

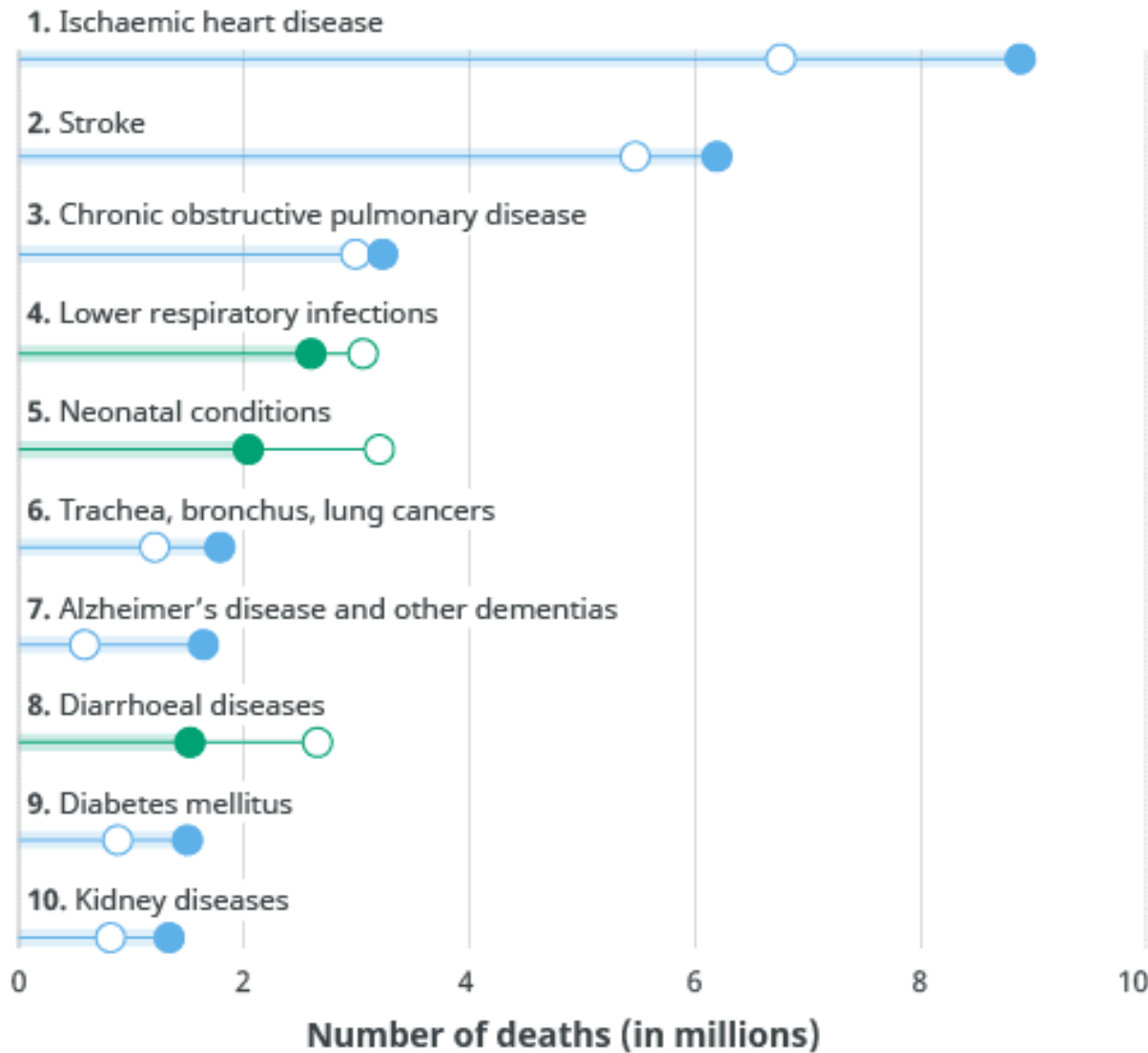


AtheroSclerotic CardioVascular Disease Prevention

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Leading causes of death globally

○ 2000 ● 2019



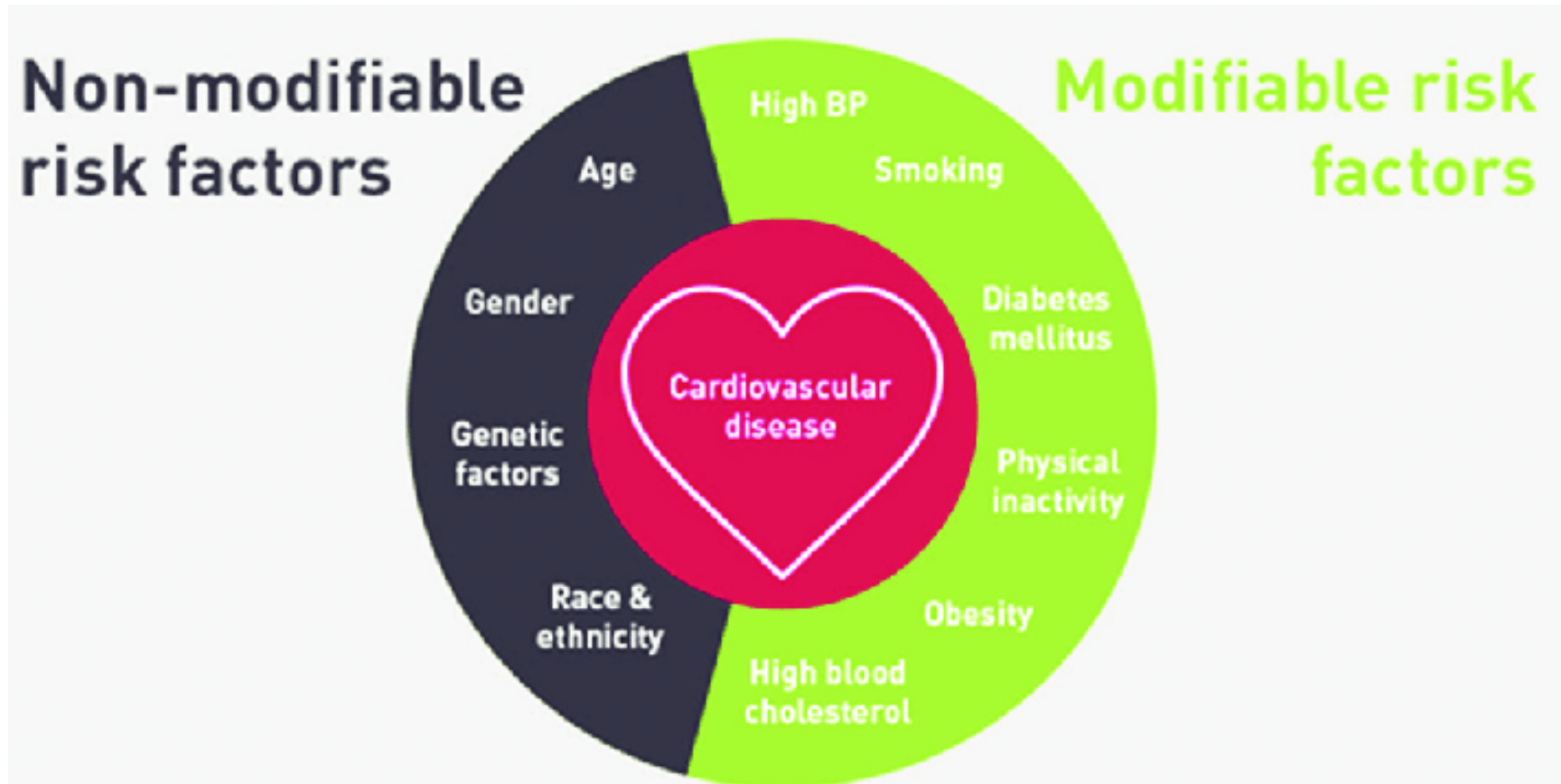
● Noncommunicable ● Communicable ● Injuries







