

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

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La dr./sa **Manuela Casula** dichiara
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ESC Classes of recommendations

	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 Levels of evidence

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.

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Risk estimation

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.

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

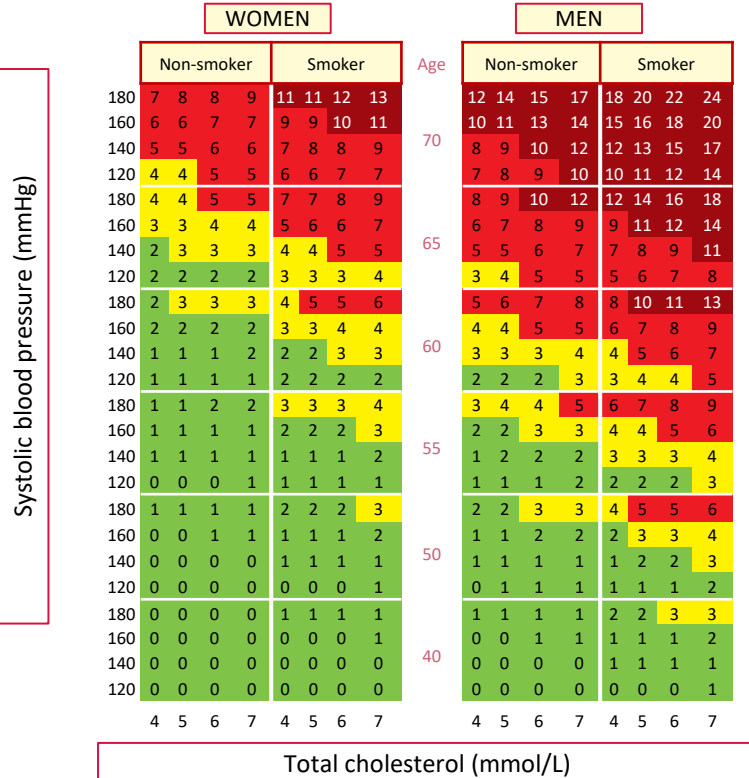
SCORE Cardiovascular Risk Chart

10-year risk of fatal CVD

Low-risk regions of Europe

SCORE chart for European populations at low cardiovascular disease risk

 <3%  3-4%  5-9%  ≥10%



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.

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, 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 m²).

A calculated SCORE ≥10% for 10-year risk of fatal CVD.

FH with ASCVD or with another major risk factor.

Cardiovascular risk categories (2)

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 ≥180/110mmHg. 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 m²). 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

Treatment targets and goals for cardiovascular disease prevention (1)

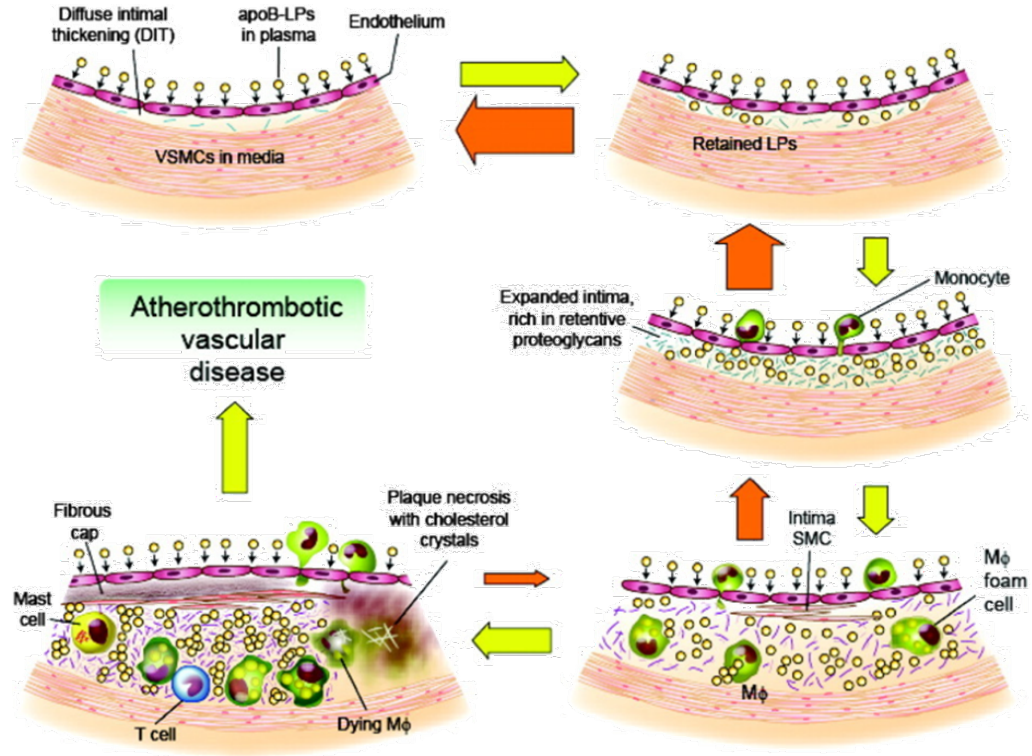
Smoking	No exposure to tobacco in any form.
Diet	Healthy diet low in saturated fat with a focus on whole grain products, vegetables, fruit and fish.
Physical activity	3.5–7 hours moderately vigorous physical activity per week or 30–60 min most days.
Body weight	BMI 20–25 kg/m ² , waist circumference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

