Training course: Pharmacotherapy in Older People

Lipid lowering agent selection in the elderly

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Receipt of grants/research supports:	
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Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins

*Cholesterol Treatment Trialists' (CTT) Collaborators**

Summary

Background Results of previous randomised trials have shown that interventions that lower LDL cholesterol concentrations can significantly reduce the incidence of coronary heart disease (CHD) and other major vascular events in a wide range of individuals. But each separate trial has limited power to assess particular outcomes or particular categories of participant.

Methods A prospective meta-analysis of data from 90 056 individuals in 14 randomised trials of statins was done. Weighted estimates were obtained of effects on different clinical outcomes per 1·0 mmol/L reduction in LDL cholesterol.

Lancet 2005; 366: 1267–78

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Cholesterol Treatment Trialists' (CTT) Collaborators Lancet 2005; 366: 1267-78.

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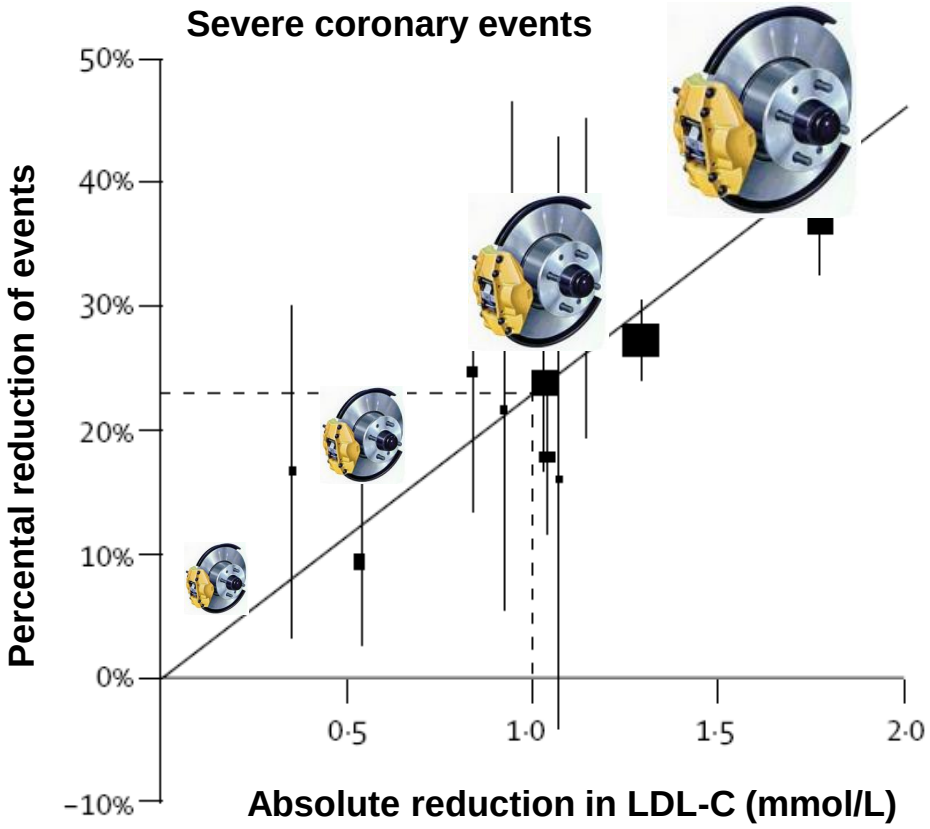
LDL-Reduction and Coronary Events: The lower, the better



