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

Main Principles for LDL-lowering Therapy

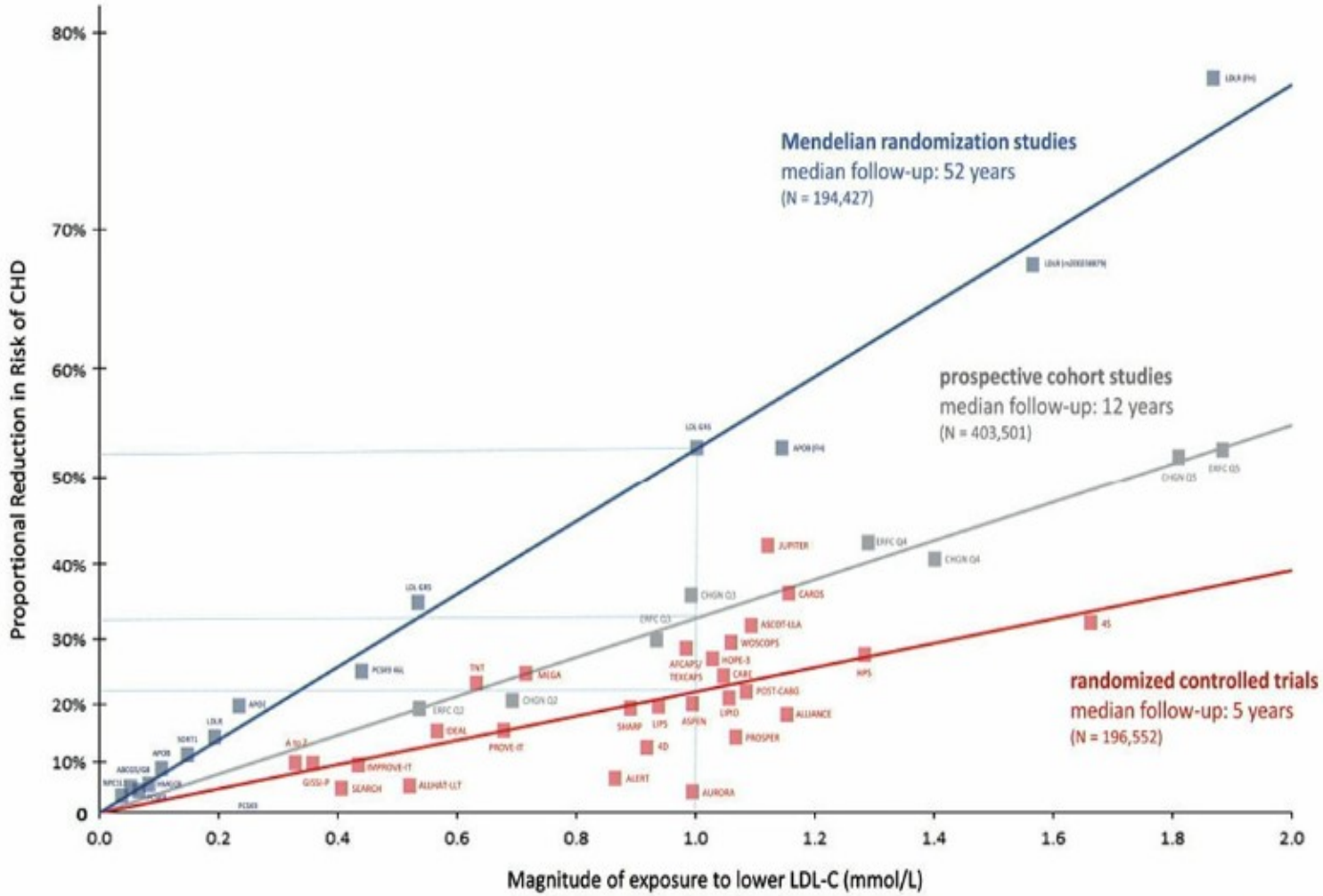
- Genetic, epidemiological and trial evidence indicates that LDL cholesterol is a CAUSE of atherosclerotic vascular disease

- Trials of LDL-lowering indicate RELATIVE RISK reduction is proportional to the ABSOLUTE REDUCTION in LDL-C