Risk Factors for Cardiovascular Disease



Leading Global Risks For Mortality In The World

	Risk factor	Deaths (millions)	Percentage of total
	<i>World</i>		
1	High blood pressure	7.5	12.8
2	Tobacco use	5.1	8.7
3	High blood glucose	3.4	5.8
4	Physical inactivity	3.2	5.5
5	Overweight and obesity	2.8	4.8
6	High cholesterol	2.6	4.5
7	Unsafe sex	2.4	4.0
8	Alcohol use	2.3	3.8
9	Childhood underweight	2.2	3.8
10	Indoor smoke from solid fuels	2.0	3.3



When to assess total cardiovascular risk?

Recommendations	Class	Level
Systematic CV risk assessment is recommended in individuals at increased CV risk, i.e., with family history of premature CVD, familial hyperlipidemia, major CV risk factors (such as smoking, high BP, DM or raised lipid levels) or comorbidities increasing CV risk.	I	C
It is recommended to repeat CV risk assessment every 5 years, and more often for individuals with risks close to thresholds mandating treatment.	I	C
Systematic CV risk assessment may be considered in men >40 years of age and in women >50 years of age or post-menopausal with no known CV risk factors.	IIb	C
Systematic CV risk assessment in men <40 of age and women <50 years of age with no known CV risk factors is not recommended.	III	C



How to estimate total cardiovascular risk?

ASCVD Risk Estimator Plus App



Estimate a patient's initial 10-year ASCVD risk using the pooled cohort equation



ESC CVD Risk Calculation App



The SCORE system estimates the 10 year risk of a first fatal atherosclerotic event

ESC Pocket Guidelines App

Anytime - Anywhere



- All ESC Pocket Guidelines
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 - Algorithms
 - Calculators
 - Charts & Scores
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- Online & Offline

Learn more in the Guidelines area



ASCVD Risk Estimator Plus



AMERICAN
COLLEGE *of*
CARDIOLOGY*





Case Study

- 50 y/o smoker man
- Chol = 300 / LDL = 130 / HDL = 45 / TG = 210
- BP = 125 / 75
- No history of DM
- No history of CVD



10 years ASCVD risk calculator

Baseline Risk	Updated Risk
Gender	☒ Male ☐ Female
Age (years)	50
Race	Asian / Pacific Islander - East Asian
Total Cholesterol	200
LDL Cholesterol	130
HDL Cholesterol	45



10 years ASCVD risk calculator

Treatment With Statin

☐

Systolic Blood Pressure

125

Treatment For Hypertension

☐

History Of Diabetes

☐

Current Smoker

☒

Aspirin Therapy

☐

8.2%

Baseline 10 years ASCVD Risk

Calculate Baseline Risk



10 years ASCVD risk calculator

Low-risk (<5%)

Borderline risk (5% to 7.4%)

Intermediate risk (7.5% to 19.9%)

High risk ($\geq 20\%$)



