European Heart Journal |

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08.11.2019

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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*

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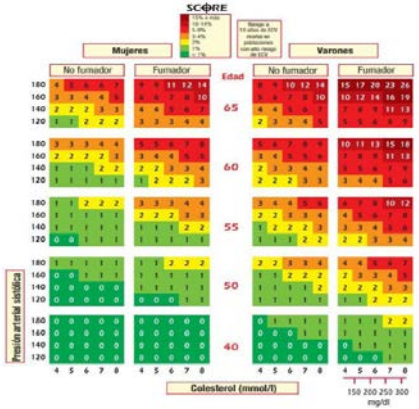
Total cardiovascular risk estimation



Sistema SCORE *(Systematic Coronary Risk Estimation)* para países de bajo riesgo cardiovascular.

SCORE para el sur de Europa

DIABETES: x3 (Varón). x5 (Mujer)

Bajo riesgo: RCV a 10 años según SCORE < 1%.
Riesgo moderado: RCV a 10 años según SCORE > 1% y < 5%.
Riesgo alto: RCV a 10 años según SCORE ≥ 5% y < 10%.
Riesgo muy alto: RCV a 10 años según SCORE ≥ 10%.

- Indicación cálculo RCV.
  - * Varón > 40 años
  - * Mujer > 50 años ó postmenopáusica.

Risk scores developed for the general population are not recommended for CV risk assessment in patients with DM or FH.	III	C

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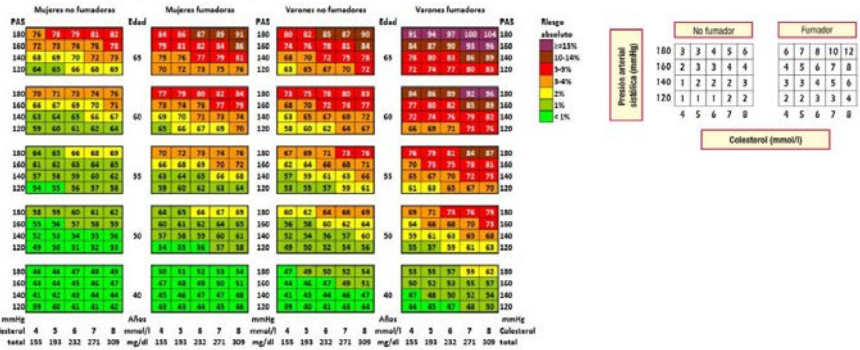
- SCORE: Riesgo a 10 años de evento cardiovascular "fatal".

Cardiovascular risk categories

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

[a]Target organ damage is defined as microalbuminuria, retinopathy, or neuropathy

Edad cardiovascular y riesgo relativo



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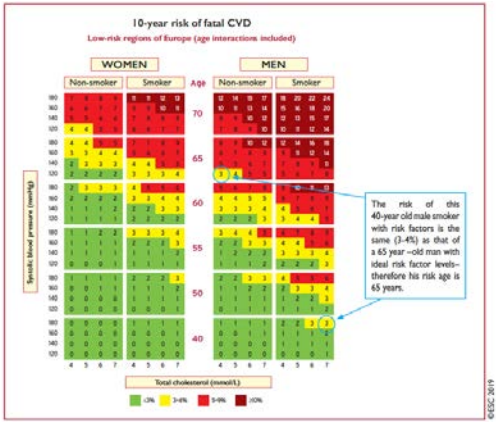

Supplementary Figure 2 Illustration of the risk age concept. CVD = cardiovascular disease.

Lp(a) LDL particle with an Apo(a) y ApoB

Lipid analyses for CVD risk estimation

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.