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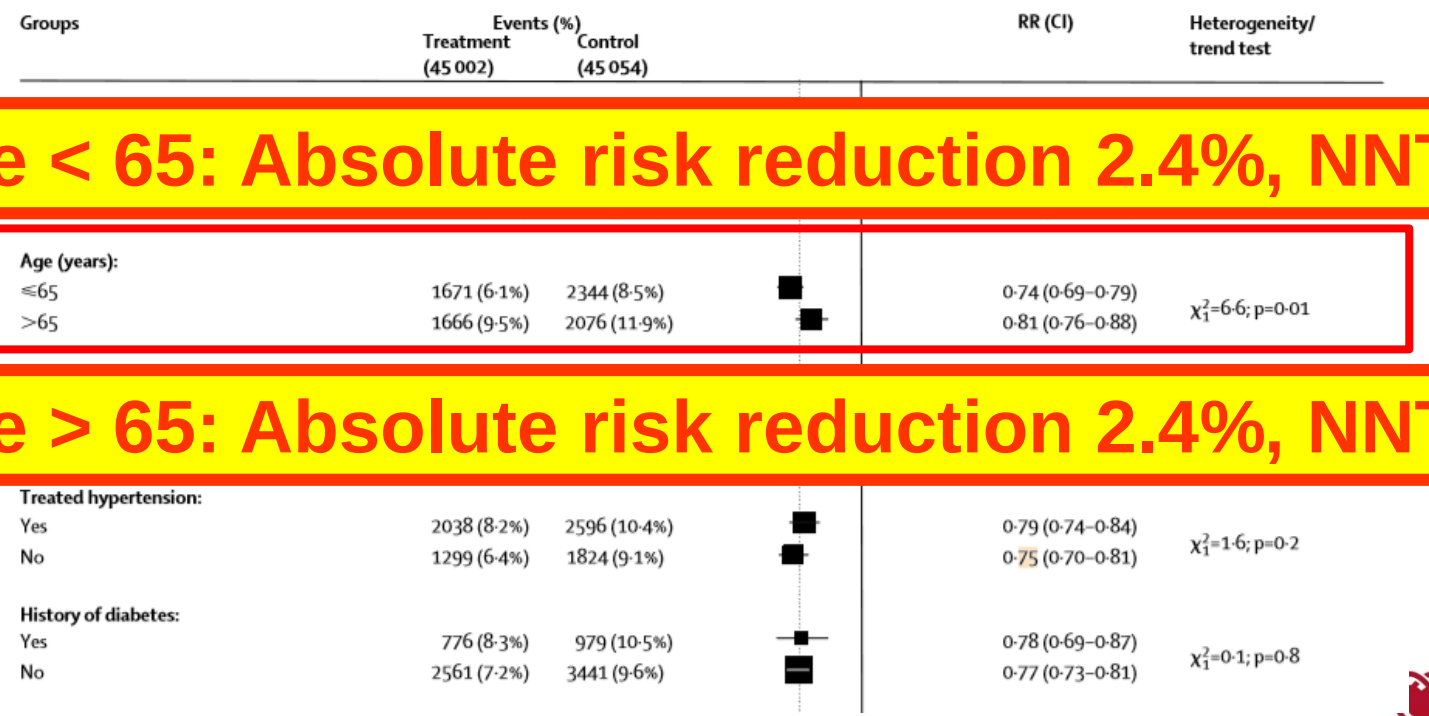
Effects on major coronary events per mmol/L LDL cholesterol reduction subdivided by baseline prognostic factors



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Cholesterol Treatment Trialists' (CTT) Collaborators Lancet 2005; 366: 1267-78.

Circulation

CHOLESTEROL CLINICAL PRACTICE GUIDELINES

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

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2018 AHA/ACC Guidelines on the Management of Blood Cholesterol

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2018 AHA/ACC Guidelines on the Management of Blood Cholesterol
Recommendations for Statin Therapy in Patients with ASCVD

COR	LOE	Recommendations
		6. At mid-2018 list prices, PCSK9 inhibitors
IIa	B-R	7. In patients older than 75 years of age with clinical ASCVD, it is reasonable to initiate moderate- or high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug–drug interactions, as well as patient frailty and patient preferences.[S4.1-23–S4.1-31]
IIa	C-LD	8. In patients older than 75 years of age who are tolerating high-intensity statin therapy, it is reasonable to continue high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug-drug interactions, as well as patient frailty and patient preferences.[S4.1-3,S4.1-10,S4.1-23,S4.1-26,S4.1-31–S4.1-36]
		moderate-intensity statin therapy to reduce the occurrence of ASCVD events.[S4.1-37]

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ESC/EAS Guidelines on Dyslipidaemia 2019

