Recommandations ESC 2025

Les lipides

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Mars 2026

Déclaration de liens d'intérêt de <u>Jacques Blacher</u> :

- **Absence de participation financière dans le capital d'une entreprise liée aux médicaments.**

-**Interventions ponctuelles en rapport avec des entreprises liées aux médicaments (essais cliniques, travaux scientifiques, conseils, comités scientifiques, rapports d'expertise, conférences, colloques, actions de formation, participation à divers symposia, rédaction de brochures...) avec, le cas échéant, facturation d'honoraires ; et ceci avec la majorité des entreprises du médicaments commercialisant des produits cardiovasculaires et autres produits en rapport avec mes domaines de spécialité (Astra-Zeneca, Bayer, Elkendi, Hikma, Leurquin Mediolanum, Novartis, Omron, Organon, Sanofi, Vivactis et Vivoptim)**

- **HAS, ANSM, CNAM, MGEN, Santé Publique France, Epi-Phare**

Les lipides

Avant les recommandations ESC 2025

PRISE EN CHARGE DU PATIENT DYSLIPIDEMIQUE

AFSSAPS 2005

Quand modifier son mode de vie et son alimentation ?

→ - Patient à risque et/ou
- LDL-cholestérol **> 1,6 g/l**

Quel est l'objectif thérapeutique ?

Patient à haut risque cardiovasculaire :
- Antécédents de maladie cardiovasculaire avérée
- Diabète de type 2 à haut risque**
- Risque de survenue d'un événement coronarien dans les 10 ans ≥ 20%

→ LDL-cholestérol **< 1,0 g/l**

≥ 3 facteurs de risque* → LDL-cholestérol **< 1,3 g/l**

2 facteurs de risque* → LDL-cholestérol **< 1,6 g/l**

1 seul facteur de risque* → LDL-cholestérol **< 1,9 g/l**

Aucun facteur de risque* → LDL-cholestérol **< 2,2 g/l**

* **Facteurs de risque cardiovasculaire associés à une dyslipidémie**

- **Age** - homme de 50 ans ou plus
  - femme de 60 ans ou plus
- **Antécédents familiaux de maladie coronaire précoce**
  - infarctus du myocarde ou mort subite avant 55 ans chez le père ou chez un parent du 1er degré de sexe masculin ;
  - infarctus du myocarde ou mort subite avant 65 ans chez la mère ou chez un parent du 1er degré de sexe féminin.
- **Tabagisme actuel** ou arrêté depuis moins de 3 ans
- **Hypertension artérielle permanente traitée ou non traitée** (*se reporter aux recommandations spécifiques*)
- **Diabète de type 2 traité ou non traité** (*se reporter aux recommandations spécifiques*)
- **HDL-cholestérol < 0, 40 g/l (1,0 mmol/l)** quel que soit le sexe

Facteur protecteur

- **HDL-cholestérol ≥ 0,60 g/l (1,5 mmol/l)** : soustraire alors "un risque" au score de niveau de risque

** **Diabète de type 2 à haut risque**

- atteinte rénale,
- ou au moins deux des facteurs de risque suivants : âge, antécédents familiaux de maladie coronaire précoce, tabagisme, hypertension artérielle, HDL-cholestérol < 0,40 g/l, microalbuminurie (> 30 mg/24 h).

Les lipides : recommandations HAS 2017

Niveau de risque cardio-vasculaire	Objectif de C-LDL	Intervention de première intention*	Intervention de deuxième intention
Faible	< 1,9 g/L (4,9 mmol/L)	Modification du mode de vie	Modification du mode de vie + Traitement hypolipémiant
Modéré	< 1,3 g/L (3,4 mmol/L)		
Élevé	< 1,0 g/L (2,6 mmol/L)	Modification du mode de vie + Traitement hypolipémiant	Modification du mode de vie + Intensification du traitement hypolipémiant
Très élevé	< 0,70 g/L (1,8 mmol/L)		

Les lipides : recommandations HAS 2017

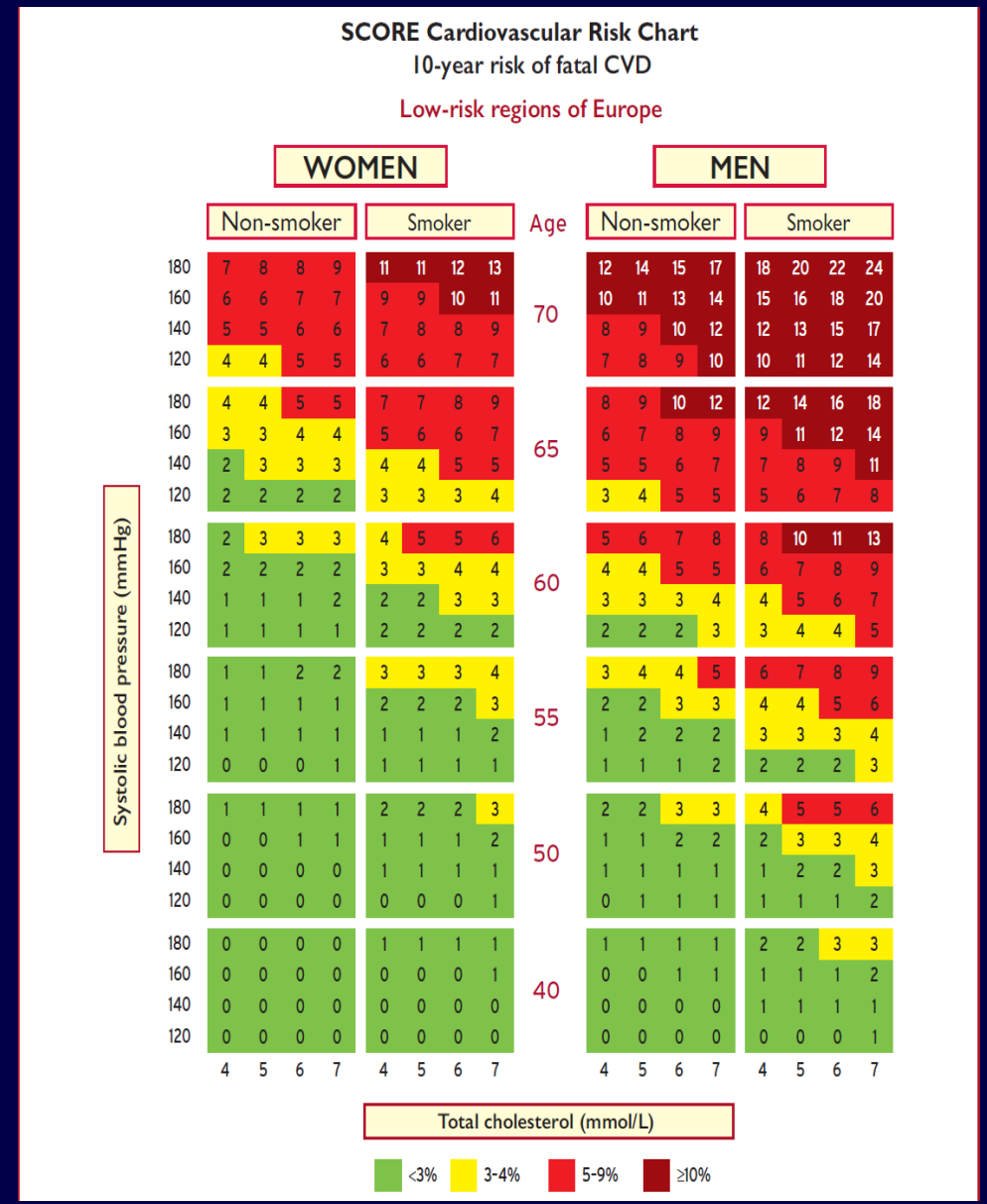
Niveau de risque cardio-vasculaire	Objectif de C-LDL	Intervention de première intention*	Intervention de deuxième intention
Faible	< 1,9 g/L (4,9 mmol/L)	Modification du mode de vie	Modification du mode de vie + Traitement hypolipémiant
Modéré	< 1,3 g/L (3,4 mmol/L)		
Élevé	< 1,0 g/L (2,6 mmol/L)	Modification du mode de vie + Traitement hypolipémiant	Modification du mode de vie + Intensification du traitement hypolipémiant
Très élevé	0,70 g/L (1,8 mmol/L)		

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)