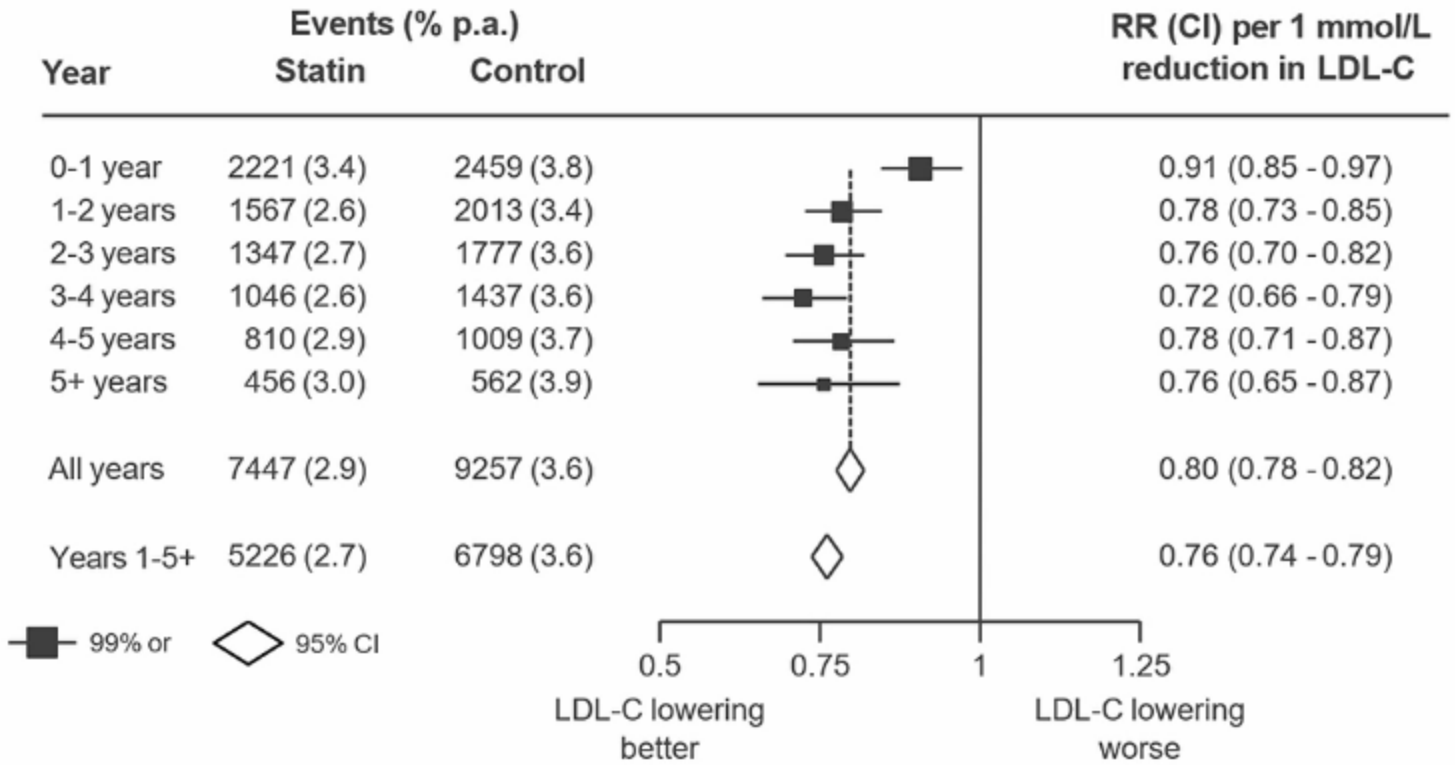
- Lower is better: lowering LDL-C with statins, ezetimibe, or PCSK9-inhibitors safe and effective to <1.4 mmol/L (55 mg/dL). The extent of the benefit is independent of the type of drug but related to the LDL reduction

- Intensity of LDL-lowering should be based on risk, irrespective of cause(s) of the risk (e.g., primary or secondary prevention, diabetes, or chronic kidney disease)

Effect Of LDL-C By Magnitude And Duration Of Exposure



Effect of statin therapy on MAJOR VASCULAR EVENTS : 22 trials of statin vs control



Test for heterogeneity between RR in first year and RR in years 1-5+: $p<0.0001$

Linee Guida ESC/EAS: Principi per la Stima del Rischio

- Nelle persone apparentemente sane, **il rischio di CVD è il più delle volte il risultato dell'interazione di molteplici fattori di rischio**. Questa è la base per la stima e la gestione del rischio CV totale

- Un **sistema per la stima del rischio così come lo SCORE,** può aiutare a prendere decisioni razionali per la gestione e **può aiutare ad evitare sia il sotto che il sovra-trattamento**

- Alcuni individui sono a rischio di CVD alto o molto alto senza bisogno di un punteggio del rischio e tutti i fattori di rischio richiedono un'attenzione immediata. Questo vale per i pazienti con CVD documentata, anziani con DM di lunga data, ipercolesterolemia familiare, malattia renale cronica, placche carotidee o femorali, punteggio del calcio coronarico >100 o elevazione estrema della Lp(a)

1. Mach F. et al., 2020

Cardiovascular risk estimation: New Recommendations (1)

Recommendations	Class	Level
Recommendations for cardiovascular risk estimation in persons without known cardiovascular disease		
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.	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.	I	B