ESC European Society of Cardiology

European Heart Journal (2019) **00**, 1–78
doi:10.1093/eurheartj/ehz455

ESC/EAS GUIDELINES

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

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Authors/Task Force Members: François Mach* (Chairperson) (Switzerland), Colin Baigent* (Chairperson) (United Kingdom), Alberico L. Catapano[1]* (Chairperson) (Italy), Konstantinos C. Koskinas (Switzerland), Manuela Casula[1] (Italy), Lina Badimon (Spain), M. John Chapman[1] (France), Guy G. De Backer (Belgium), Victoria Delgado (Netherlands), Brian A. Ference (United Kingdom), Ian M. Graham (Ireland), Alison Halliday (United Kingdom), Ulf Landmesser (Germany), Borislava Mihaylova (United Kingdom), Terje R. Pedersen (Norway), Gabriele Riccardi[1] (Italy), Dimitrios J. Richter (Greece), Marc S. Sabatine (United States of America), Marja-Riitta Taskinen[1] (Finland), Lale Tokgozoglu[1] (Turkey), Olov Wiklund[1] (Sweden)

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Mach F et al. Eur Heart J 2019.

New recommendations (2)

EAS ESC European Society of Cardiology

Drug treatments of patients with hypertriglyceridaemia
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 2g/day) should be considered in combination with statins.

Treatment of patients with heterozygous FH
In primary prevention, for individuals with FH 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) should be considered.

Treatment of dyslipidaemias in older people
Treatment with statins is recommended for primary prevention, according to the level of risk, in older people aged ≤75.

Treatment of dyslipidaemias in older people
Initiation of statin treatment for primary prevention in older people aged >75 may be considered, if at high risk or above.

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

Low-risk regions of Europe (age interactions included)

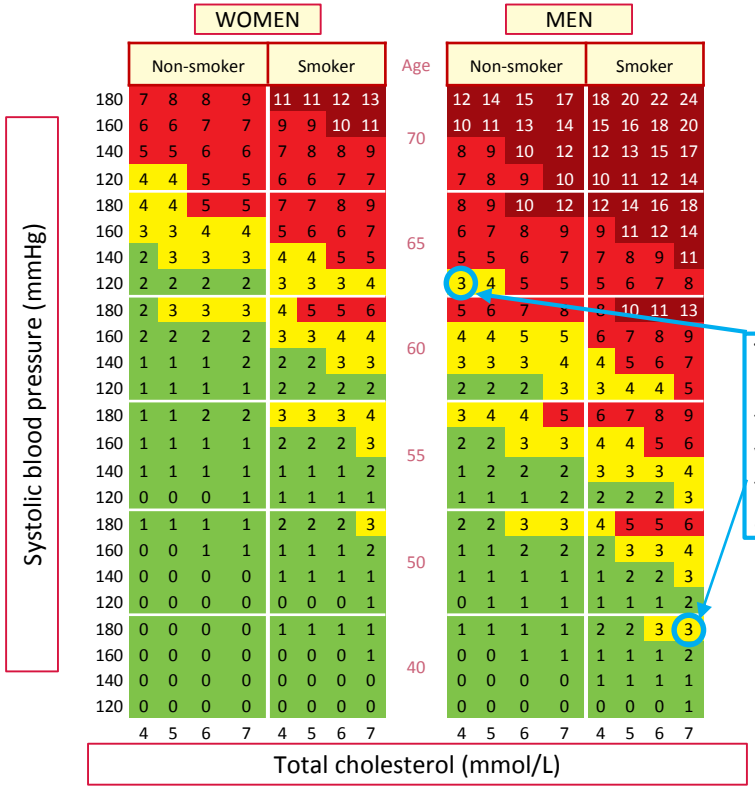

Illustration of the risk age concept

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.

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.

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

[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

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 the treatment of dyslipidaemias in older people (aged >65 years)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
Treatment with statins is recommended for older people with ASCVD in the same way as for younger patients.	I	A
Treatment with statins is recommended for primary prevention, according to level of risk, in older people aged ≤ 75.	I	A
Initiation of statin treatment for primary prevention in older people aged > 75 may be considered, if at high risk or above.	IIb	B
It is recommended that the statin is started at a low dose if there is significant renal impairment and/or the potential for drug interactions, and then titrated upwards to achieve LDL-C treatment goals.	I	C

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 the management of dyslipidaemias in patients with severe mental illness