SCORE Cardiovascular Risk Chart
10-year risk of fatal CVD
Low-risk regions of Europe
WOMEN
MEN
Non-smoker
Smoker
Age
Systolic blood pressure (mmHg)
180 160 140 120
70 65 60 55 50 40
7 8 8 9 | 11 11 12 13 | 12 14 15 17 | 18 20 22 24
6 6 7 7 | 9 9 10 11 | 10 11 13 14 | 15 16 18 20
5 5 6 6 | 7 8 8 9 | 8 9 10 12 | 12 13 15 17
4 4 5 5 | 6 6 7 7 | 7 8 9 10 | 10 11 12 14
4 4 5 5 | 7 7 8 9 | 8 9 10 12 | 12 14 16 18
3 3 4 4 | 5 6 6 7 | 6 7 8 9 | 9 11 12 14
2 3 3 3 | 4 4 5 5 | 5 5 6 7 | 7 8 9 11
2 2 2 2 | 3 3 3 4 | 3 4 5 5 | 5 6 7 8
2 3 3 3 | 4 5 5 6 | 5 6 7 8 | 8 10 11 13
2 2 2 2 | 3 3 4 4 | 4 4 5 5 | 6 7 8 9
1 1 1 2 | 2 2 3 3 | 3 3 3 4 | 4 5 6 7
1 1 1 1 | 2 2 2 2 | 2 2 2 3 | 3 4 4 5
1 1 2 2 | 3 3 3 4 | 3 4 4 5 | 6 7 8 9
1 1 1 1 | 2 2 2 3 | 2 2 3 3 | 4 4 5 6
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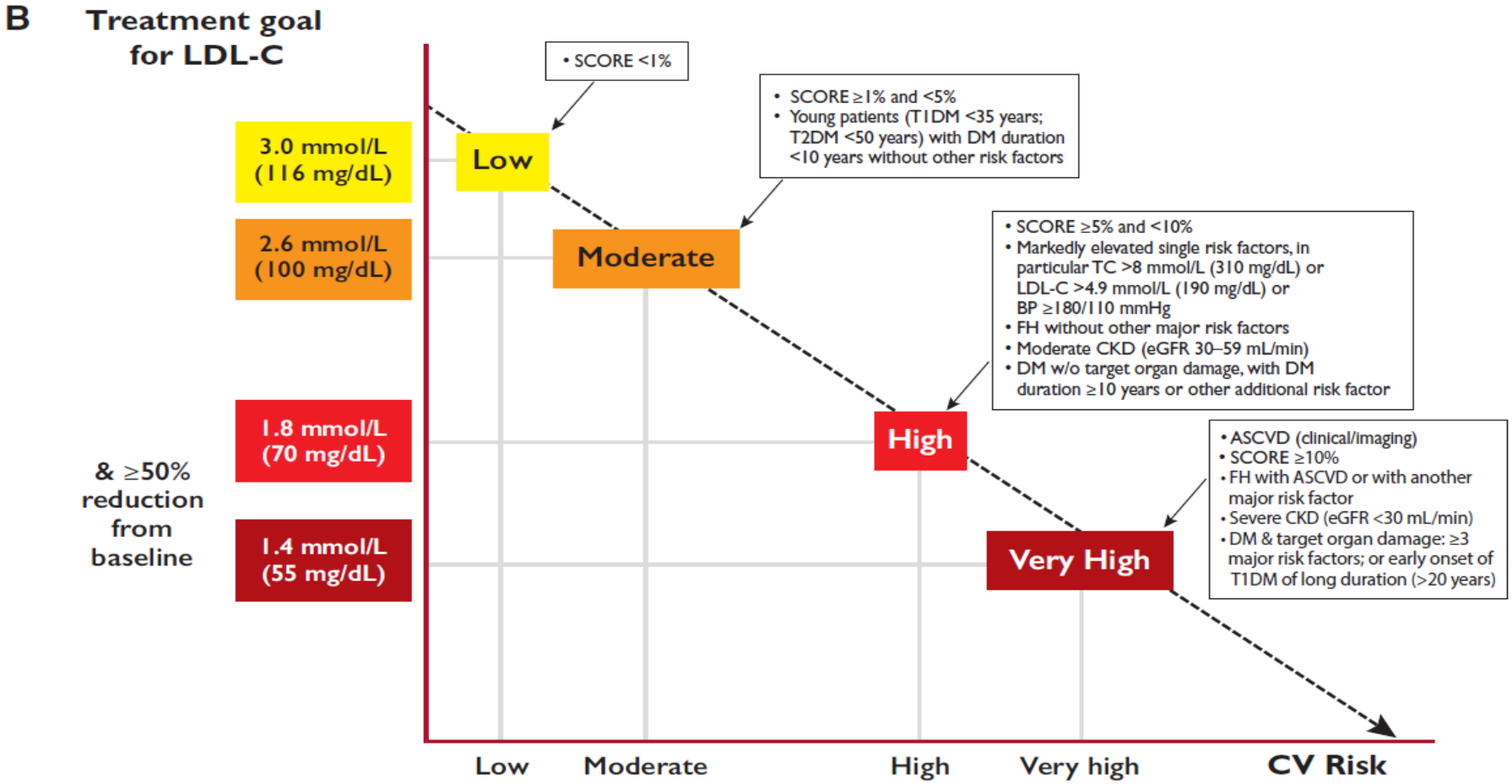
0 0 0 1 | 1 1 1 1 | 1 1 1 2 | 2 2 2 3
1 1 1 1 | 2 2 2 3 | 2 2 3 3 | 4 5 5 6
0 0 1 1 | 1 1 1 2 | 1 1 2 2 | 2 3 3 4
0 0 0 0 | 1 1 1 1 | 1 1 1 1 | 1 2 2 3
0 0 0 0 | 0 0 0 1 | 0 1 1 1 | 1 1 1 2
0 0 0 0 | 1 1 1 1 | 1 1 1 1 | 2 2 3 3
0 0 0 0 | 0 0 0 1 | 0 0 1 1 | 1 1 1 2
0 0 0 0 | 0 0 0 0 | 0 0 0 0 | 1 1 1 1
0 0 0 0 | 0 0 0 0 | 0 0 0 0 | 0 0 0 1
4 5 6 7 | 4 5 6 7 | 4 5 6 7 | 4 5 6 7
Total cholesterol (mmol/L)
<3%
3-4%
5-9%
≥10%



2019 ESC/EAS Guidelines

Les lipides

Depuis les recommandations ESC 2025

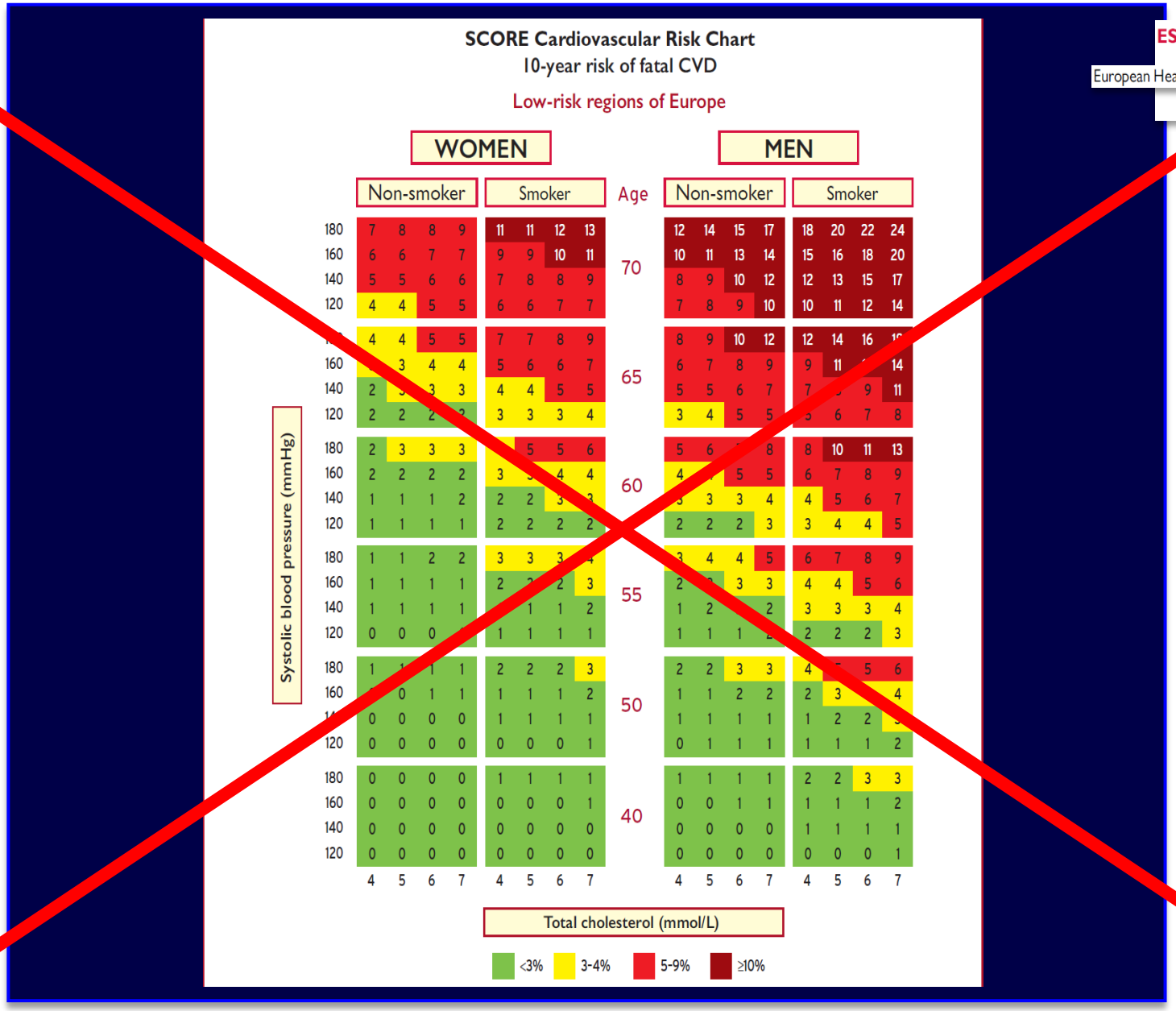
ESC European Society of Cardiology
European Heart Journal (2025) **46**, 4359–4378
https://doi.org/10.1093/eurheartj/ehaf190