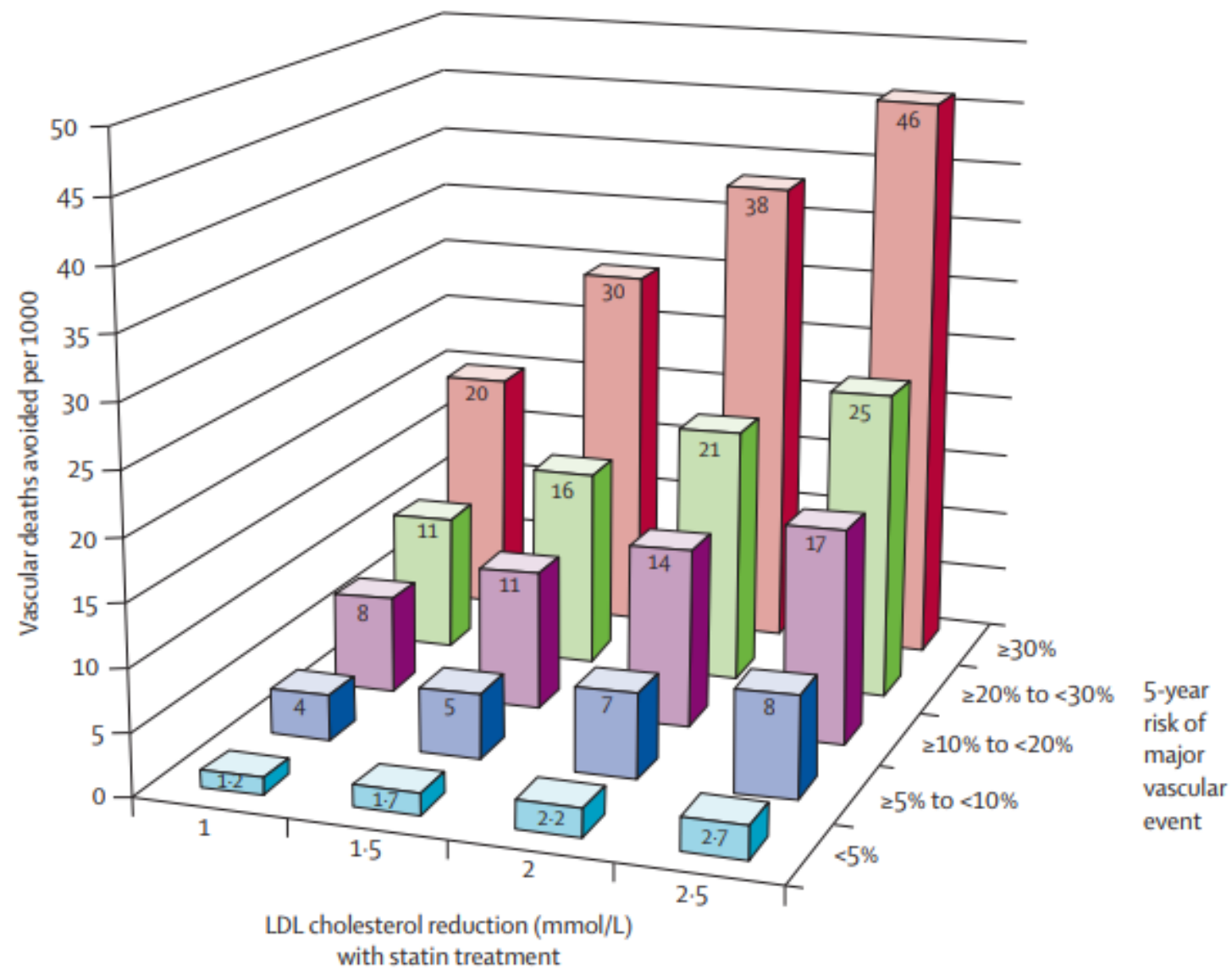
Cholesterol and CV risk

- Serum cholesterol and its lipoprotein carriers (LDL, VLDL, and HDL) are known to be related to ASCVD.
- Although LDL-C is a primary cause of atherosclerosis, other risk factors contribute, as well. The major risk factors include:
 - Cigarette smoking
 - Hypertension
 - Dysglycemia
 - Lipoprotein abnormalities
 - Age



Cholesterol and CV risk

- Throughout the range of LDL-C levels, '**lower is better**' with no lower threshold, at least down to 1 mmol/L.
- Lowering LDL-C may yield worthwhile benefits in patients with average or below average LDL-C who are already receiving LDL-C-lowering treatment.
- The proportional reduction in ASCVD risk achieved by lowering LDL-C (e.g. with a statin, ezetimibe, or PCSK9-inhibitor) depends on the absolute reduction in LDL-C, with each 1 mmol/L reduction corresponding to a reduction of about one-fifth in ASCVD.





Lipid Lowering Agents

- **Statins (HMG-CoA reductase inhibitors)**
 - Prevent the production of cholesterol in the liver. Their major effect is to lower LDL cholesterol. Some names are **lovastatin**, **pravastatin**, **simvastatin**, **fluvastatin**, **atorvastatin** and **rosuvastatin**.
- **other drugs**
 - **Bile acid binders (resins)** cause the intestine to get rid of more cholesterol. Some names are **cholestyramine** and **cholestipol**.
 - **Ezetimibe (cholesterol absorption inhibitors)** works by preventing cholesterol from being absorbed in the intestine.
 - **PCSK9 Inhibitors** bind to and inactivate a protein in liver in order to lower LDL cholesterol. Some names are **alirocumab** and **evolocumab**.
 - **Fibrates** are especially good for lowering triglyceride (blood fat) levels and have a mild LDL-lowering action. Some names are **gemfibrozil** and **fenofibrate**.
 - **Niacin (nicotinic acid)** is a B vitamin that limits the production of blood fats in the liver. It lowers triglycerides and has mild LDL-lowering action.



High-, Moderate-, and Low-Intensity Statins

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering	≥50%	30%–49%	<30%
Statins	Atorvastatin 40 mg, 80 mg Rosuvastatin 20 mg, 40 mg	Atorvastatin 10 mg, 20 mg Rosuvastatin 5 mg, 10 mg Simvastatin 20–40 mg Pravastatin 40 mg, 80 mg Lovastatin 40 mg, 80 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 1–4 mg	Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg



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%



4 major statin-benefit groups

Group 1

Clinical ASCVD

CHD, stroke, and
peripheral arterial disease,
all of presumed
atherosclerotic origin

Group 2

LDL-C ≥ 190 mg/dL
(~5 mmol/L)

Group 3

Diabetes mellitus

+ age of 40–75 years
+ LDL-C 70–189 mg/dL
(~1.8–5 mmol/L)

Group 4

ASCVD risk $\geq 7.5\%$

No diabetes
+ age of 40–75 years
+ LDL-C 70–189 mg/dL
(~1.8–5 mmol/L)