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

Low-density lipoproteins **cause** atherosclerotic cardiovascular disease

Plausibility

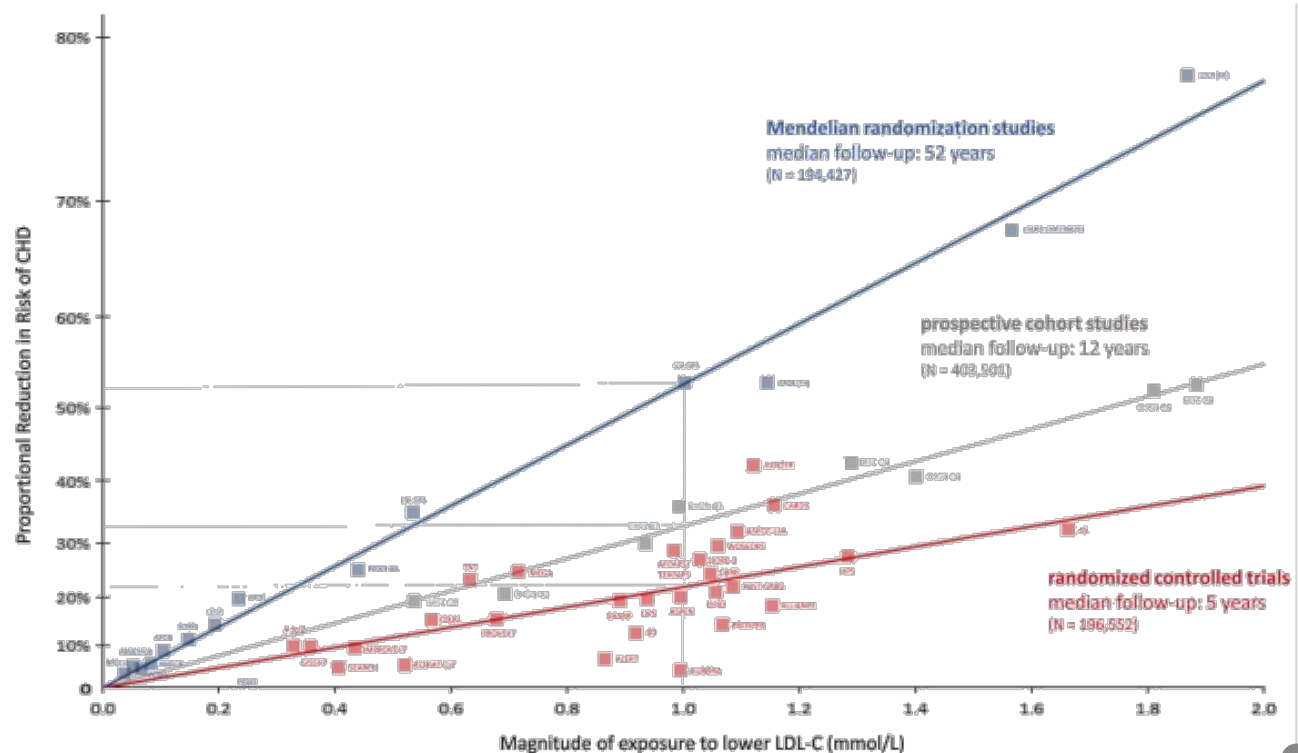
LDL and other apolipoprotein (apo) B-containing lipoproteins are directly implicated in the initiation and progression of ASCVD