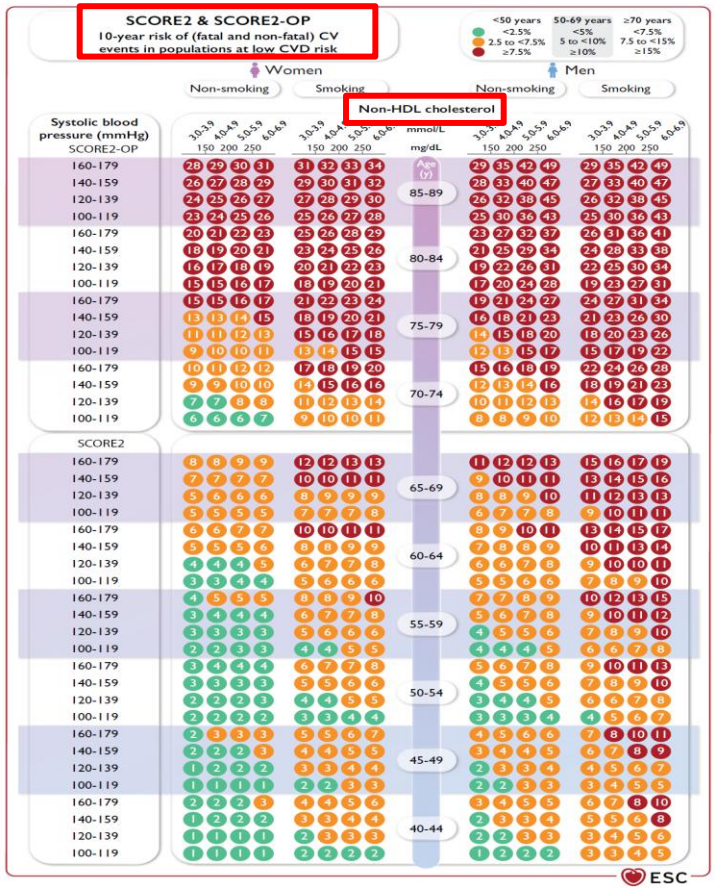
2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias

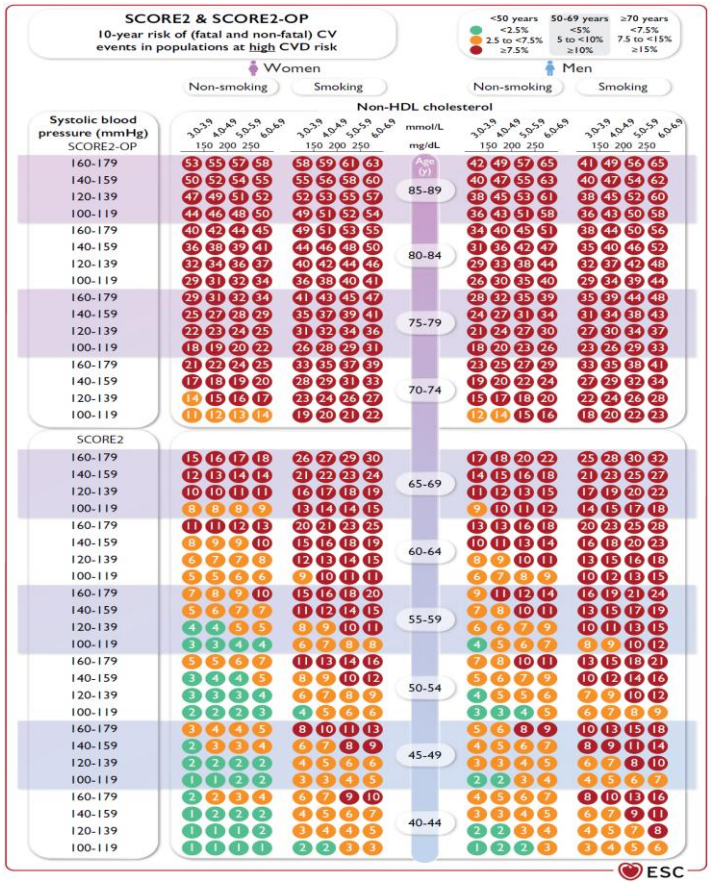
Developed by the task force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Authors/Task Force Members: François Mach *†, (ESC Chairperson) (Switzerland), Konstantinos C. Koskinas*†, (ESC Chairperson) (Switzerland), Jeanine E. Roeters van Lennep *†, (EAS Chairperson) (Netherlands), Lale Tokgözoğlu, (Task Force Co-ordinator) (Türkiye), Lina Badimon (Spain), Colin Baigent (United Kingdom), Marianne Benn (Denmark), Christoph J. Binder (Austria), Alberico L. Catapano (Italy), Guy G. De Backer (Belgium), Victoria Delgado (Spain), Natalia Fabin (Italy), Brian A. Ference (United Kingdom), Ian M. Graham (Ireland), Ulf Landmesser (Germany), Ulrich Laufs (Germany), Borislava Mihaylova (United Kingdom), Børge Grønne Nordestgaard (Denmark), Dimitrios J. Richter (Greece), Marc S. Sabatine (United States of America), and ESC/EAS Scientific Document Group

European Heart Journal (2019)




SCORE2 & SCORE2-OP
10-year risk of (fatal and non-fatal) CV events in populations at low CVD risk
<50 years
50-69 years
≥70 years
<2.5%
2.5 to <7.5%
≥7.5%
<5%
5 to <10%
≥10%
<7.5%
7.5 to <15%
≥15%
Women
Men
Non-smoking
Smoking
Non-HDL cholesterol
Systolic blood pressure (mmHg)
SCORE2-OP
SCORE2
mmol/L
mg/dL
Age (y)
85-89
80-84
75-79
70-74
65-69
60-64
55-59
50-54
45-49
40-44
ESC


SCORE2 & SCORE2-OP
10-year risk of (fatal and non-fatal) CV events in populations at high CVD risk
<50 years
50-69 years
≥70 years
<2.5%
2.5 to <7.5%
≥7.5%
<5%
5 to <10%
≥10%
<7.5%
7.5 to <15%
≥15%
Women
Men
Non-smoking
Smoking
Non-HDL cholesterol
Systolic blood pressure (mmHg)
SCORE2-OP
SCORE2
mmol/L
mg/dL
Age (y)
85-89
80-84
75-79
70-74
65-69
60-64
55-59
50-54
45-49
40-44
ESC

Box 1 Risk modifiers for consideration beyond the risk estimation based on the SCORE2 and SCORE2-OP algorithms

Demographic/clinical conditions

- Family history of premature CVD (men: <55 years; women: <60 years)
- High-risk ethnicity (e.g. Southern Asian)
- Stress symptoms and psychosocial stressors
- Social deprivation
- Obesity
- Physical inactivity
- Chronic immune-mediated/inflammatory disorders
- Major psychiatric disorders
- History of premature menopause
- Pre-eclampsia or other hypertensive disorders of pregnancy
- Human immunodeficiency virus infection
- Obstructive sleep apnoea syndrome

Biomarkers

- Persistently elevated hs-CRP (>2 mg/L)
- Elevated Lp(a) [>50 mg/dL (>105 nmol/L)].

Recommendation Table 1 — Recommendations for cardiovascular risk estimation in persons without known cardiovascular disease (see also Supplementary data online, Evidence Table 1)

Recommendations	Class[a]	Level[b]
SCORE2 is recommended in apparently healthy people <70 years of age without established ASCVD, DM, CKD, genetic/rare lipid or BP disorders for estimation of 10-year fatal and non-fatal CVD risk.[2] [c]	I	B
SCORE2-OP is recommended in apparently healthy people ≥70 years of age without established ASCVD, DM, CKD, genetic/rare lipid or BP disorders for estimation of 10-year fatal and non-fatal CVD risk.[3] [c]	I	B
Presence of subclinical coronary atherosclerosis by imaging or increased CAC score by CT should be considered as risk modifiers in individuals at moderate risk or individuals around treatment decision thresholds to improve risk classification.[24,27,28,36] [d]	IIa	B
Risk modifiers[e] should be considered in individuals at moderate risk or individuals around treatment decision thresholds to improve risk classification.[17,27,37] [f]	IIa	B
In primary prevention,[g] pharmacological LDL-C-lowering therapy is recommended in persons: • at very high risk and LDL-C ≥1.8 mmol/L (70 mg/dL), or • at high risk and LDL-C ≥2.6 mmol/L (100 mg/dL) despite optimization of non-pharmacological measures, to lower CVD risk.[1,13,38,39]	I	A
In primary prevention,[g] pharmacological LDL-C-lowering therapy should be considered in persons: • at very high risk and LDL-C ≥1.4 mmol/L (55 mg/dL) but <1.8 mmol/L (70 mg/dL), or • at high risk and LDL-C ≥1.8 mmol/L (70 mg/dL) but <2.6 mmol/L (100 mg/dL), or • at moderate risk and LDL-C ≥2.6 mmol(L (100 mg/dL) but <4.9 mmol/L (190 mg/dL), or • at low risk and LDL-C ≥3.0 mmol/L (116 mg/dL) but <4.9 mmol/L (190 mg/dL) despite optimization of non-pharmacological measures, to lower CVD risk.[1,13,38,39]	IIa	A

ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CAC, coronary artery calcium; CKD, chronic kidney disease; CT, computed tomography; CVD, cardiovascular disease; DM, diabetes mellitus; LDL-C, low-density lipoprotein cholesterol; SCORE2, Systematic Coronary Risk Evaluation 2; SCORE2-OP, Systematic Coronary Risk Evaluation 2-Older Persons

[a]Class of recommendation.

[b]Level of evidence.