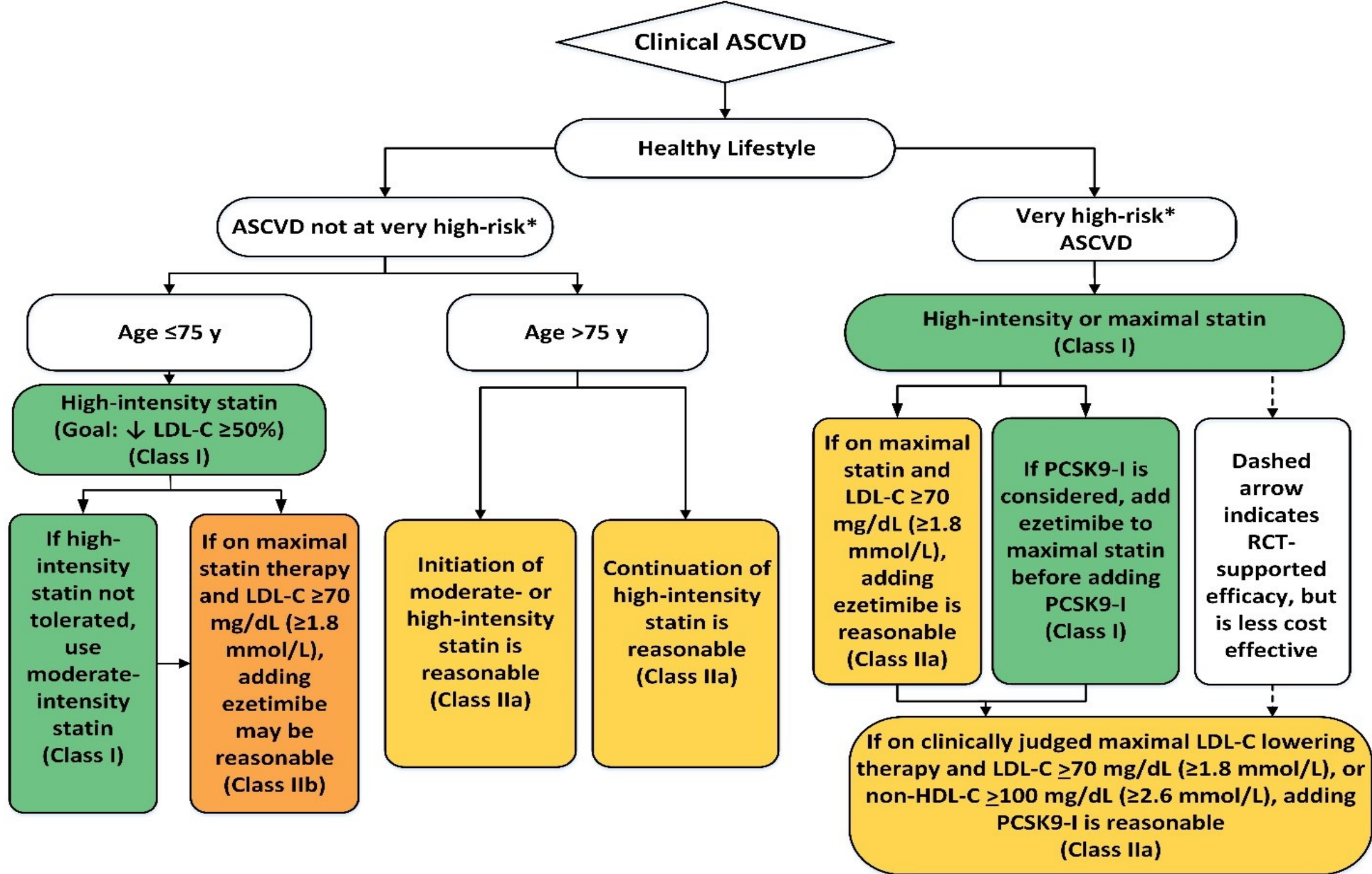
Statin Therapy in Secondary Prevention of Cardiovascular Disease



Secondary Prevention in Patients With Clinical ASCVD

Clinical ASCVD consists of

- ACS,
- history of MI,
- stable or unstable angina
- coronary other arterial revascularization
- stroke,
- TIA
- PAD including aortic aneurysm
- atherosclerotic origin





Very High-Risk of Future ASCVD Events

Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic PAD
High-Risk Conditions
Age ≥ 65 y
Heterozygous FH
History of prior coronary artery bypass surgery or PCI outside of the major ASCVD event(s)
DM
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m ²)
Current smoking
Persistently elevated LDL-C (LDL-C ≥ 100 mg/dL) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF



Very High-Risk of Future ASCVD Events

Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk condition.



Patients with Severe Hypercholesterolemia (LDL-C $\geq$ 190 mg/dL)

Recommendations for Primary Severe Hypercholesterolemia (LDL-C $\geq$ 190 mg/dL)		
COR	LOE	Recommendations
I	B-R	In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher, maximally tolerated statin therapy is recommended.
IIa	B-R	In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher who achieve less than a <u>50% reduction</u> in LDL-C while receiving maximally tolerated statin therapy and/or have an <u>LDL-C level of 100</u> mg/dL or higher, ezetimibe therapy is reasonable.
IIb	B-R	In patients 30 to 75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL ($\geq$ 2.6 mmol/L) or higher while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered.



Patients with Diabetes Mellitus

Recommendations for Patients With Diabetes Mellitus		
COR	LOE	Recommendations
I	A	In adults 40 to 75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, <u>moderate-intensity</u> statin therapy is indicated.
Ila	B-NR	In adults 40 to 75 years of age with diabetes mellitus and an LDL-C level of 70 to 189 mg/dL, it is reasonable to assess the 10-year risk of a first ASCVD event by using the race and sex-specific PCE to help stratify ASCVD risk.

Recommendations for Patients With Diabetes Mellitus		
COR	LOE	Recommendations
Ila	B-R	In adults with diabetes mellitus who have <u>multiple ASCVD risk factors</u> , it is reasonable to prescribe <u>high-intensity statin therapy</u> with the aim to <u>reduce LDL-C levels by 50% or more</u> .
Ila	B-NR	In adults older than 75 years of age with diabetes mellitus and who are already on statin therapy, it is reasonable to <u>continue</u> statin therapy.
IIb	C-LD	In adults with diabetes mellitus and <u>10-year ASCVD risk of 20% or higher</u> , it may be reasonable to add <u>ezetimibe</u> to maximally tolerated statin therapy to reduce LDL-C levels by 50% or more.