Linee Guida ESC/EAS: Criteri del Livello di Rischio per CVD – Update 2025

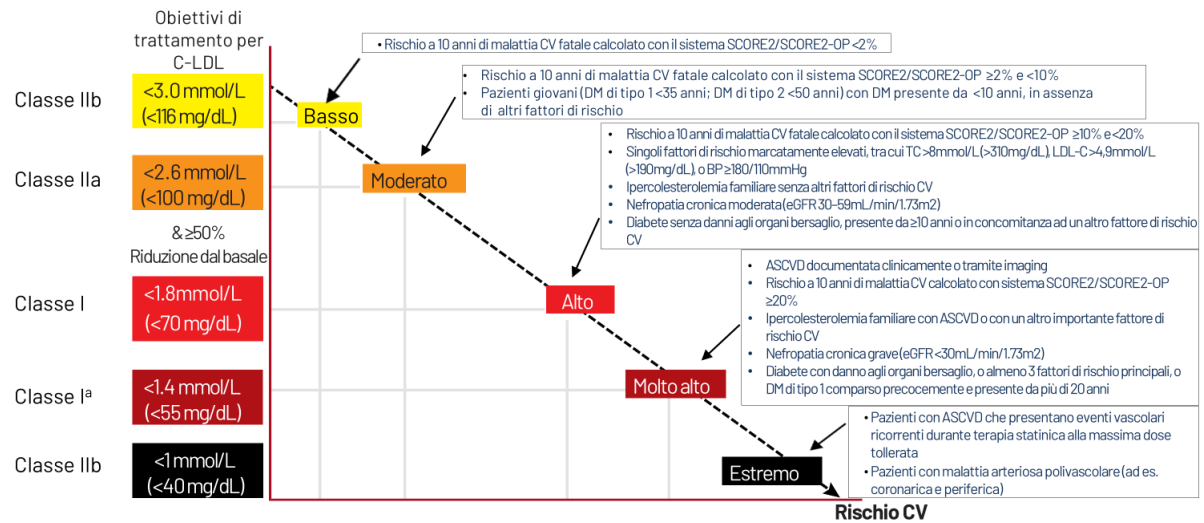
Livello di rischio	Persone Con Una delle Seguenti Condizioni:
Molto alto	• ASCVD documentata clinicamente o tramite imaging. ASCVD documentata include pregressa sindrome coronarica acuta (infarto miocardico o angina instabile), sindromi coronariche croniche, rivascolarizzazione coronarica (PCI, CABG e altre procedure di rivascolarizzazione arteriosa), ictus e TIA, e malattia arteriosa periferica. Chiara ASCVD documentata tramite imaging include riscontri noti per essere associati allo sviluppo futuro di eventi clinici, come una placca rilevante all'angiografia coronarica, o alla TAC o all'ultrasonografia carotidea. • Diabete con danno agli organi bersaglio, o almeno 3 fattori di rischio principali, o DM di tipo 1 comparso precocemente e presente da più di 20 anni • Nefropatia cronica grave (eGFR <30mL/min/1.73m2) • Rischio a 10 anni di malattia CV calcolato con sistema SCORE ≥10% • Ipercolesterolemia familiare con ASCVD o con un altro importante fattore di rischio CV
Alto	• Singoli fattori di rischio marcatamente elevati, tra cui TC >8mmol/L (>310mg/dL), LDL-C >4,9mmol/L (>190mg/dL), o BP ≥180/110mmHg • Ipercolesterolemia familiare senza altri fattori di rischio CV • Diabete senza danni agli organi bersaglio, presente da ≥10 anni o in concomitanza ad un altro fattore di rischio CV • Nefropatia cronica moderata (eGFR 30–59mL/min/1.73m2) • Rischio a 10 anni di malattia CV fatale calcolato con il sistema SCORE ≥10% e <20%
Moderato	• Pazienti giovani (DM di tipo 1 <35 anni; DM di tipo 2 <50 anni) con DM presente da <10 anni, in assenza di altri fattori di rischio • Rischio a 10 anni di malattia CV fatale calcolato con il sistema SCORE ≥2% e <10%
Basso	• Rischio a 10 anni di malattia CV fatale calcolato con il sistema SCORE <1%

ASCVD, malattia cardiovascolare aterosclerotica; BP, pressione arteriosa; CT, tomografia computerizzata; CVD, malattia cardiovascolare; DM, diabete mellito; EAS, European Atherosclerosis Society; eGFR, tasso di filtrazione glomerulare stimato; ESC, European Society of Cardiology; LDL-C, colesterolo lipoproteico a bassa densità; SCORE, Systematic Coronary Risk Estimation; TC, colesterolo totale

1. European Heart Journal (2025) 00, 1–20

Rischio particolarmente elevato
Livelli target di C-LDL <40 mg/dl
Rischio molto alto o prevenzione secondaria
Riduzione del LDL-C ≥50% rispetto al basale e livelli target di C-LDL <55 mg/dl
Rischio alto
Riduzione del LDL-C ≥50% rispetto al basale e livelli target di C-LDL <70 mg/dl
Rischio moderato
Livelli target di C-LDL <100 mg/dl
Rischio basso
Livelli target di C-LDL <116 mg/dl

Obiettivi di trattamento per il C-LDL



[a]:Classe IIa per pazienti in prevenzione primaria con ipercolesterolemia familiare a rischio molto alto

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

1. European Heart Journal (2025) 00, 1-20

le carte del rischio precedenti :

Non includevano alcuni fattori prognosticamente rilevanti tra cui:
durata dell’esposizione al rischio,
familiarità,
predisposizione genetica,
obesità,
pre-diabete/sindrome metabolica
L’area geografica
I cosidetti MODIFICATORI DEL RISCHIO