Table 6 Physical and chemical characteristics of human plasma lipoproteins

	Density (g/mL)	Diameter (nm)	TGs (%)	Cholesteryl esters (%)	PLs (%)	Cholesterol (%)	Apolipoproteins	
							Major	Others
Chylomicrons	<0.95	80–100	90–95	2–4	2–6	1	ApoB-48	ApoA-I, A-II, A-IV, A-V
VLDL	0.95–1.006	30–80	50–65	8–14	12–16	4–7	ApoB-100	ApoA-I, C-II, C-III, E, A-V
IDL	1.006–1.019	25–30	25–40	20–35	16–24	7–11	ApoB-100	ApoC-II, C-III, E
LDL	1.019–1.063	20–25	4–6	34–35	22–26	6–15	ApoB-100	
HDL	1.063–1.210	8–13	7	10–20	55	5	ApoA-I	ApoA-II, C-III, E, M
Lp(a)	1.006–1.125	25–30	4–8	35–46	17–24	6–9	Apo(a)	ApoB-100

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Lipid analyses for CVD risk estimation

ApoB analysis is recommended for risk assessment, particularly in people with high TG, DM, 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, DM, obesity, or very low LDL-C.

- In general, LDL-C, non-HDL-C, and ApoB concentrations are very highly correlated (ASCVD risk)
- Si TG > 400 mg/dl → Col no HDL y ApoB

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Mendelian randomization studies ??

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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

RCV moderado

RCV bajo

LDL-C	A goal of <2.6 mmol/L (<100 mg/dL).	A goal of <3.0 mmol/L (<116 mg/dL).
Non-HDL-C	< 130 mg/dl	
ApoB	< 100 mg/dl	

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

Risk category	LDL goals (starting with untreated LDL-C)	
	2016	2019
Very-high risk	<1.8 mmol/L (70 mg/dL) or >50% ↓ if LDL-C 1.8–3.5 mmol/L (70–135 mg/dL)	<1.4 mmol/L (55 mg/dL) and >50% ↓
High-risk	<2.6 mmol/L (100 mg/dL) or >50% ↓ if LDL-C 2.6–5.2 mmol/L (100–200 mg/dL)	<1.8 mmol/L (70 mg/dL) and >50%↓
Moderate-risk	<3.0 mmol/L (115 mg/dL)	<2.6 mmol/L (100 mg/dL)
Low-risk	<3.0 mmol/L (115 mg/dL)	<3.0 mmol/L (115 mg/dL)

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Hope-3

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Blood-Pressure and Cholesterol Lowering in Persons without Cardiovascular Disease

Salim Yusuf, M.B., B.S., D.Phil., Eva Lonn, M.D., Prem Pais, M.D., Jackie Bosch, Ph.D.,

N Engl J Med 2016;Apr 2:[

†A complete list of the Heart Outcomes Prevention Evaluation (HOPE)–3 trial

12705 pacientes
RCV intermedio (No ECV)
DM 2: 5.8 %
HTA: 33%
2X2: Rosu 10mg, Candesartan 16, HTZ 12.5 mg
Seguimiento: 5.6 años

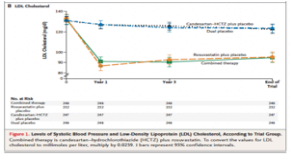

Figure 1. Levels of Systolic Blood Pressure and Low-Density Lipoprotein (LDL) Cholesterol, According to Trial Group.

LDL basal: 128 mg/dl
Descenso LDL: 33.7 mg/dl
Descenso PA: 6.2 mmHg /3 mmHg

2. Cholesterol lowering:

First co-primary endpoint:
- Composite of CV death/MI/stroke for rosuvastatin vs. placebo: 3.7% vs. 4.8%, HR 0.76, 95% CI 0.64-0.91, P=0.002, NNT=91

↓24% lower risk of cardiovascular events

HTA + RCV leve- moderado = Estatinas (JUPITER) HOPE-3

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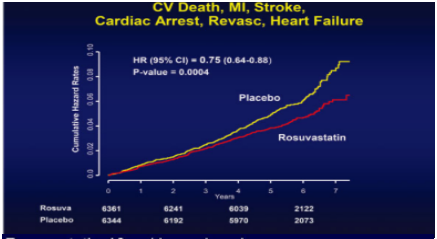
4 Study Objectives