[c]Revised recommendation replacing the respective recommendation based on SCORE in the 2019 ESC/EAS Guidelines.

[d]Revised recommendation replacing the recommendation on CAC score for CV risk assessment in the 2019 ESC/EAS Guidelines.

[e]Listed in *Box 1*.

[f]New recommendation.

[g]Persons without known clinical atherosclerotic cardiovascular disease.

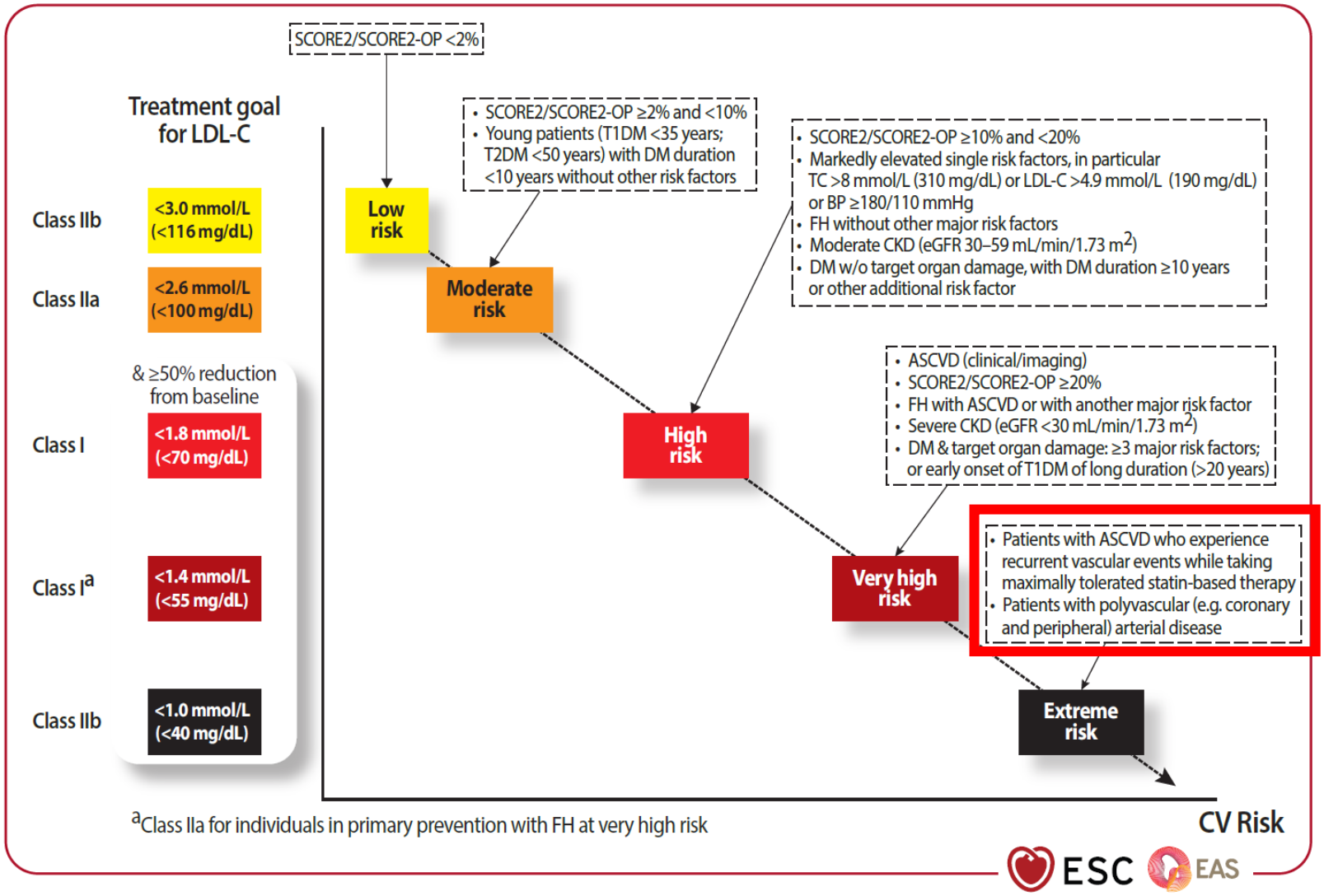


Figure 1 Treatment goals for low-density lipoprotein cholesterol across categories of total cardiovascular risk. ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FH, familial hypercholesterolaemia; LDL-C, low-density lipoprotein cholesterol; SCORE2, Systematic Coronary Risk Evaluation 2; SCORE2-OP, Systematic Coronary Risk Evaluation 2-Older Persons; T1DM, type 1 DM; T2DM, type 2 DM; TC, total cholesterol.

European Heart Journal (2025) **46**, 4359–4378
https://doi.org/10.1093/eurheartj/ehaf190

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 13, 2023 VOL. 388 NO. 15

Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients

S.E. Nissen, A.M. Lincoff, D. Brennan, K.K. Ray, D. Mason, J.J.P. Kastelein, P.D. Thompson, P. Libby, L. Cho, J. Plutzky, H.E. Bays, P.M. Moriarty, V. Menon, D.E. Grobbee, M.J. Louie, C.-F. Chen, N. Li, L.A. Bloedon, P. Robinson, M. Horner, W.J. Sasiela, J. McCluskey, D. Davey, P. Fajardo-Campos, P. Petrovic, J. Fedacko, W. Zmuda, Y. Lukyanov, and S.J. Nicholls, for the CLEAR Outcomes Investigators*

Table 1. Demographic and Baseline Patient Characteristics in the Intention-to-Treat Population.*

Characteristic	Bempedoic Acid (N=6992)	Placebo (N=6978)
Age		
Mean — yr	65.5±9.0	65.5±8.9
Distribution — no. (%)		
<65 yr	2859 (40.9)	2907 (41.7)
≥65 to <75 yr	3070 (43.9)	3027 (43.4)
≥75 yr	1063 (15.2)	1044 (15.0)
Female sex — no. (%)	3361 (48.1)	3379 (48.4)
White race — no. (%)†	6397 (91.5)	6335 (90.8)
Hispanic or Latinx — no. (%)†	1190 (17.0)	1143 (16.4)
Body-mass index‡	29.9±5.2	30.0±5.2
LDL cholesterol		
Mean value — mg/dl	139.0±34.9	139.0±35.2
Distribution — no. (%)		
<130 mg/dl	3074 (44.0)	3089 (44.3)
≥130 to <160 mg/dl	2213 (31.7)	2250 (32.2)
≥160 mg/dl	1705 (24.4)	1639 (23.5)
HDL cholesterol — mg/dl	49.6±13.3	49.4±13.3
Non-HDL cholesterol — mg/dl	173.8±39.5	173.9±40.2
Total cholesterol — mg/dl	223.5±40.6	223.3±41.1
Median triglycerides (IQR) — mg/dl	159.5 (118.0–216.5)	158.5 (118.0–215.0)
Median high-sensitivity CRP (IQR) — mg/liter	2.3 (1.2–4.5)	2.3 (1.2–4.5)
Estimated GFR — no. (%)		
≥90 ml/min/1.73 m^2	1216 (17.4)	1233 (17.7)
≥60 to <90 ml/min/1.73 m^2	4322 (61.8)	4282 (61.4)
≥30 to <60 ml/min/1.73 m^2	1437 (20.6)	1444 (20.7)
Cardiovascular risk category — no. (%)		
Primary prevention	2100 (30.0)	2106 (30.2)
Secondary prevention	4892 (70.0)	4872 (69.8)
Coronary artery disease	3574 (51.1)	3536 (50.7)
Peripheral arterial disease	794 (11.4)	830 (11.9)
Cerebrovascular atherosclerotic disease	1027 (14.7)	1040 (14.9)
Glycemic status — no. (%)		
Diabetes§	3144 (45.0)	3229 (46.3)
Inadequately controlled diabetes¶	1356 (19.4)	1369 (19.6)
Statin use — no. (%)	1601 (22.9)	1573 (22.5)
Ezetimibe use — no. (%)	803 (11.5)	809 (11.6)