Risk Enhancers

- Long duration (≥ 10 years for type 2 diabetes mellitus or ≥ 20 years for type 1 diabetes mellitus)
- Albuminuria ≥ 30 mcg of albumin/mg creatinine
- eGFR < 60 mL/min/1.73 m²
- Retinopathy
- Neuropathy
- ABI < 0.9

Table 10.2—Recommendations for statin and combination treatment in adults with diabetes

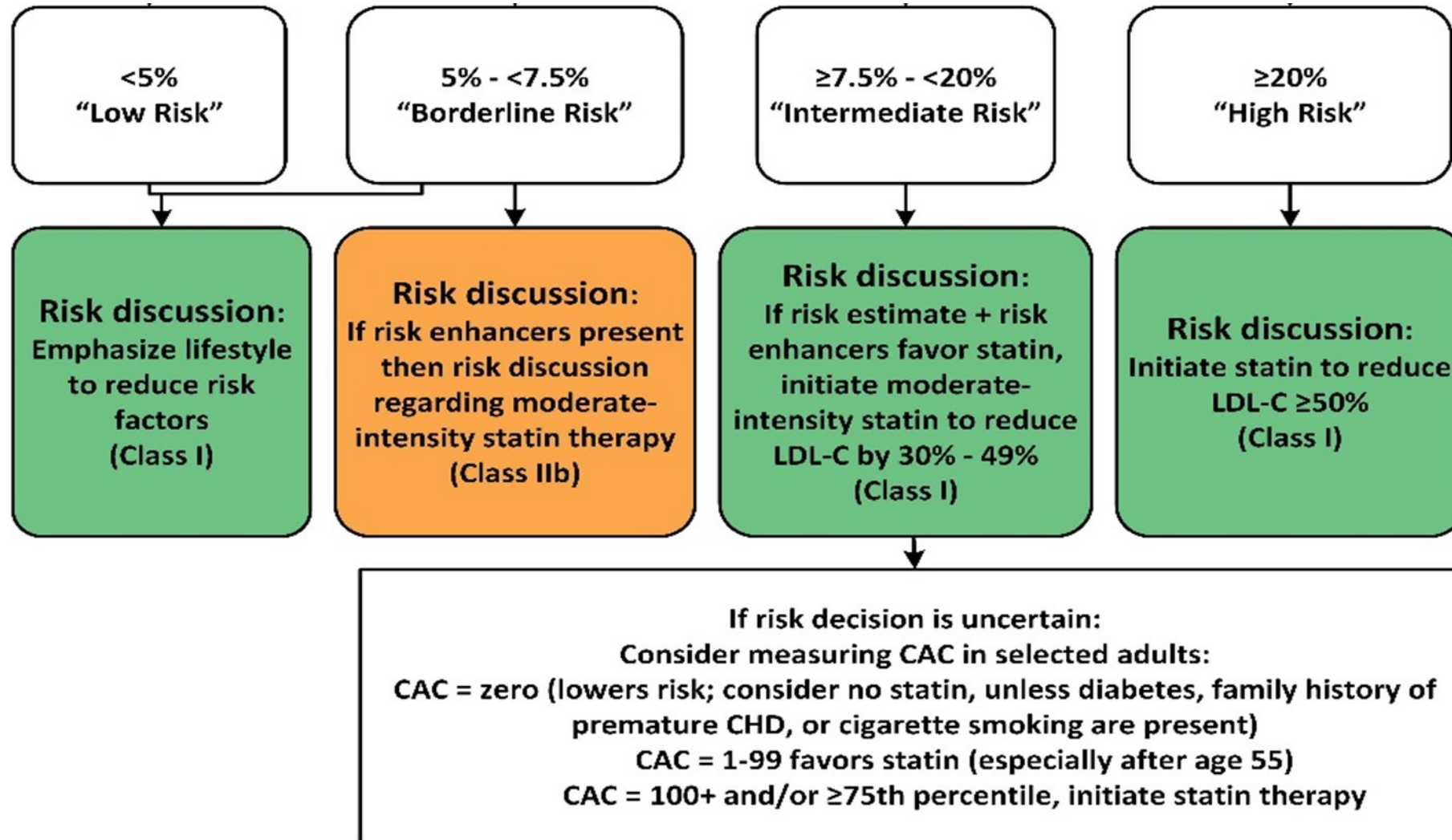
Age	ASCVD or 10-year ASCVD risk >20%	Recommended statin intensity [^] and combination treatment [*]
<40 years	No	None [†]
	Yes	High • In patients with ASCVD, if LDL cholesterol ≥ 70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)[#]
≥ 40 years	No	Moderate [‡]
	Yes	High • In patients with ASCVD, if LDL cholesterol ≥ 70 mg/dL despite maximally tolerated statin dose, consider adding additional LDL-lowering therapy (such as ezetimibe or PCSK9 inhibitor)



ASCVD Risk $\geq$ 7.5%



Primary prevention of CVD





Recommendations for drug treatment of patients with hypertriglyceridemia

Recommendations	Class ^a	Level ^b
Statin treatment is recommended as the first drug of choice to reduce CVD risk in high-risk individuals with hypertriglyceridaemia [TG levels >2.3 mmol/L (>200 mg/dL)]. ³⁵⁵	I	B
In high-risk (or above) patients with TG levels between 1.5–5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2×2 g/day) should be considered in combination with a statin. ¹⁹⁴	IIa	B
In primary prevention patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins. ^{305–307,356}	IIb	B
In high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins. ^{305–307,356}	IIb	C



Measurements of LDL-C and Non-HDL-C

Recommendations for Measurements of LDL-C and Non-HDL-C		
COR	LOE	Recommendations
I	B-NR	In adults who are <u>20 years</u> of age or older and not on lipid-lowering therapy, measurement of either a <u>fasting</u> or a <u>nonfasting</u> plasma lipid profile is effective in estimating ASCVD risk and documenting baseline LDL-C.
I	B-NR	In adults who are 20 years of age or older and in whom an initial <u>nonfasting</u> lipid profile reveals a <u>triglycerides</u> level of <u>400</u> mg/dL or higher, a repeat lipid profile in the fasting state should be performed for assessment of <u>fasting</u> triglyceride levels and baseline LDL-C.