Low-density lipoproteins cause atherosclerotic cardiovascular disease

Strength and Biological gradient

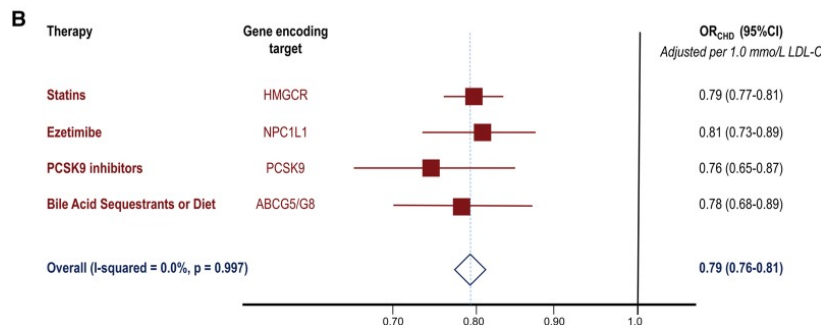
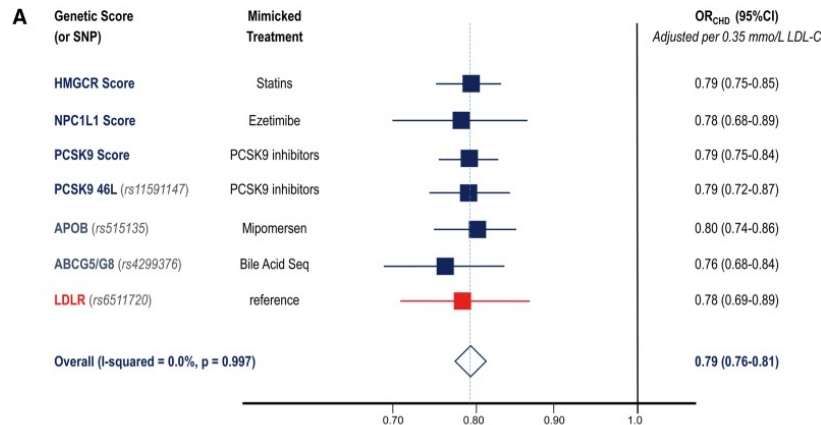
Monogenic lipid disorders, prospective cohort studies, Mendelian randomization studies, and randomized intervention trials uniformly demonstrate a dose-dependent, log-linear association between the absolute magnitude of exposure to LDL and risk of ASCVD



Low-density lipoproteins cause atherosclerotic cardiovascular disease

Consistency

Over 200 studies involving more than 2 million participants with over 20 million person-years of follow-up and more than 150 000 cardiovascular events consistently demonstrate a dose-dependent, log-linear association between the absolute magnitude of exposure to LDL and risk of ASCVD



Treatment targets and goals for cardiovascular disease prevention (2)

LDL-C

Very-high-risk in primary or secondary prevention: A therapeutic regimen that achieves at least a 50% LDL-C reduction from baseline^b and an LDL-C goal of <1.4 mmol/L (<55 mg/dL).

No current statin use: this is likely to require high-intensity LDL-lowering therapy.

Current LDL-lowering treatment: an increased treatment intensity is required.