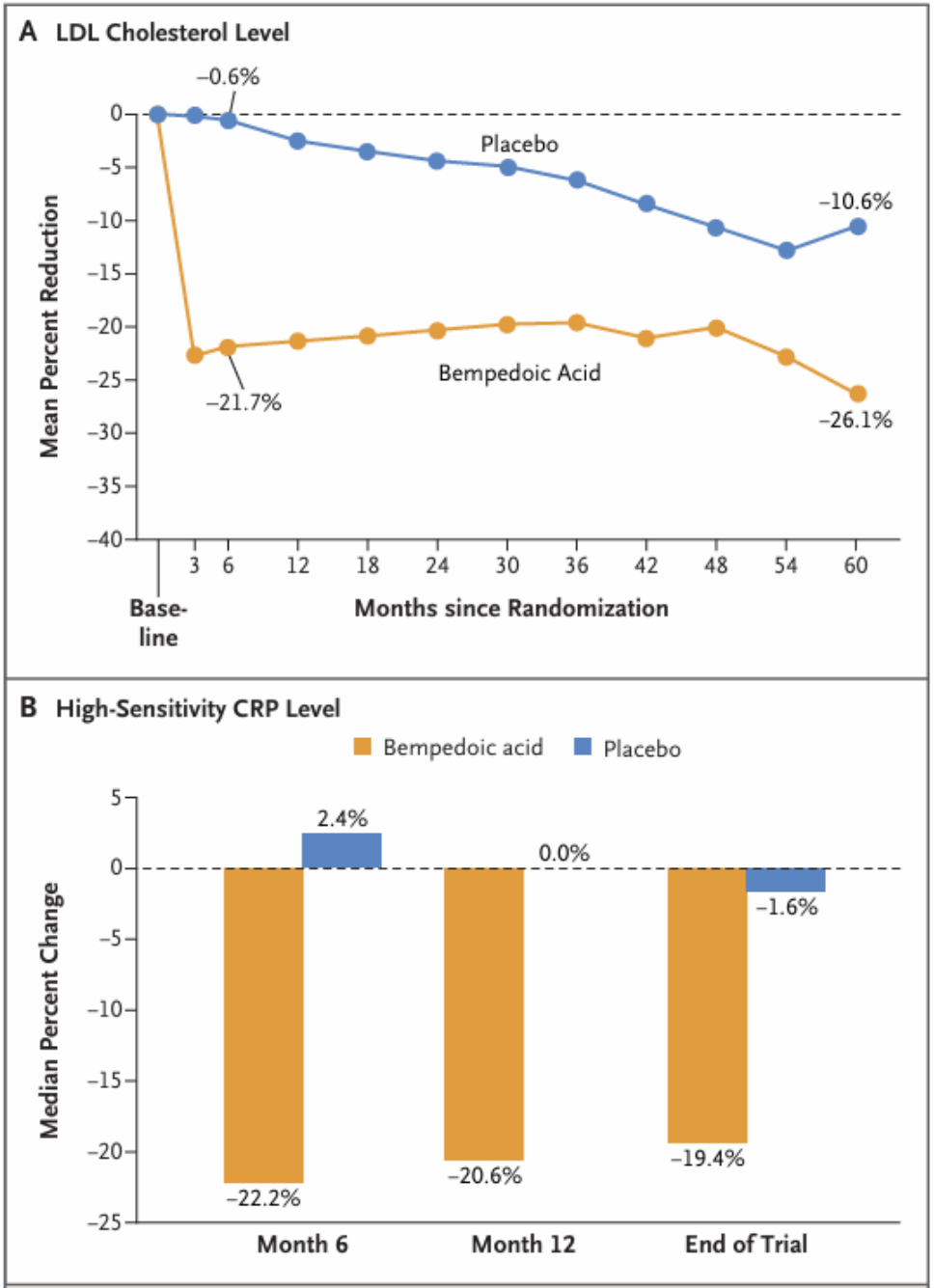

Figure 1. Changes in LDL Cholesterol and High-Sensitivity CRP Levels over Time.

Table 2. Efficacy End Points in the Intention-to-Treat Population.*

Outcome	Bempedoic Acid (N = 6992)	Placebo (N = 6978)	Difference (95% CI)*	P Value†
Primary efficacy end point				
Four-component MACE — no. (%)‡	819 (11.7)	927 (13.3)	0.87 (0.79 to 0.96)	0.004
Key secondary efficacy end points				
Three-component MACE — no. (%)§	575 (8.2)	663 (9.5)	0.85 (0.76 to 0.96)	0.006
Fatal or nonfatal myocardial infarction — no. (%)	261 (3.7)	334 (4.8)	0.77 (0.66 to 0.91)	0.002
Coronary revascularization — no. (%)	435 (6.2)	529 (7.6)	0.81 (0.72 to 0.92)	0.001
Fatal or nonfatal stroke — no. (%)	135 (1.9)	158 (2.3)	0.85 (0.67 to 1.07)	0.16
Death from cardiovascular causes — no. (%)	269 (3.8)	257 (3.7)	1.04 (0.88 to 1.24)	
Death from any cause — no. (%)	434 (6.2)	420 (6.0)	1.03 (0.90 to 1.18)	
Additional secondary end points				
Death from any cause, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization — no. (%)	962 (13.8)	1062 (15.2)	0.89 (0.82 to 0.97)	
Five-component MACE — no. (%)¶	831 (11.9)	952 (13.6)	0.86 (0.78 to 0.94)	
Hospitalization for unstable angina — no. (%)	91 (1.3)	137 (2.0)	0.66 (0.50 to 0.86)	
New-onset type 2 diabetes mellitus — no./total no. (%)‖	429/3848 (11.1)	433/3749 (11.5)	0.95 (0.83 to 1.09)	
Change from baseline in secondary lipid and biomarker efficacy end points				
Mean percent change in mean LDL cholesterol level at 6 mo (95% CI)**	−21.1 (−21.6 to −20.5)	−0.8 (−1.4 to −0.2)	−20.3 (−21.1 to −19.5)	
Median percent change in high-sensitivity CRP level at 6 mo (95% CI)	−22.2 (−23.5 to −20.8)	2.4 (0.0 to 4.2)	−21.6 (−23.7 to −19.6)	
Mean percentage-point change in glycated hemoglobin level at 12 mo in patients with inadequately controlled type 2 diabetes mellitus (95% CI)**††	−0.04 (−0.12 to 0.03)	−0.01 (−0.09 to 0.06)	−0.03 (−0.14 to 0.08)	

* The patients were followed for a median of 40.6 months. Differences are given as the hazard ratio for the primary efficacy end point, the key secondary efficacy end points, and the additional secondary end points and as the percentage-point difference for the changes from baseline in secondary lipid and biomarker efficacy end points.

† As prespecified in the hierarchical testing procedure, all P values after the first nonsignificant P value are not presented.

‡ The primary efficacy end point was a four-component composite of adjudicated major adverse cardiovascular events (MACE), defined as death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization, as assessed in a time-to-first-event analysis.

§ The first key secondary end point was a three-component MACE, defined as death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

¶ The five-component MACE was defined as death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or hospitalization for unstable angina.

‖ New-onset type 2 diabetes mellitus was defined as a glycated hemoglobin level of 6.5% or greater or two or more fasting glucose measurements of 126 mg per deciliter (7.0 mmol per liter) or greater in patients with a baseline glycemic status of no diabetes.

** Results were adjusted for baseline LDL cholesterol or glycated hemoglobin levels with the use of a pattern-mixture model for missing data.

†† Inadequately controlled type 2 diabetes was defined as type 2 diabetes and a glycated hemoglobin level of 7% or greater at baseline.

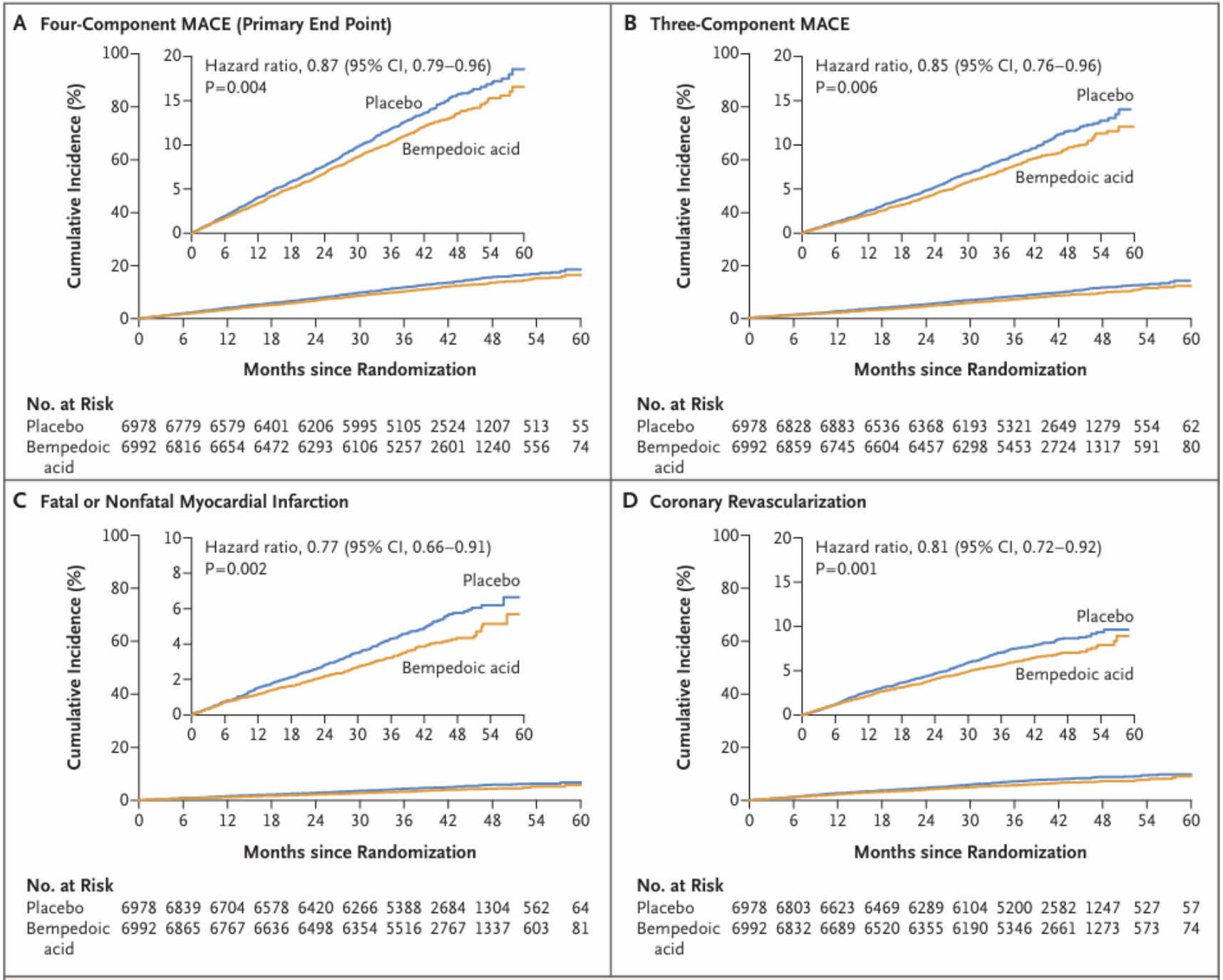

Figure 2. Cumulative Incidence of Cardiovascular Events.