Measurements of LDL-C and Non-HDL-C

Recommendations for Measurements of LDL-C and Non-HDL-C		
COR	LOE	Recommendations
Ia	C-LD	For patients with an <u>LDL-C level less than 70 mg/dL</u> , measurement of <u>direct LDL-C</u> or <u>modified LDL-C</u> estimate is reasonable to improve accuracy over the Friedewald formula.
Ia	C-LD	In adults who are <u>20 years</u> of age or older and without a personal history of ASCVD but with a <u>family history</u> of premature ASCVD or genetic hyperlipidemia, measurement of a <u>fasting</u> plasma lipid profile is reasonable as part of an initial evaluation to aid in the understanding and identification of familial lipid disorders.



lipid analyses for CVD 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



Monitoring in Response to LDL-C–Lowering Therapy

Recommendation for Monitoring		
COR	LOE	Recommendation
I	A	1. Adherence to changes in lifestyle and effects of LDL-C–lowering medication should be assessed by measurement of fasting lipids and appropriate safety indicators 4 to 12 weeks after statin initiation or dose adjustment and every 3 to 12 months thereafter based on need to assess adherence or safety.



Recommendations for the treatment of dyslipidemias in older people (aged >65 years)

Recommendations	Class ^a	Level ^b
Treatment with statins is recommended for older people with ASCVD in the same way as for younger patients. ²¹⁷	I	A
Treatment with statins is recommended for primary prevention, according to the level of risk, in older people aged ≤75 years. ²¹⁷	I	A
Initiation of statin treatment for primary prevention in older people aged >75 years may be considered, if at high-risk or above. ²¹⁷	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*

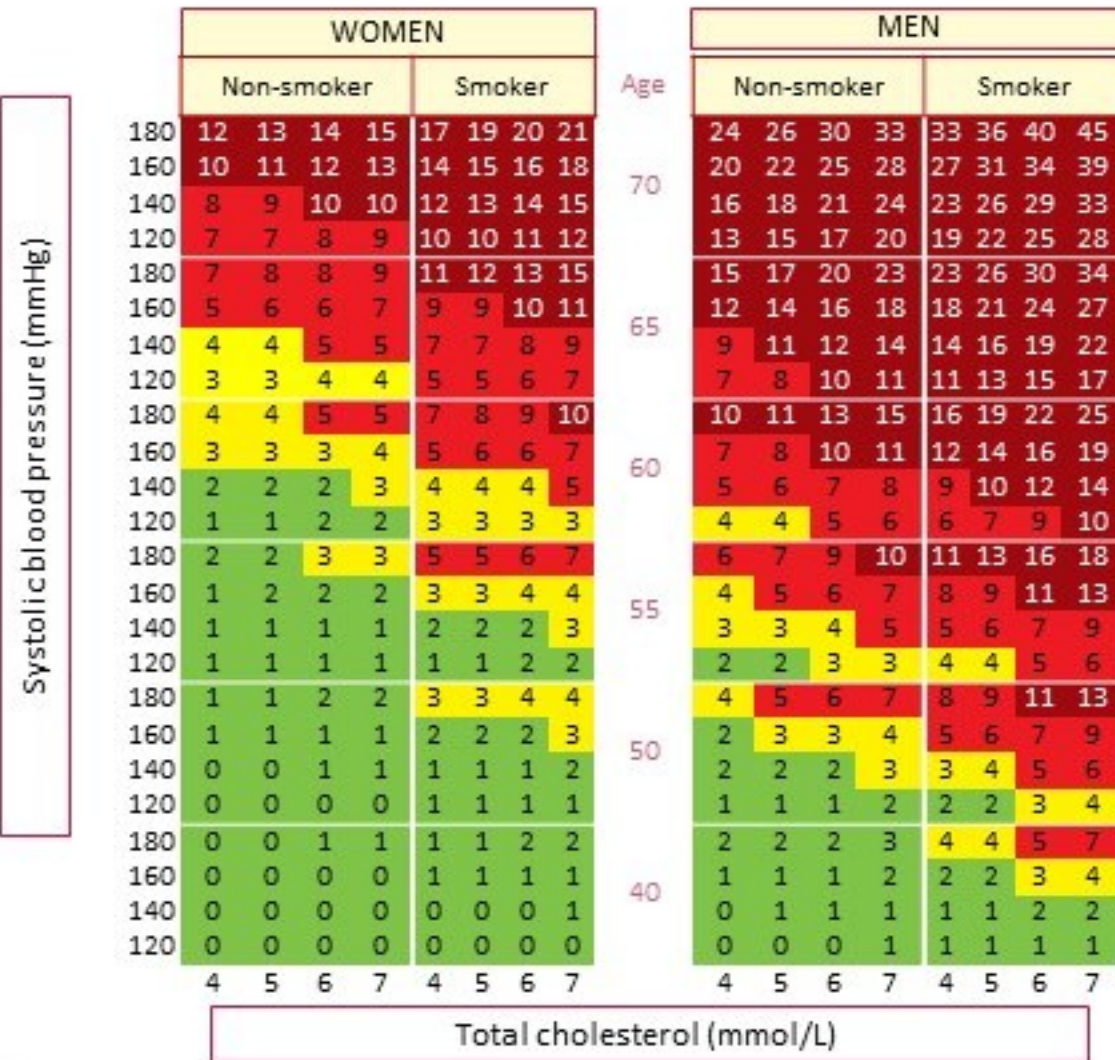
SCORE Cardiovascular Risk Chart

10-year risk of fatal CVD

High-risk regions of Europe

SCORE chart for European populations at high cardiovascular disease risk

 <3%  3-4%  5-9%  ≥10%



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).

(>20 years). Severe CKD (eGFR <30 mL/min/1.73m²).