High risk: A therapeutic regimen that achieves at least a 50% LDL-C reduction from baseline^b and an LDL-C goal of <1.8 mmol/L (<70 mg/dL).

Moderate risk: A goal of <2.6 mmol/L (<100 mg/dL).

Low risk: A goal of <3.0 mmol/L (<116 mg/dL)

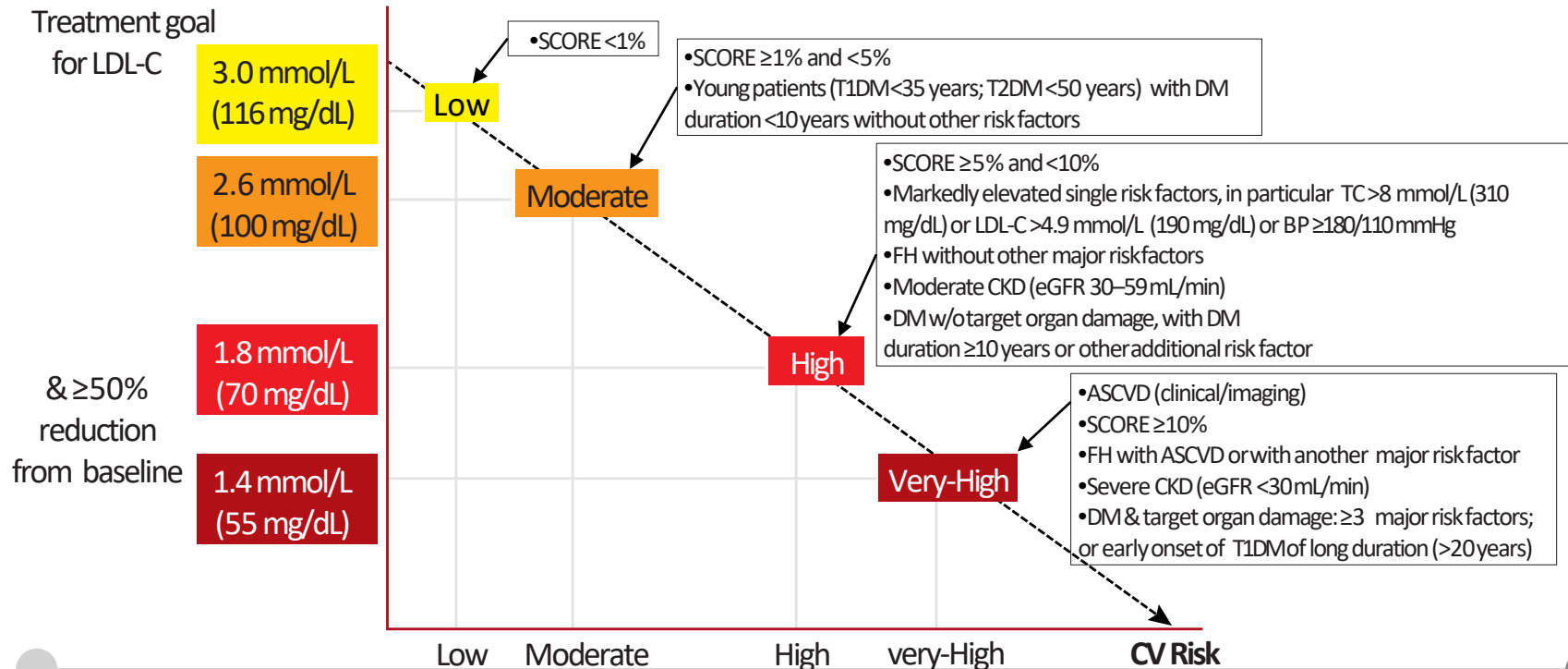
^bThe term 'baseline' refers to the LDL-C level in a person not taking any lipid lowering medication, or to the extrapolated baseline value for those who are on current treatment.

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

EAS



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European Society
of Cardiology



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

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

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.

Treatment targets and goals for cardiovascular disease prevention (3)

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).