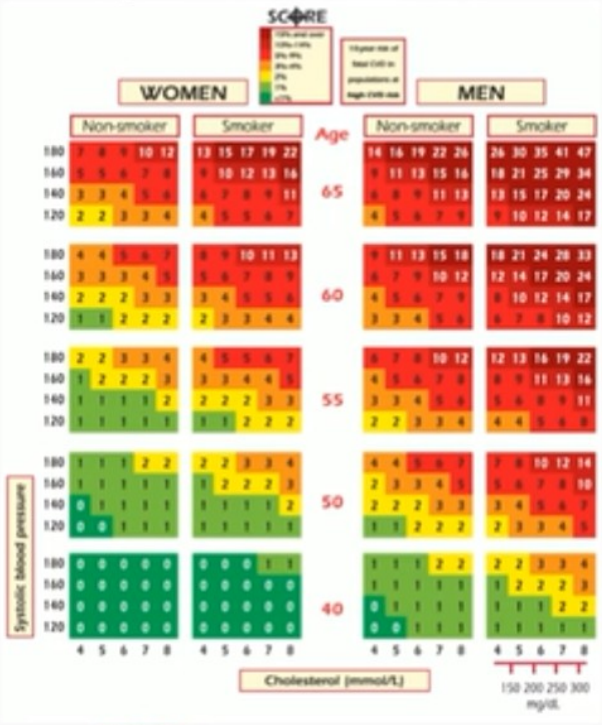
Non sempre sono in grado di discriminare individui con aterosclerosi precoce

Le carte del rischio:

1) Non includono alcuni fattori prognosticamente rilevanti tra cui durata della esposizione al riscio familiarità, predisposizione genetica ,obesità,prediabete /sindomre metabolica
2) Non sempre sono in grado di discriminare individui con aterosclerosi precoce
3) Risentono delle caratteristiche della popolazione di riferimento:la stima del rischio sovra/sottostimata quando applicata ad altre popolazioni
4) **tutte le precedenti**