Table 3. Investigator-Reported Adverse Events and Laboratory Safety-Related Findings in the Safety Population.*

Event	Bempedoic Acid (N=7001)	Placebo (N=6964)
Any adverse event that started or worsened after the first dose of a trial agent — no. (%)	6040 (86.3)	5919 (85.0)
Serious adverse event that started or worsened after the first dose of a trial agent — no. (%)	1767 (25.2)	1733 (24.9)
Adverse event leading to discontinuation of the trial regimen — no. (%)	759 (10.8)	722 (10.4)
Prespecified adverse events of special interest		
Myalgia — no. (%)	393 (5.6)	471 (6.8)
Discontinuation of the trial regimen because of myalgia — no. (%)	124 (1.8)	129 (1.9)
New-onset diabetes in patients without diabetes at baseline — no./total no. (%)	621/3856 (16.1)	640/3740 (17.1)
New-onset diabetes in patients with prediabetes at baseline — no./total no. (%)†	569/2918 (19.5)	586/2877 (20.4)
New-onset diabetes in patients with normoglycemia at baseline — no./total no. (%)†	52/938 (5.5)	54/863 (6.3)
Worsening hyperglycemia — no./total no. (%)‡	713/3145 (22.7)	746/3224 (23.1)
Hypoglycemia — no. (%)	304 (4.3)	267 (3.8)
Metabolic acidosis — no. (%)	13 (0.2)	11 (0.2)
Elevated hepatic-enzyme level — no. (%)	317 (4.5)	209 (3.0)
Renal impairment — no. (%)	802 (11.5)	599 (8.6)
Neurocognitive disorders — no. (%)	58 (0.8)	69 (1.0)
Atrial fibrillation — no. (%)	229 (3.3)	246 (3.5)
Adjudicated tendon rupture — no. (%)	86 (1.2)	66 (0.9)
Tendinopathies — no. (%)	118 (1.7)	128 (1.8)
Malignant conditions — no. (%)	321 (4.6)	341 (4.9)
Other adverse events — no. (%)		
Hyperuricemia	763 (10.9)	393 (5.6)
Gout	215 (3.1)	143 (2.1)
Cholelithiasis	152 (2.2)	81 (1.2)
Laboratory results after 6 mo — mg/dl		
Change from baseline in uric acid level	0.76±1.2	−0.03±1.0
Change from baseline in creatinine level	0.05±0.2	0.01±0.2
Laboratory results after 12 mo		
Change from baseline in glycated hemoglobin level — %§	0.04±0.74	0.06±0.70
Abnormal enzyme level at any visit — no. (%)		
Creatine kinase level >5× ULN, single occurrence	45 (0.6)	40 (0.6)
Creatine kinase level >5× ULN, repeated and confirmed	8 (0.1)	8 (0.1)
Creatine kinase level >10× ULN, single occurrence	18 (0.3)	15 (0.2)
Creatine kinase level >10× ULN, repeated and confirmed	2 (<0.1)	4 (0.1)
Alanine aminotransferase level >3× ULN¶	83 (1.2)	53 (0.8)
Aspartate aminotransferase level >3× ULN¶	80 (1.1)	43 (0.6)

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ESTABLISHED IN 1812 APRIL 13, 2023 VOL. 388 NO. 15

Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients

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CONCLUSIONS

Among statin-intolerant patients, treatment with bempedoic acid was associated with a lower risk of major adverse cardiovascular events (death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or coronary revascularization). (Funded by Esperion Therapeutics; CLEAR Outcomes ClinicalTrials.gov number, NCT02993406.)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two Phase 3 Trials of Inclisiran in Patients with Elevated LDL Cholesterol

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Conclusions: Reductions in LDL cholesterol levels of approximately 50% were obtained with inclisiran, administered subcutaneously every 6 months. More injection-site adverse events occurred with inclisiran than with placebo. (Funded by the Medicines Company; ORION-10 and ORION-11 ClinicalTrials.gov numbers, NCT03399370 and NCT03400800.).

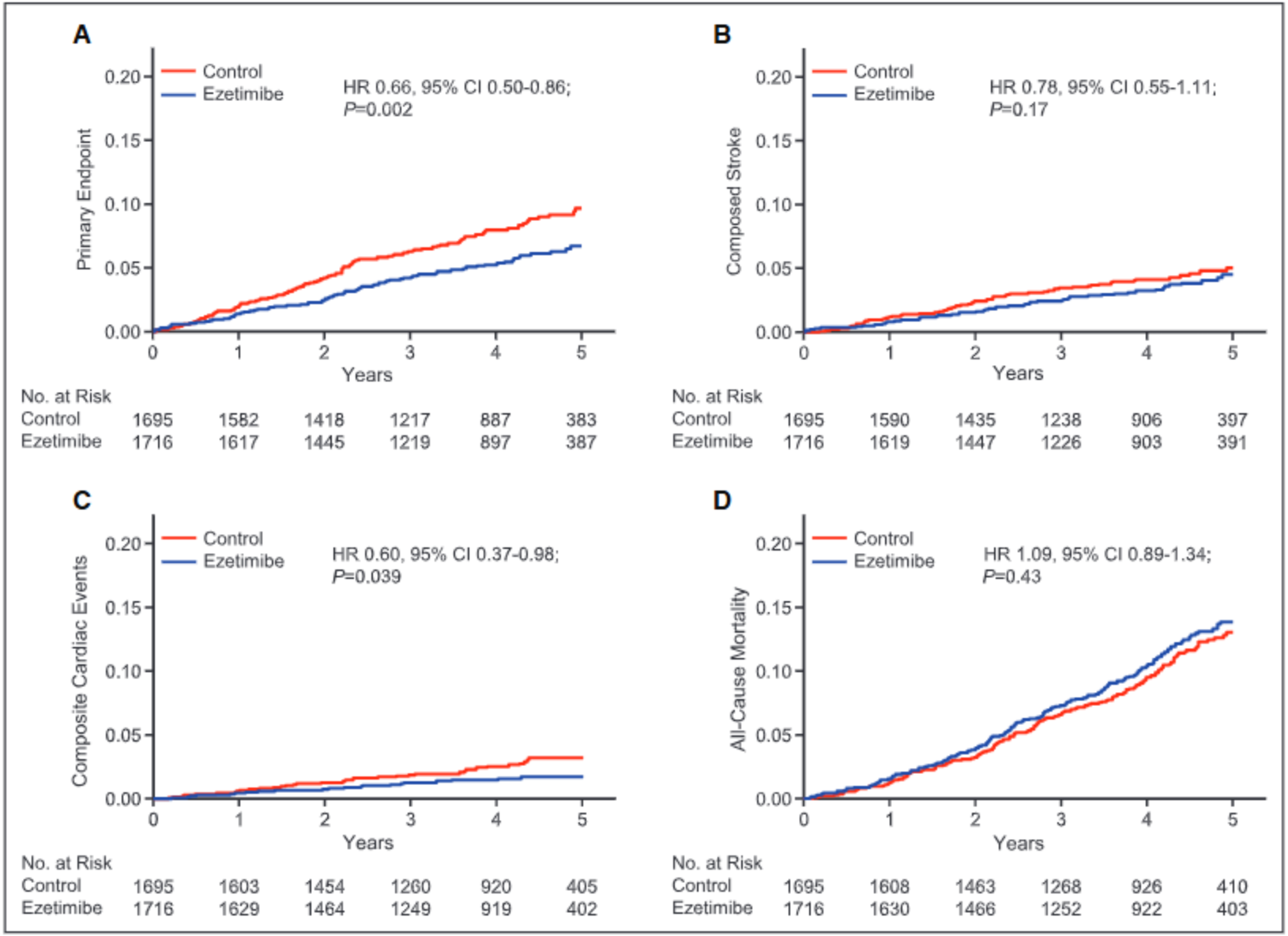

Figure 3. Kaplan–Meier estimates of the incidences of outcome events in the ezetimibe group and the control group.

A, Primary outcome. B, Composed stroke. C, Composite cardiac events. D, All-cause mortality.