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

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 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

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

Recommendations	Class	Level
For secondary prevention, patients at very-high risk not achieving their goal 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.	Ila	C

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

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 is not achieved, statin combination with a bile acid sequestrant may be considered.	IIb	C

Recommendations for the treatment of dyslipidaemias in diabetes (1)

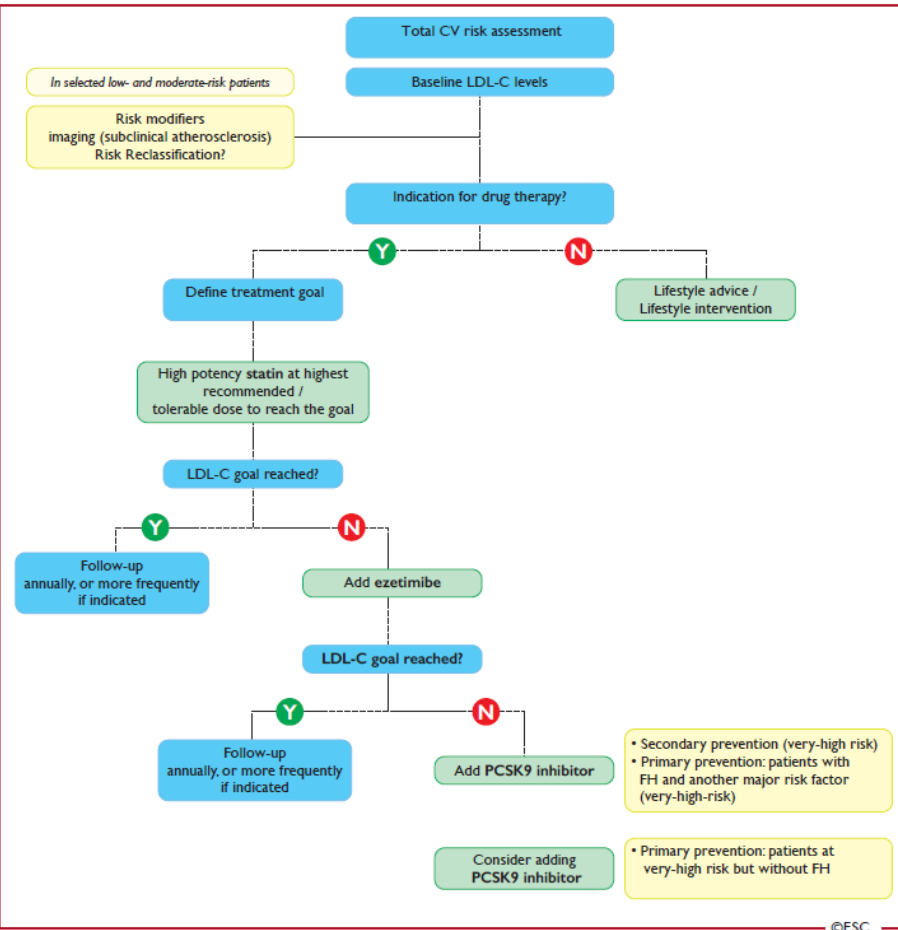
Recommendations	Class ^a	Level ^b
In patients with T2DM at very-high-risk^c , an LDL-C reduction of at least 50% from baseline and LDL-C goal of <1.4 mmol/L (<55 mg/dL) is recommended.	I	A
In patients with T2DM at high-risk^c an LDL-C reduction of at least 50% from baseline and an LDL-C goal of <1.8 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

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^c See Table in Full Text.

Recommendations for the treatment of dyslipidaemias in diabetes (1)

Recommendations	Class ^a	Level ^b
Intensification of statin therapy should be considered before the introduction of combination therapy.	IIa	C
If the goal is not reached, statin combination with ezetimibe should be considered.	IIa	B
Statin therapy is not recommended in pre-menopausal patients with diabetes who are considering pregnancy or not using adequate contraception.	III	C
Statin therapy may be considered in both T1DM and T2DM patients under the age of 30 years with evidence of end organ damage and/or LDL-C >2.5 mmol/L as long as pregnancy is not being planned.	IIb	C



Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering

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Thanks