EAS ESC European Society of Cardiology

Recommendations	Class	Level
It is recommended that SMI is used as a modifier for estimating total ASCVD risk.	I	C
It is recommended that the same guidelines for the management of total ASCVD risk are used in patients with SMI as are used in patients without such disease.	I	C
It is recommended that in patients with SMI intensified attention is paid to adherence to lifestyle changes and to compliance with drug treatment.	I	C

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

Lipid lowering agent selection in the elderly
Conclusions

1. Guidelines set an arbitrary age cut-off: 75 y
2. Absolute risk increases with age
3. Absolute risk reduction > 65 y is equal to < 65 y
4. Start of therapy at old age is at lower dosage,
5. Evidence level for that is C

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A Case Approach

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Achievable reductions of low-density lipoprotein cholesterol as a function of the therapeutic approach (1)

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Starting LDL-C, mmol/L (mg/dL)	Achievable LDL-C levels with different therapeutic strategies				
	Moderate-intensity statins		High-intensity statins		PCSK9 inhibitor plus high- intensity statin
		Plus ezetimibe		Plus ezetimibe	
4.5 (175)	3.2 (123)	2.5 (96)	2.3 (88)	1.6 (61)	0.9 (35)
4.3 (165)	3.0 (116)	2.4 (91)	2.2 (83)	1.5 (58)	0.9 (33)

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

Training course:
Pharmacotherapy in Older People

Thank you!

Lipid lowering agent selection in the elderly

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Achievable reductions of low-density lipoprotein cholesterol as a function of the therapeutic approach (2)

EAS ESC European Society of Cardiology

Starting LDL-C, mmol/L (mg/dL)	Achievable LDL-C levels with different therapeutic strategies				
	Moderate-intensity statins		High-intensity statins		PCSK9 inhibitor plus high- intensity statin
		Plus ezetimibe		Plus ezetimibe	
4.0 (155)	2.8 (109)	2.2 (85)	2.0 (78)	1.4 (54)	0.8 (31)
3.7 (145)	2.6 (102)	2.0 (80)	1.9 (73)	1.3 (51)	0.7 (29)

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 (3)

Starting LDL-C, mmol/L (mg/dL)	Achievable LDL-C levels with different therapeutic strategies				
	Moderate-intensity statins		High-intensity statins		PCSK9 inhibitor plus high- intensity statin
		Plus ezetimibe		Plus ezetimibe	
3.5 (135)	2.5 (95)	1.9 (74)	1.8 (68)	1.2 (47)	0.7 (27)
3.2 (125)	2.2 (88)	1.8 (69)	1.6 (63)	1.1 (44)	0.6 (25)

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 (4)

Starting LDL-C, mmol/L (mg/dL)	Achievable LDL-C levels with different therapeutic strategies				
	Moderate-intensity statins		High-intensity statins		PCSK9 inhibitor plus high- intensity statin
		Plus ezetimibe		Plus ezetimibe	
3.0 (116)	2.1 (81)	1.7 (63)	1.5 (58)	1.1 (40)	0.6 (23)
2.7 (105)	1.9 (74)	1.5 (58)	1.4 (53)	0.9 (37)	0.5 (21)

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 (5)

EAS ESC European Society of Cardiology

Starting LDL-C, mmol/L (mg/dL)	Achievable LDL-C levels with different therapeutic strategies				
	Moderate-intensity statins		High-intensity statins		PCSK9 inhibitor plus high- intensity statin
		Plus ezetimibe		Plus ezetimibe	
2.5 (95)	1.8 (67)	1.4 (52)	1.3 (48)	0.9 (33)	0.5 (19)
2.2 (85)	1.5 (60)	1.2 (47)	1.1 (43)	0.8 (30)	0.4 (17)

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 (6)

EAS ESC European Society of Cardiology

Starting LDL-C, mmol/L (mg/dL)	Achievable LDL-C levels with different therapeutic strategies				
	Moderate-intensity statins		High-intensity statins		PCSK9 inhibitor plus high- intensity statin
		Plus ezetimibe		Plus ezetimibe	
1.9 (75)	1.3 (53)	1.0 (41)	1.0 (38)	0.7 (26)	0.4 (15)

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

Training course:

Pharmacotherapy in [illegible] People

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Cardiovascular risk categories (1)

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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.

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)

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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

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