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 $\geq$180/110mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage*, with DM duration $\geq$10 years or another additional risk factors. Moderate CKD (eGFR 30–59 mL/min/1.73m²). A calculated SCORE $\geq$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 $\geq$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

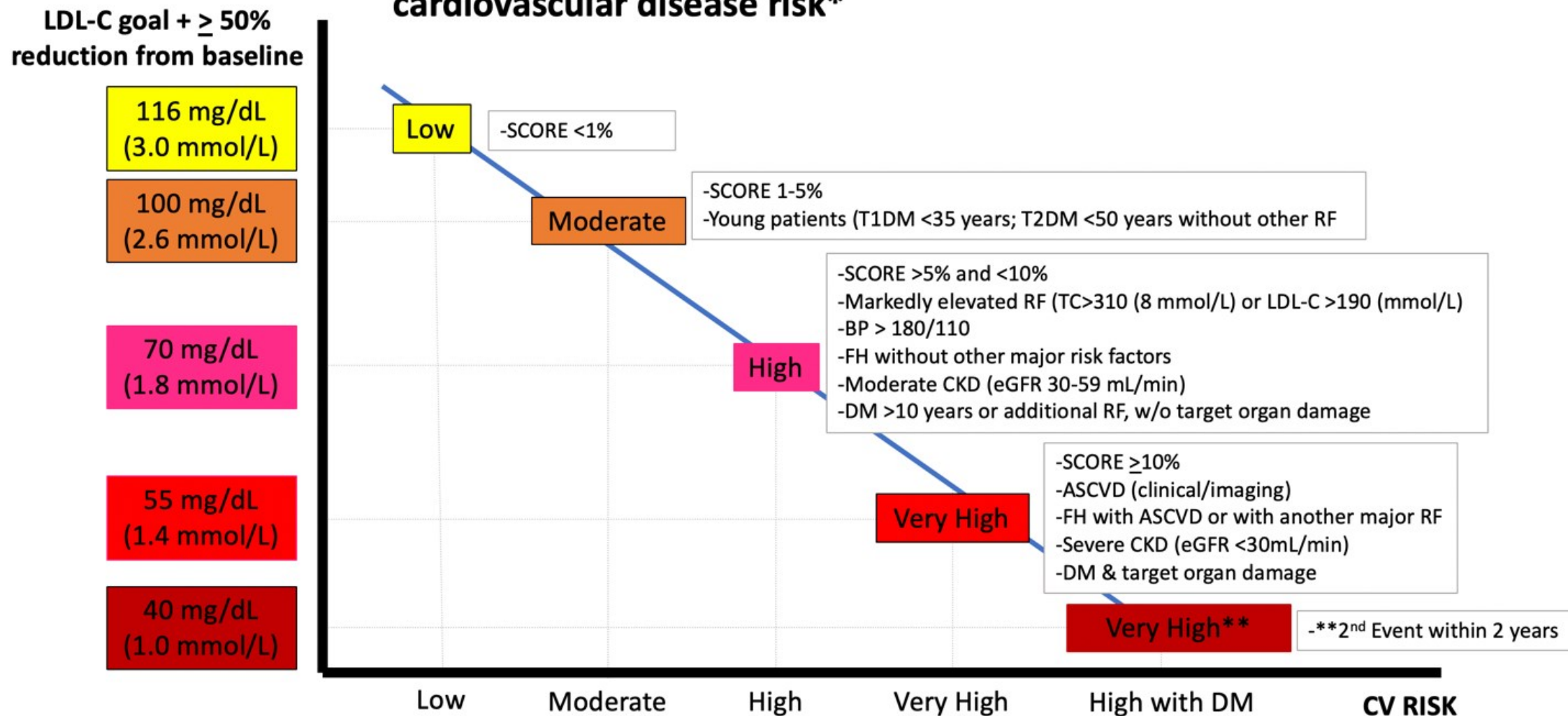
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Intervention strategies as a function of total cardiovascular risk and untreated low-density lipoprotein cholesterol levels

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

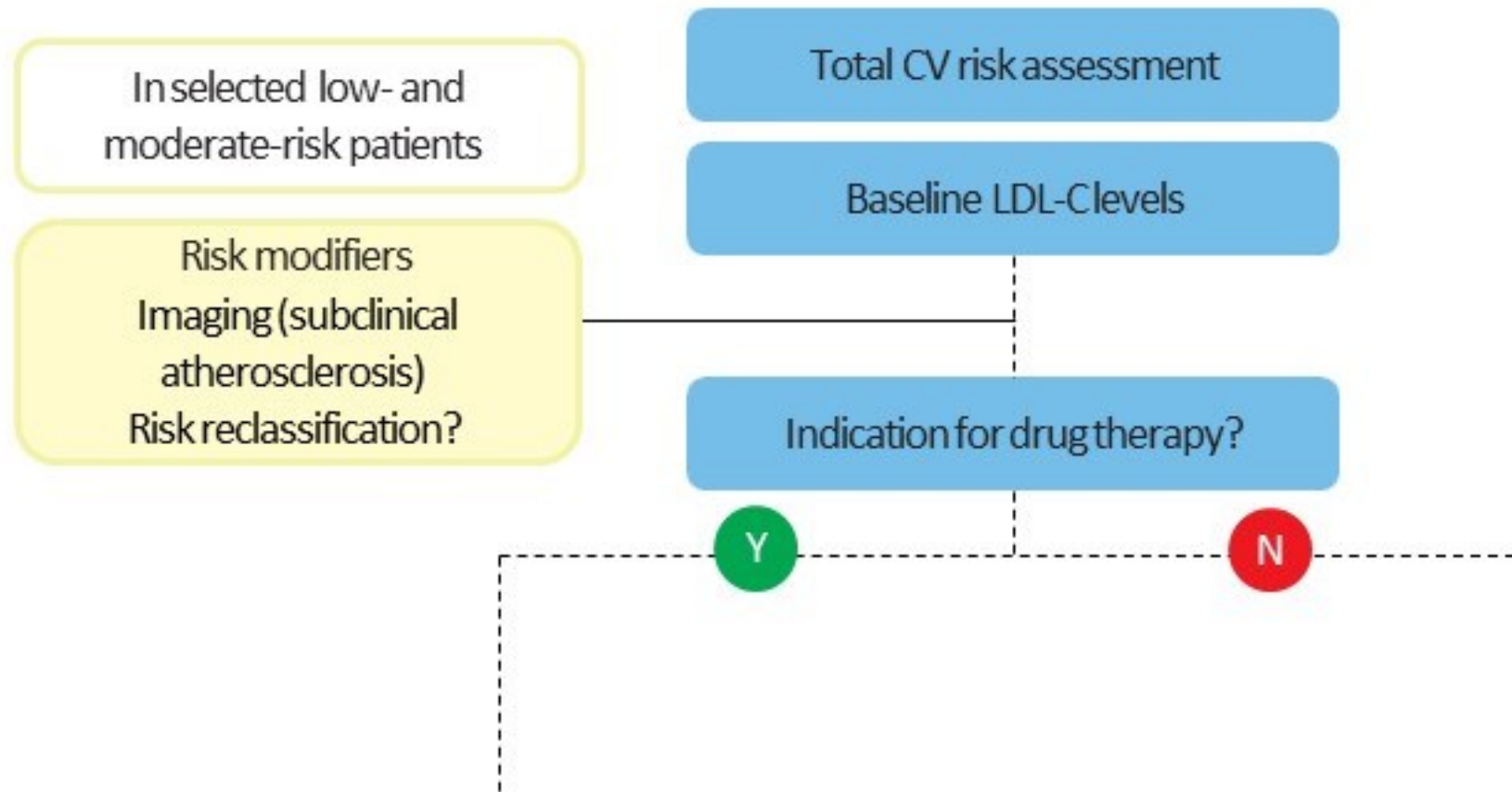
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European Treatment goals for LDL-C across categories of total cardiovascular disease risk*