To evaluate in an intermediate risk population without CVD the effects on CV events of:
BP lowering with combined Candesartan 16 mg + HCTZ 12.5 mg daily
Cholesterol lowering with Rosuvastatin 10 mg daily
Combined BP and cholesterol lowering



Rosuvastatin 10mg/day reduced:

- LDL-C by 34.6 mg/dl (0.9 mmol/l; i.e. 26% in LDL-C)
- ***CVD by 25%***

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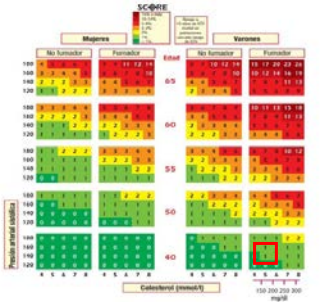
JUPITER
HOPE-3

Varón 47 años…



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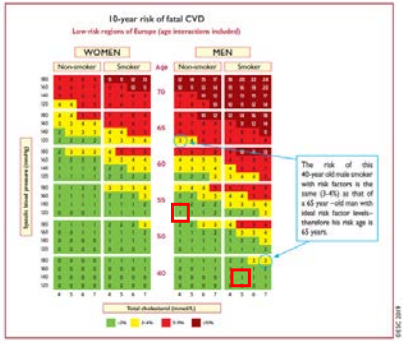
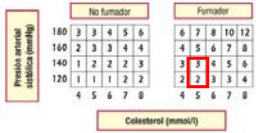
Edad cardiovascular y riesgo relativo



Supplementary Figure 2 Illustration of the risk age concept. CVD = cardiovascular disease.



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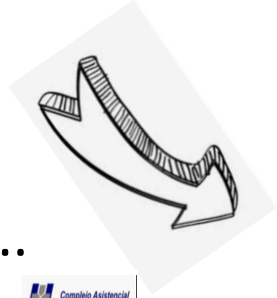

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Risk estimation: key messages

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

RCV alto y muy alto

Cardiovascular risk categories

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

high Lp(a), IIa C

[a]Target organ damage is defined as microalbuminuria, retinopathy, or neuropathy

	RCV muy alto	RCV alto
LDL-C	**Very-high risk in primary or secondary prevention:** A therapeutic regimen that achieves ≥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 ≥50% LDL-C reduction from baseline[b] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL).	
Non-HDL-C	< 85 mg/dl	< 100 mg/dl
ApoB	< 65 mg/dl	< 80 mg/dl

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.

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

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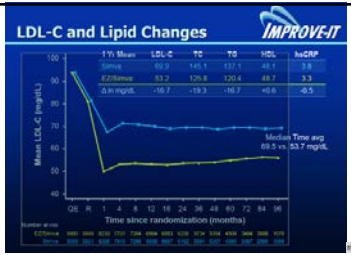

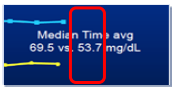

Descenso Objetivo primario: 6.4%

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥30 days), or stroke

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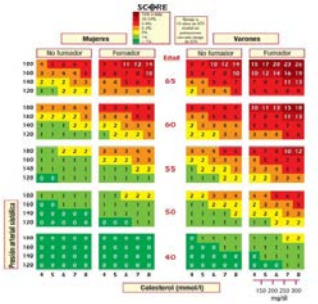
EVIDENCE FOR EFFICACY OF LDL-LOWERING THERAPIES DOWN TO BELOW 1.4 MMOL/L (55 MG/DL)

Source of evidence	Mean reduction in LDL cholesterol; mmol/L [mg/dL]	Outcome	RR (95% CI) [per mmol/L]
CTT meta-analysis[1] (high-intensity vs standard statin; subgroup <2.0 mmol/L)	1.71 [66] vs 1.32 [50]	MI, CHD death, stroke, coronary revascularisation	0.71 (0.56–0.91)
IMPROVE-IT[2] (ezetimibe plus statin vs statin)	1.55 [70] vs 1.40 [54]	CV death, MI, stroke, UA, coronary revascularisation	0.94 (0.89–0.99)
FOURIER[3] (evolocumab plus high-dose statin ± ezetimibe vs high-dose statin ± ezetimibe)	2.37 [92] vs 0.78 [30]	CV death, MI, stroke, UA, coronary revascularisation	0.85 (0.79–0.92)
ODYSSEY OUTCOMES[4] (alirocumab plus high-dose statin ± ezetimibe vs high-dose statin ± ezetimibe)	2.37 [92] vs 1.37 [53]	MI, CHD death, stroke, UA	0.85 (0.78–0.93)