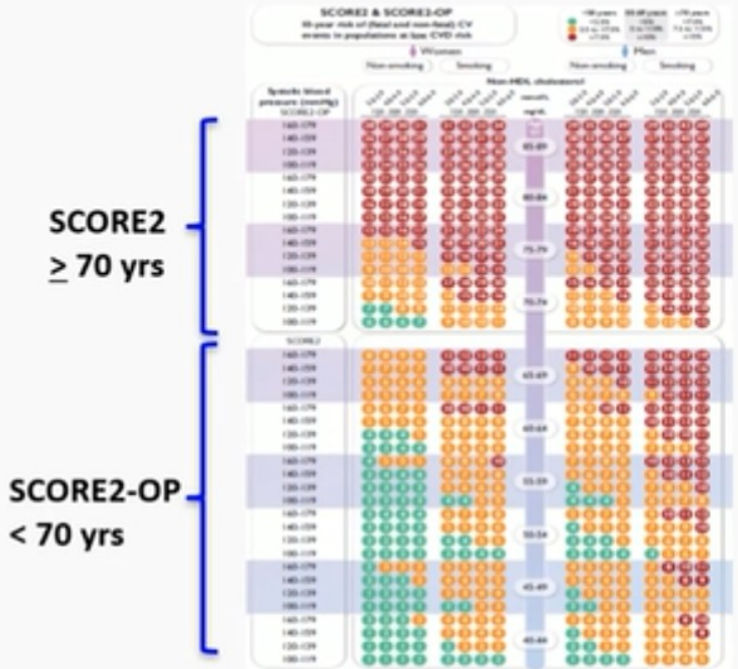
SCORE

- Age 40-70 y
- 10-year risk of fatal CVD

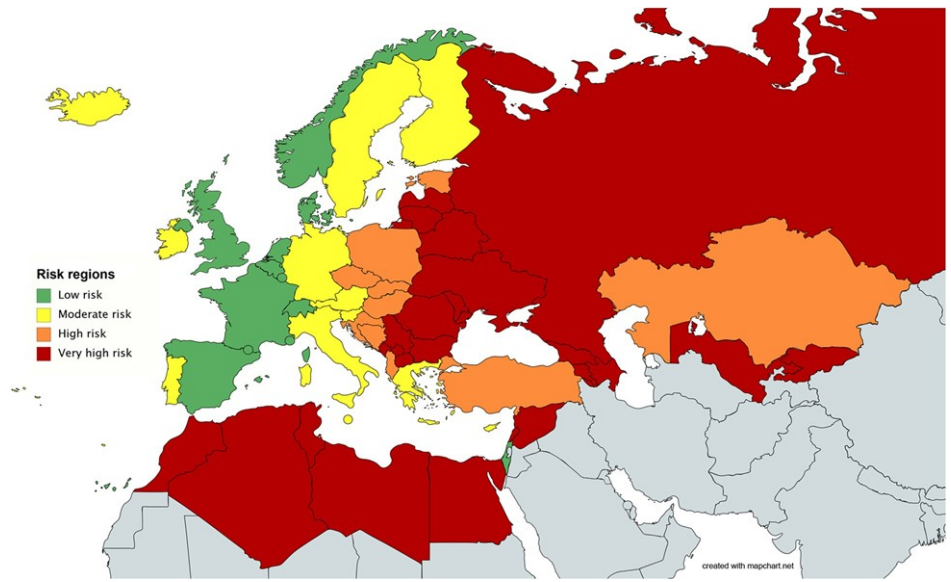


SCORE2 / SCORE2-OP

- Age 40-89 y
- 10-year risk of fatal and non-fatal CVD

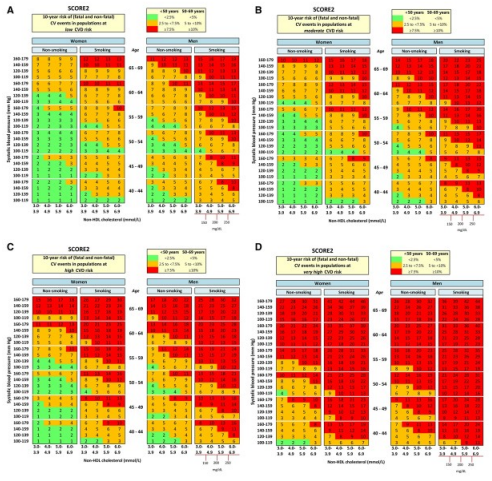


basso rischio (<100 decessi per malattie cardiovascolari ogni 100.000),
rischio moderato (da 100 a <150 decessi per malattie cardiovascolari ogni 100.000),
alto rischio (da 150 a <300 decessi per malattie cardiovascolari ogni 100.000)
e rischio molto alto (≥300 decessi per malattie cardiovascolari ogni 100.000)

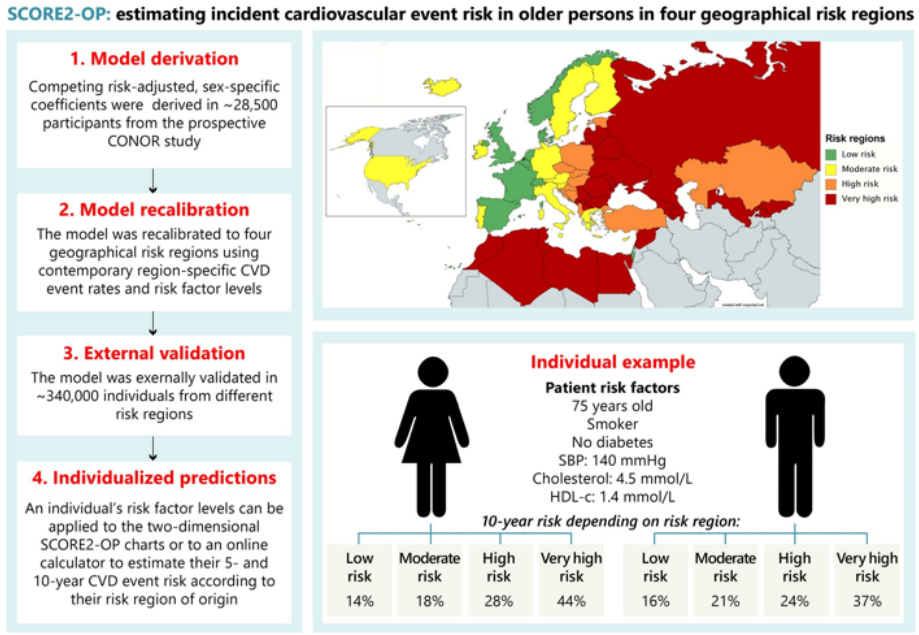


A differenza del vecchio algoritmo, basato sul colesterolo totale, SCORE2 e SCORE2-OP utilizzano il colesterolo non-HDL e consentono di calcolare non solo il rischio di eventi fatali, ma anche non fatali, includendo le persone sopra i 70 anni.

Figure 3 SCORE2 charts for estimation of CVD risk in four European risk regions.



Eur Heart J, Volume 42, Issue 25, 1 July 2021, Pages 2439–2454, https://doi.org/10.1093/eurheartj/ehab309



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

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 any of the following: • 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	People with any of the following: • 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

Cardiovascular risk categories (1)

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

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), **chronic coronary syndromes**, 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** or on carotid **or femoral** ultrasound **or markedly elevated CAC score by CT**. • 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 m^2). • A calculated **SCORE2 or SCORE2-OP** ≥20% for 10-year risk of fatal or non-fatal CVD. • FH with ASCVD or with another major risk factor.

