	2.0	1.4	0.8
(155)	(109)	(85)	(78)	(54)	(31)
3.7	2.6	2.0	1.9	1.3	0.7
(145)	(102)	(80)	(73)	(51)	(29)
3.5	2.5	1.9	1.8	1.2	0.7
(135)	(95)	(74)	(68)	(47)	(27)
3.2	2.2	1.8	1.6	1.1	0.6
(125)	(88)	(69)	(63)	(44)	(25)
3.0	2.1	1.7	1.5	1.1	0.6
(116)	(81)	(63)	(58)	(40)	(23)
2.7	1.9	1.5	1.4	0.9	0.5
(105)	(74)	(58)	(53)	(37)	(21)
2.5	1.8	1.4	1.3	0.9	0.5
(95)	(67)	(52)	(48)	(33)	(19)
2.2	1.5	1.2	1.1	0.8	0.4
(85)	(60)	(47)	(43)	(30)	(17)
1.9	1.3	1.0	1.0	0.7	0.4
(75)	(53)	(41)	(38)	(26)	(15)

LDL-C = low-density lipoprotein cholesterol; PCSK9 = proprotein convertase subtilisin/kexin type 9.

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

EAS ESC European Society of Cardiology

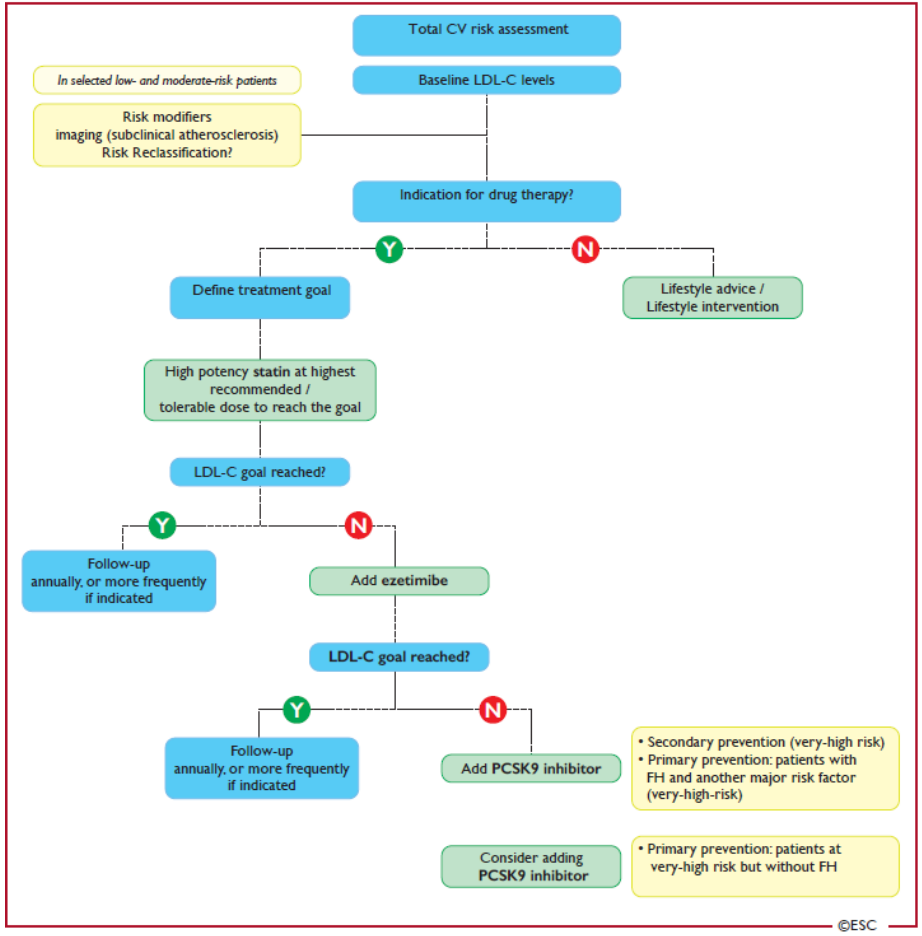
LDL-C on optimized Rx (mmol/L; mg/dL)	RRR	10%	20%	30%	40%
5.0 194	53%	38	25	19	15	13	10	9
4.0 155	45%	44	30	22	18	15	13	11
3.0 114	36%	56	37	28	22	19	16	14
2.0 77	26%	77	51	38	31	26	22	19

Absolute risk over 10 years

NNT (>5 years) as function of estimated 10-year risk of ACVE, starting LDL-C (on optimized statin/ezetimibe therapy), and average relative risk reduction associated with LDL-C drop of 60%

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)



EAS ESC
European Society
of Cardiology

Treatment algorithm for pharmacological LDL-C lowering

©ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for drug treatments of patients with hypertriglyceridaemia (1)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
Statin treatment is recommended 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
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.	IIa	B

© ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for drug treatments of patients with hypertriglyceridaemia (2)

EAS ESC European Society of Cardiology

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

© ESC

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Intervention strategies as a function of total cardiovascular risk and untreated low-density lipoprotein cholesterol levels

EAS ESC European Society of Cardiology

	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	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	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	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

www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)