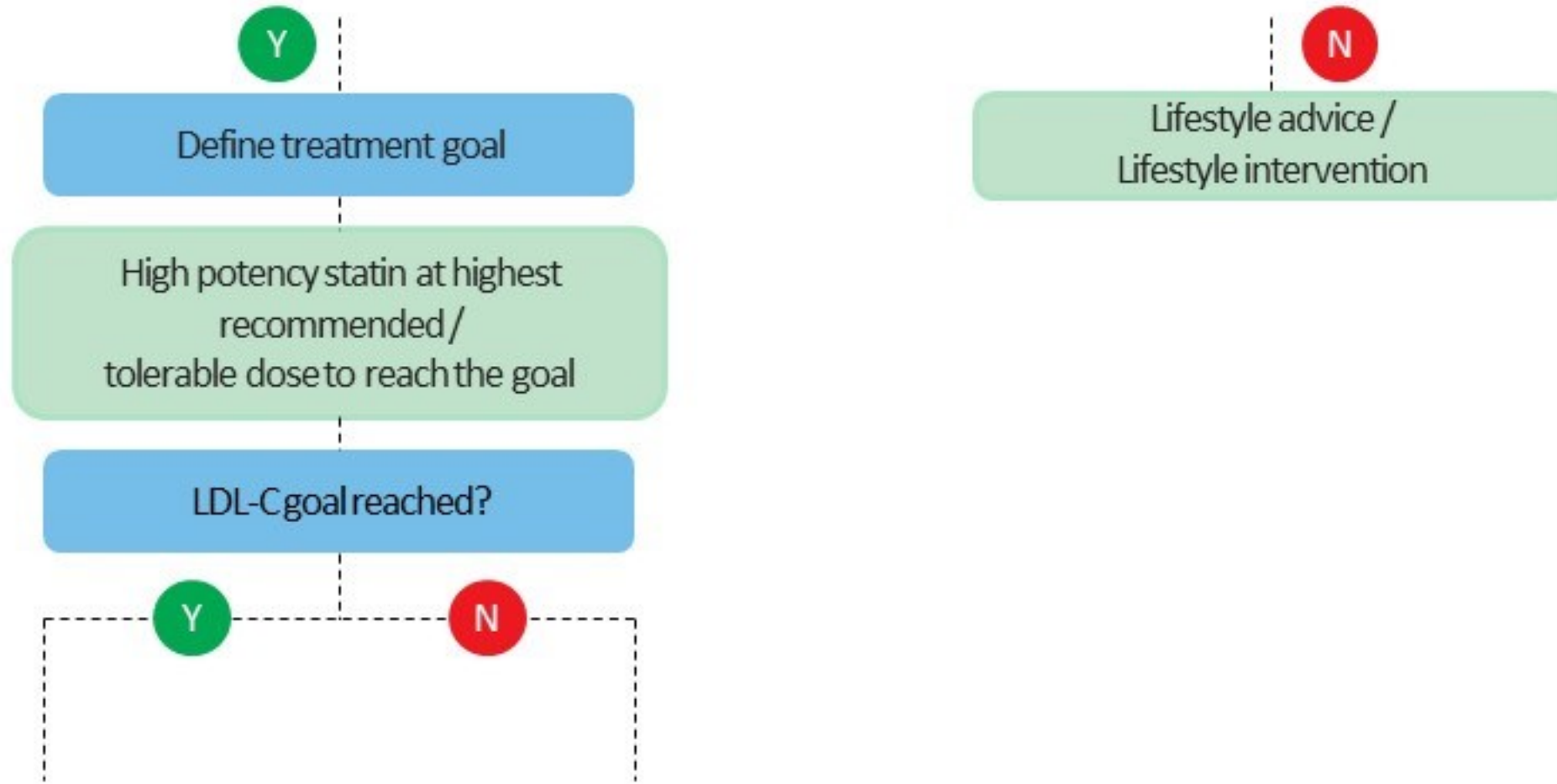


*Adapted from slideset available on www.escardio.org/guidelines which is from 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk

Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (1)



Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (2)



Central Illustration Lower panel: Treatment algorithm for pharmacological LDL-C lowering (3)