Table 5 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							
	Class[a]/Level[b]	I/C	I/C	IIa/A	IIa/A	IIa/A	IIa/A
	≥5 to <10, or high-risk (see Table 4)	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	IIa/A	IIa/A	I/A	I/A	I/A
	≥10, or at very-high risk due to a risk condition (see Table 4)	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/B	IIa/A	I/A	I/A	I/A	I/A
Secondary prevention	Very-high-risk	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	I/A	I/A	I/A	I/A	I/A

Varón 47 años…



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Modificadores de RCV

Factors modifying SCORE risks (1)

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Family history of premature CVD (men: <55 years; women: <60 years).
Elevated biomarkers including apoB, Lp(a), CRP, TG; or atherosclerosis on non-invasive imaging
Social deprivation – the origin of many of the causes of CVD.
Obesity and central obesity as measured by the body mass index and waist circumference, respectively.
Physical inactivity.
Left ventricular hypertrophy.
Chronic kidney disease; Obstructive sleep apnoea syndrome; Non-alcoholic fatty liver disease

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Table 6 Risk modifiers increasing cardiovascular risk estimated by the Systemic COronary Risk Evaluation (SCORE) system[33]

Social deprivation, the origin of many causes of CVD
Obesity (measured by BMI) and central obesity (measured by waist circumference)
Physical inactivity
Psychosocial stress, including vital exhaustion
Family history of premature CVD (occurring at age <55 years in men and <60 years in women)
Autoimmune and other inflammatory disorders
Major psychiatric disorders
Treatment for infection with human immunodeficiency virus
Atrial fibrillation
LV hypertrophy
CKD
Obstructive sleep apnoea syndrome

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BMI = body mass index; CKD = chronic kidney disease; CVD = cardiovascular disease; LV = left ventricular.

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- Modificadores de Riesgo / Reclasificación

- Lp(a)

  - 1 Vez en la vida
  - Si > 180 mg/dL. RCV moderado → RCV Alto

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

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

ASCVD Risk Enhancers:

- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g. preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity factors (e.g. South Asian ancestory)

Lipid/Biomarkers:

- Persistently elevated triglycerides (≥175 mg/mL)

In selected individuals if measured:

- hs-CRP ≥2.0 mg/L
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

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Factors modifying SCORE risks (1)

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Physical inactivity
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Family history of premature CVD (occurring at age <55 years in men and <60 years in women)
Autoimmune and other inflammatory disorders
Major psychiatric disorders
Treatment for infection with human immunodeficiency virus
Atrial fibrillation
LV hypertrophy
CKD
Obstructive sleep apnoea syndrome

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BMI = body mass index; CKD = chronic kidney disease; CVD = cardiovascular disease; LV = left ventricular.

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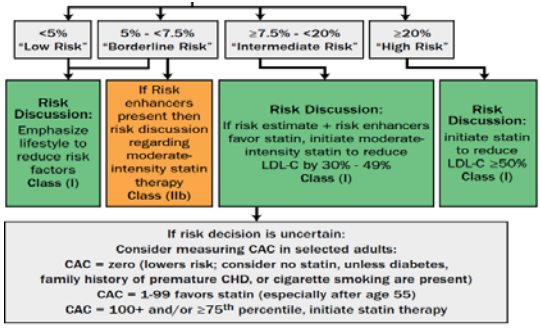
Fourth Statin Benefit Group

Primary Prevention



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Causes of death in the US

What Americans die from, what they search on Google, and what the media reports on

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