Cardiovascular risk estimation: New Recommendations (2)

Recommendations	Class	Level
Recommendations for cardiovascular risk estimation in persons without known cardiovascular disease		
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.	IIa	B
Risk modifiers should be considered in individuals at moderate risk or individuals around treatment decision thresholds to improve risk classification.	IIa	B

Modificatori del rischio

Clinici

Anatomici

Bioumorali

Clinico-demografici
Storia familiare di malattia cardiovascolare precoce (uomini <55 anni; donne <60 anni)
Popolazioni ad alto rischio (es. sud-asiatiche)
Sintomi da stress e fattori di stress psicosociali
Obesità
Inattività fisica
Malattie croniche infiammatorie/immuno-mediate
Disordini psichiatrici maggiori
Menopausa precoce
Pre-eclampsia e altri disordini ipertensivi in gravidanza
Infezione da HIV
Sindrome delle apnee ostruttive del sonno

Anatomici
Aterosclerosi coronarica subclinica all'imaging
Score del calcio coronarico elevato
Bioumorali
Livelli di hs-PCR persistentemente elevati (>2 mg/l)
Livelli elevati di Lp(a) (>50 mg/dl [>105 nmol/l])

ESC European Society of Cardiology
European Journal of Preventive Cardiology (2022) 29, 1553–1714
https://doi.org/10.1093/eurjpc/zwac087
FULL RESEARCH PAPER
Prevention in practice

Improving 10-year cardiovascular risk prediction in apparently healthy people: flexible addition of risk modifiers on top of SCORE2

Steven H. J. Hageman [1], Carmen Petitjean[2,3], Lisa Pennells[2,3], Stephen Kaptoge[2,3], Romin Pajouheshnia[4], Taavi Tillmann[5], Michael J. Blaha[6], Robyn L. McClelland[7], Kunihiro Matsushita[8], Vijay Nambi[9,10], Olaf H. Klungel[4], Patrick C. Souverein[4], Yvonne T. van der Schouw[11], W. M. Monique Verschuren[12], Nils Lehmann[13], Raimund Erbel[13], Karl-Heinz Jöckel[13], Emanuele Di Angelantonio[2,3,14,15,16,17], Frank L. J. Visseren[1], and Jannick A. N. Dorresteijn[1]**

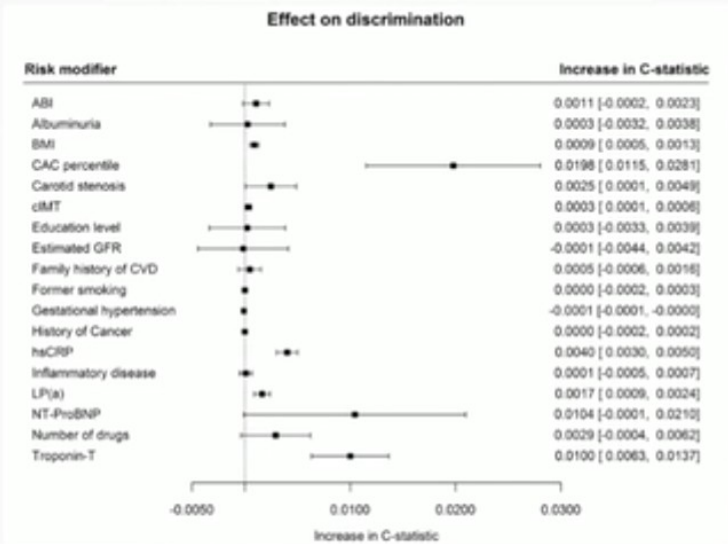
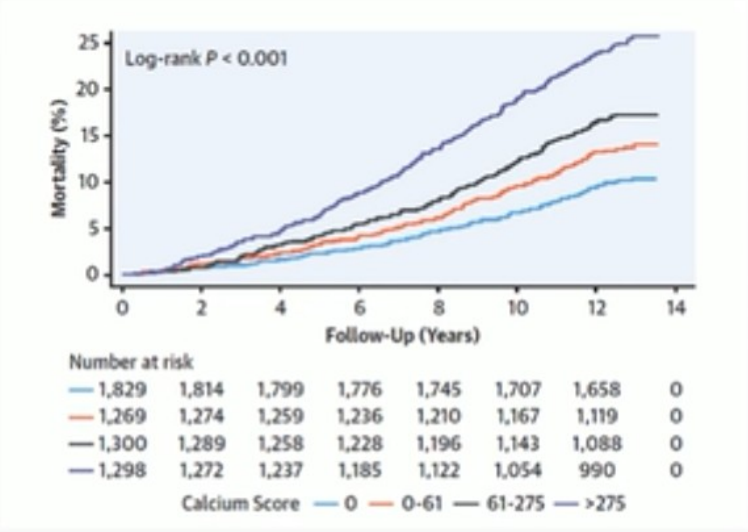