Recommendation Table 5 — Recommendations for drug treatment of patients with hypertriglyceridaemia (see also Supplementary data online, Evidence Table 5)

Recommendations	Class[a]	Level[b]
High-dose icosapent ethyl (2 × 2 g/day) should be considered in combination with a statin in high-risk or very high-risk patients with elevated triglyceride levels (fasting triglyceride level 135–499 mg/dL or 1.52–5.63 mmol/L) to reduce the risk of cardiovascular events.[8,111]	IIa	B
Volanesorsen (300 mg/week) should be considered in patients with severe hypertriglyceridaemia (>750 mg/dL or >8.5 mmol/L) due to familial chylomicronaemia syndrome, to lower triglyceride levels and reduce the risk of pancreatitis.[6,117]	IIa	B

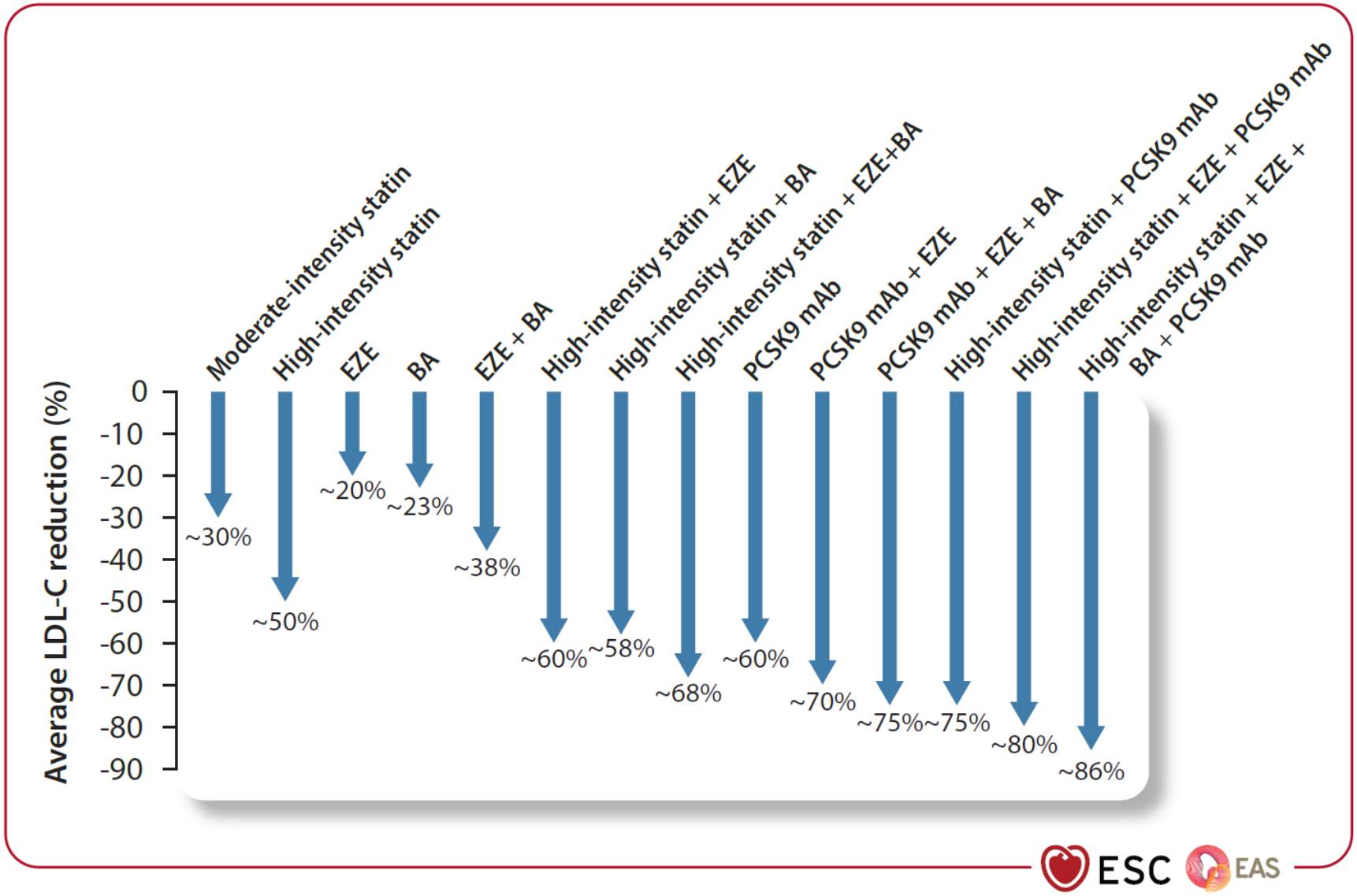

Figure 2 Average reduction in low-density lipoprotein cholesterol levels with different pharmacological therapies with proven cardiovascular benefits. BA, bempedoic acid; EZE, ezetimibe; LDL-C, low-density lipoprotein cholesterol; PCSK9 mAb, proprotein convertase subtilisin/kexin type 9 monoclonal antibody.

European Heart Journal (2025) **46**, 4359–4378
https://doi.org/10.1093/eurheartj/ehaf190

Lp(a)

Currently, there are specific Lp(a)-lowering medications being tested in randomized clinical trials. The injectable RNA (either antisense oligonucleotide or small interfering RNA)-based therapies that target apolipoprotein(a) production in the hepatocyte lower Lp(a) concentration by 80%–98%.[94–97] An oral small molecule inhibitor and a small interfering RNA that can lower Lp(a) significantly are currently under investigation.[98–100]

Recommendation Table 4 includes a new recommendation reflecting the increase in CV risk across the spectrum of elevated Lp(a) levels.[1] It is reasonable to consider elevated Lp(a) levels >50 mg/dL (≥105 nmol/L) (affecting at least 20% of the population)[83] in order to refine CV risk estimation across the spectrum of CV risk; moreover, this cut-off level should be considered as a risk modifier to potentially reclassify the CV risk category specifically in individuals at moderate risk or individuals close to treatment decision thresholds (see *Box 1* and *Recommendation*

Recommendation Table 2 — Recommendations for pharmacological low-density lipoprotein cholesterol lowering (see also Supplementary data online, Evidence Table 2)

Recommendations	Class[a]	Level[b]
Non-statin therapies with proven cardiovascular benefit,[c] taken alone or in combination, are recommended for patients who are unable to take statin therapy to lower LDL-C levels and reduce the risk of CV events. The choice should be based on the magnitude of additional LDL-C lowering needed.[4,53,54]	I	A
Bempedoic acid is recommended in patients who are unable to take statin therapy to achieve the LDL-C goal.[4]	I	B
The addition of bempedoic acid to the maximally tolerated dose of statin with or without ezetimibe should be considered in patients at high or very high risk in order to achieve the LDL-C goal.[42,55]	IIa	C
Evinacumab should be considered in patients with homozygous familial hypercholesterolaemia aged 5 years or older who are not at LDL-C goal despite receiving maximum doses of lipid-lowering therapy to lower LDL-C levels.[5,50,51]	IIa	B

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

This table complements the table of recommendations for pharmacological low-density lipoprotein cholesterol lowering in the 2019 ESC/EAS Guidelines and does not replace it.

[a]Class of recommendation.

[b]Level of evidence.

[c]Ezetimibe, PCSK9 monoclonal antibodies, bempedoic acid.

European Heart Journal (2025) **46**, 4359–4378
https://doi.org/10.1093/eurheartj/ehaf190

Recommendation Table 3 — Recommendations for lipid-lowering therapy in patients with acute coronary syndromes (see also Supplementary data online, Evidence Table 3)

Recommendations	Class[a]	Level[b]
Intensification of lipid-lowering therapy during the index ACS hospitalization is recommended for patients who were on any lipid-lowering therapy before admission in order to further lower LDL-C levels.	I	C
Initiating combination therapy with high-intensity statin plus ezetimibe during index hospitalization for ACS should be considered in patients who were treatment-naïve and are not expected to achieve the LDL-C goal with statin therapy alone.[66]	IIa	B

This table complements the ESC 2019 ESC/EAS Guidelines table and does not replace it.
ACS, acute coronary syndromes; LDL-C, low-density lipoprotein cholesterol.
[a]Class of recommendation.
[b]Level of evidence.

European Heart Journal (2025) **46**, 4359–4378
https://doi.org/10.1093/eurheartj/ehaf190

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 24, 2023 VOL. 389 NO. 8

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

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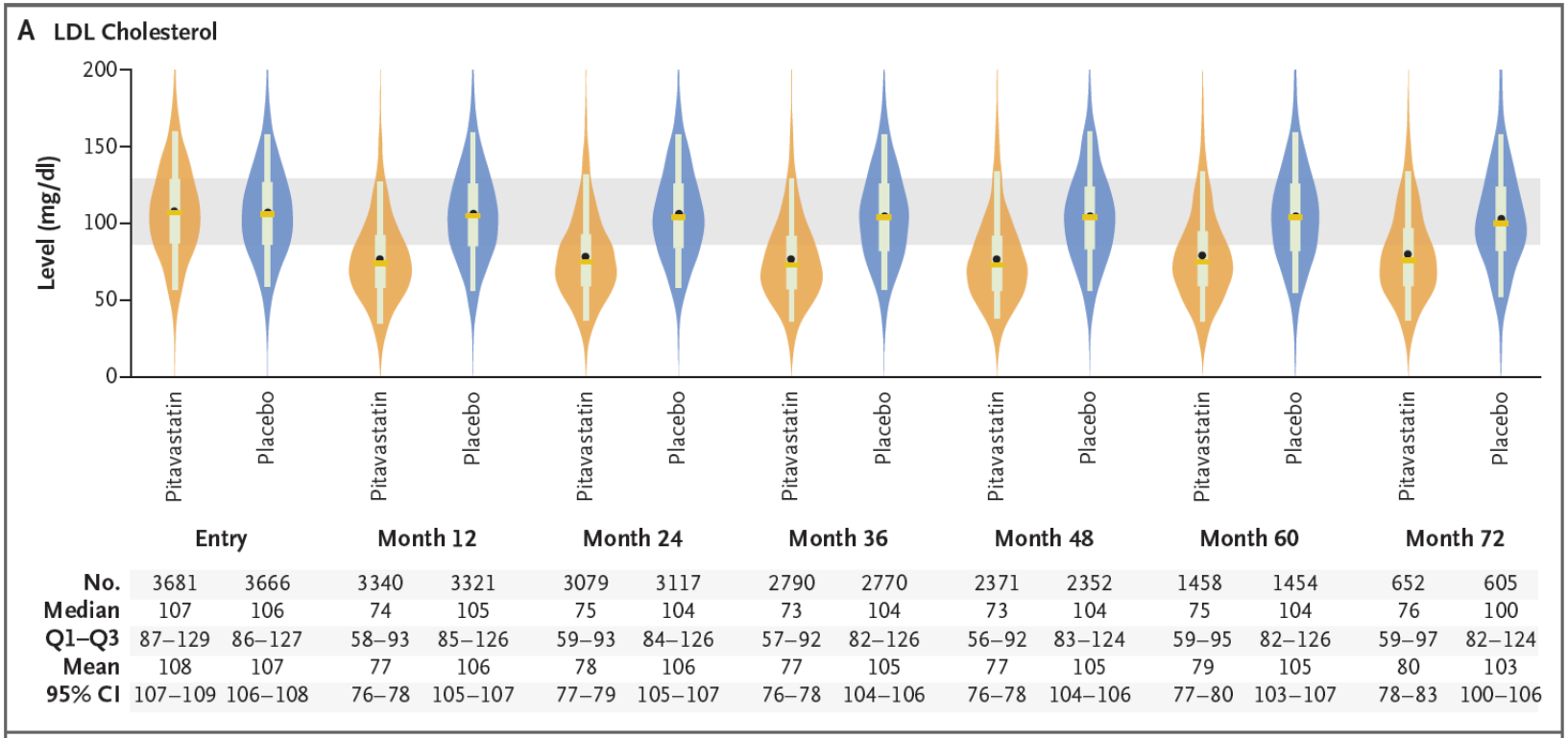
CONCLUSIONS