Table 2 Subdistribution hazard ratios of the additional predictors

Predictor	Subdistribution hazard ratio (95% CI)
Ankle–brachial index (<0.9)	1.46 (1.18–1.80)
Body mass index (kg/m^2)†	1.02 (0.81–1.32)
CAC percentile†	1.78 (1.53–2.00)
History of cancer	1.07 (1.00–1.13)
Carotid stenosis (>25%)	1.54 (1.22–1.94)
Carotid intima-media thickness (mm)‡	1.02 (0.92–1.14)
Estimated GFR (mL/min/1.73m^2)†	0.91 (0.56–1.48)
CRP (mg/L)*	1.31 (1.28–1.35)
History of chronic inflammatory disease	0.95 (0.54–1.67)
Lower education level	1.30 (1.18–1.43)
Parental history of myocardial infarction	1.36 (1.20–1.53)
Former smoking (vs. never)	1.05 (1.00–1.09)
Gestational hypertension	1.15 (0.97–1.36)
Lp(a) (mg/dL)*	1.14 (1.12–1.17)
Albuminuria (>30 mg/g)	1.34 (1.26–1.43)
Number of drugs (*n*)†	1.18 (1.05–1.32)
NT-ProBNP (pg/mL)*	1.47 (1.37–1.57)
hs-Troponin-T (pg/mL)*	1.55 (1.44–1.68)

Influence of Subclinical Atherosclerosis Burden and Progression on Mortality

- N=5,716 asymptomatic U.S. adults
- Mean age 68.9 years, 56.7% female
- Baseline: vascular ultrasound to quantify carotid plaque burden (cPB) + computed tomography for CAC
- Median follow-up: 12.4 yrs



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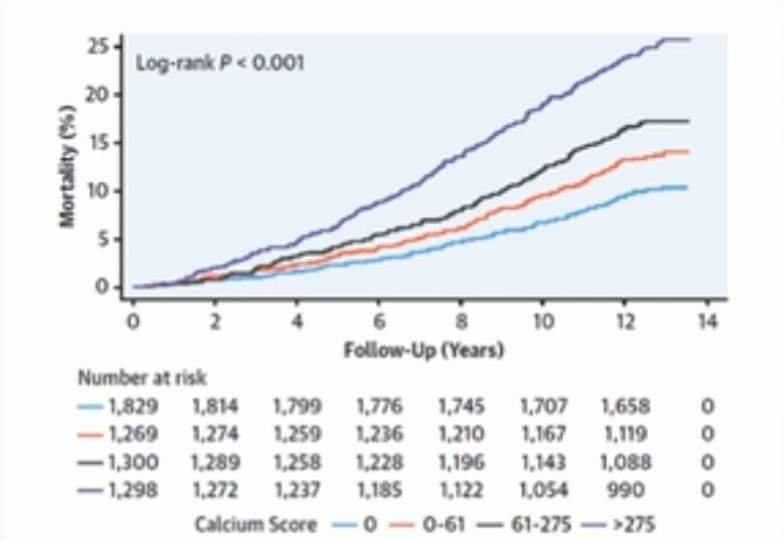
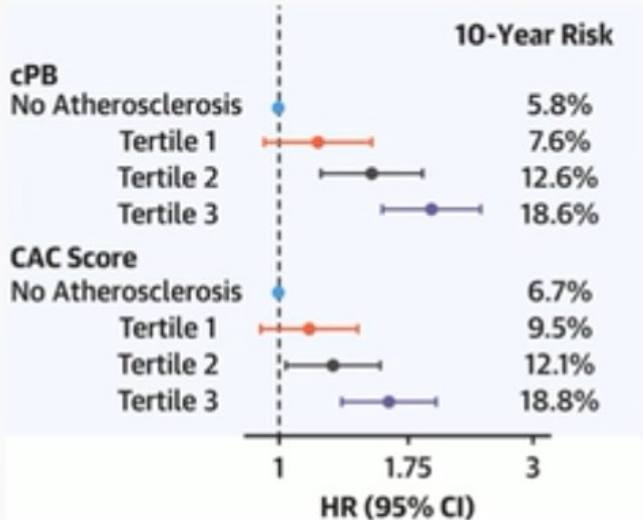




Very High Coronary Artery Calcium (≥1000) and Association With Cardiovascular Disease Events, Non–Cardiovascular Disease Outcomes, and Mortality

Results From MESA

- N= 6,814 individuals free of known CVD
- Mean age 68.9 years, 56.7% female
- **Event rates calculated as a function of CAC** and compared them with those in the placebo group of secondary prevention pts (FOURIER trial)
- Mean follow-up: 13.6 yrs