Participants with HIV infection who received pitavastatin had a lower risk of a major adverse cardiovascular event than those who received placebo over a median follow-up of 5.1 years. (Funded by the National Institutes of Health and others; REPRIEVE ClinicalTrials.gov number, NCT02344290.)

TRIAL POPULATION

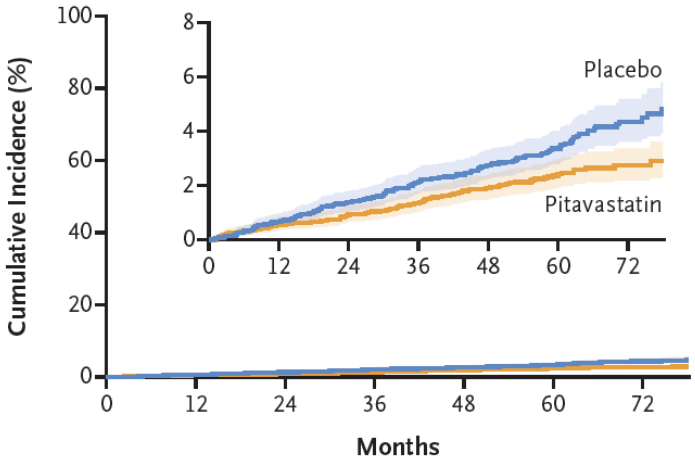
The inclusion criteria included a diagnosis of HIV infection, an age of 40 to 75 years, and receipt of stable antiretroviral therapy. All the participants had a low-to-moderate risk of atherosclerotic cardiovascular disease, as determined by the score on the American Heart Association and American College of Cardiology 2013 Pooled Cohort Equation risk calculator[15] — a risk of up to 15% for LDL cholesterol (≥70 mg per deciliter [1.81 mmol per liter]) in conjunction with LDL cholesterol levels below specific thresholds.



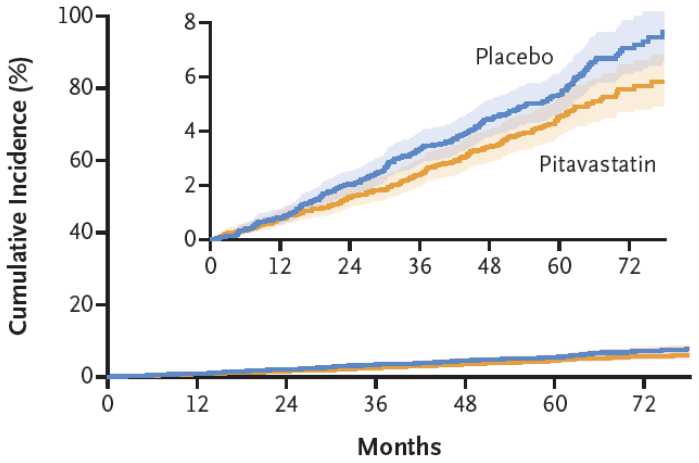
	Entry		Month 12		Month 24		Month 36		Month 48		Month 60		Month 72	
No.	3681	3666	3340	3321	3079	3117	2790	2770	2371	2352	1458	1454	652	605
Median	107	106	74	105	75	104	73	104	73	104	75	104	76	100
Q1–Q3	87–129	86–127	58–93	85–126	59–93	84–126	57–92	82–126	56–92	83–124	59–95	82–126	59–97	82–124
Mean	108	107	77	106	78	106	77	105	77	105	79	105	80	103
95% CI	107–109	106–108	76–78	105–107	77–79	105–107	76–78	104–106	76–78	104–106	77–80	103–107	78–83	100–106

Figure 3. Fasting Cholesterol Levels.

Shown are violin plots of data regarding LDL cholesterol (Panel A) and non–high-density lipoprotein (HDL) cholesterol (Panel B) in the pitavastatin group and the placebo group. In each plot, the mean value is indicated by a circle, the median by a horizontal line, and the interquartile range (Q1–Q3) by the top and bottom of a box; whiskers indicate the 5th and 95th percentiles, and the tapering points reflect the shape of the distribution. For reference, the shaded area indicates the matching interquartile ranges in the pitavastatin and placebo groups at trial entry. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.



Cumulative Incidence of Event (%)							
Placebo	0.00	0.66	1.38	2.14	2.74	3.36	4.36
Pitavastatin	0.00	0.56	0.95	1.35	1.89	2.41	2.73
No. at Risk							
Placebo	3881	3693	3506	3356	2997	2182	959
Pitavastatin	3888	3647	3475	3364	2997	1947	1052



Cumulative Incidence of Event (%)							
Placebo	0.00	0.80	2.03	3.34	4.44	5.35	7.06
Pitavastatin	0.00	0.77	1.58	2.39	3.40	4.54	5.54
No. at Risk							
Placebo	3881	3693	3506	3356	2997	1975	919
Pitavastatin	3888	3647	3475	3364	2998	1948	1027

Figure 1. Treatment Effect of Pitavastatin on Major Adverse Cardiovascular Events.

Shown is the incidence rate of a major adverse cardiovascular event (MACE) among trial participants with human immunodeficiency virus (HIV) infection in the pitavastatin group and the placebo group and the estimated treatment effect, according to stratified Cox proportional-hazards analysis (Panel A). Also shown are the cumulative incidence of the primary outcome (first MACE) (Panel B) and a key secondary outcome (first MACE or death from any cause) (Panel C). In Panels B and C, the insets show the data on an expanded y axis. At the top of Panel A, the primary outcome of the trial is shown in bold text. Panel A also shows the treatment effect for secondary and supportive analyses. Cox proportional-hazards models were stratified according to sex at birth and the CD4 cell count at screening. Aside from the primary result, the widths of the confidence intervals have not been adjusted for multiplicity and therefore may not be used in place of hypothesis testing. TIA denotes transient ischemic attack.

Recommendation Table 6 — Recommendations for statin therapy in primary prevention for people with human immunodeficiency virus infection (see also Supplementary data online, Evidence Table 6)

Recommendation	Class[a]	Level[b]
Statin therapy is recommended for people in primary prevention aged ≥40 years with HIV, irrespective of estimated cardiovascular risk and LDL-C levels, to reduce the risk of cardiovascular events; the choice of statin should be based on potential drug interactions.[7]	I	B

HIV, human immunodeficiency virus; LDL-C, low-density lipoprotein cholesterol.
[a]Class of recommendation.
[b]Level of evidence.

European Heart Journal (2025) **46**, 4359–4378
https://doi.org/10.1093/eurheartj/ehaf190

Recommendation Table 7 — Recommendations for statin therapy in patients receiving cancer therapy (see also Supplementary data online, Evidence Table 7)

Recommendation	Class[a]	Level[b]
Statins should be considered in adult patients at high or very high risk of developing chemotherapy-related cardiovascular toxicity[c] to reduce the risk of anthracycline-induced cardiac dysfunction.[9,132–134]	IIa	B

[a]Class of recommendation.
[b]Level of evidence.
[c]Baseline cardiovascular toxicity risk stratification discussed in detail in the 2022 ESC Guidelines on cardio-onocology.[135]

Recommendation Table 8 — Recommendations for dietary supplements (see also Supplementary data online, Evidence Table 8)

Recommendation	Class[a]	Level[b]
Dietary supplements or vitamins without documented safety and significant LDL-C-lowering efficacy are not recommended to lower the risk of ASCVD.[10,11]	III	B

ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol.

[a]Class of recommendation.

[b]Level of evidence.

European Heart Journal (2025) **46**, 4359–4378
https://doi.org/10.1093/eurheartj/ehaf190

Conclusion

Avec les recommandations ESC 2025, qui va échapper au traitement hypolipémiant ?