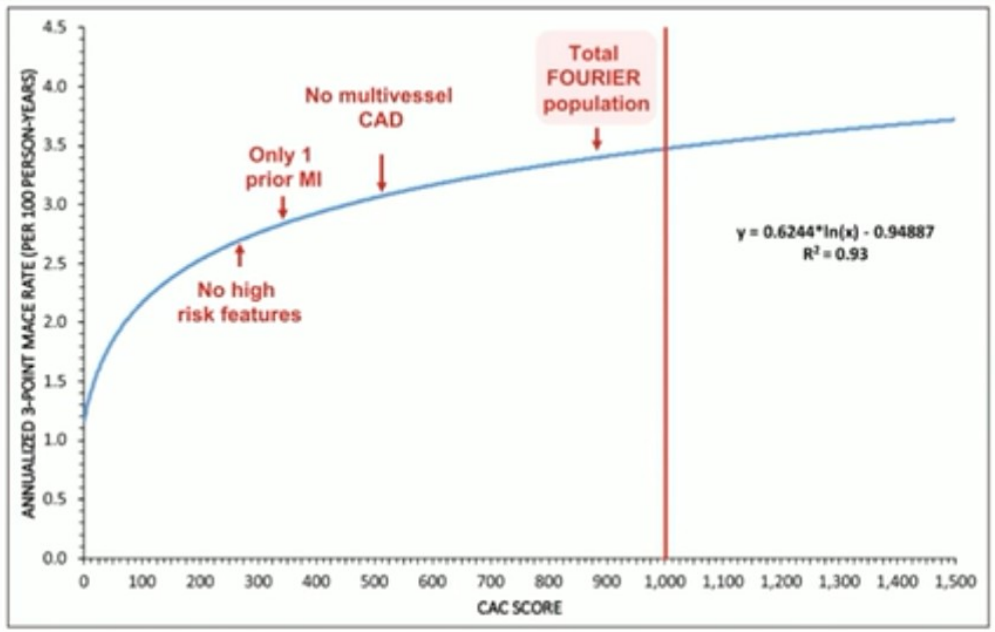


Figure 2. Annualized 3-point major adverse cardiovascular event (MACE) rate (per 100 person-years) as a function of coronary artery calcium (CAC) score.

Peng AW et al. Circulation 2021;143:1571-1583

A person with evidence of atherosclerosis on imaging

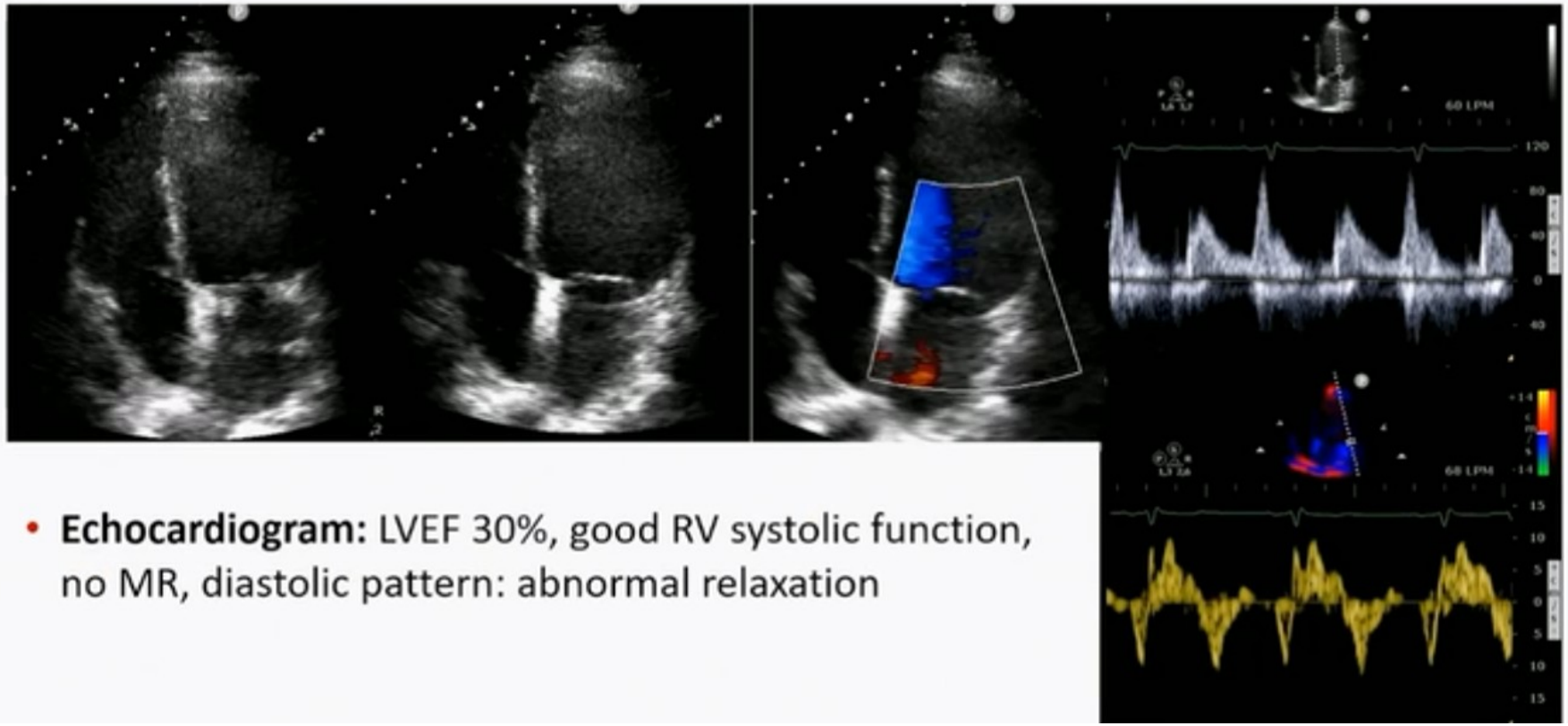
- 55 year-old male, ex-smoker, 198 cm height and 146 kg weight (BMI 37.2), no other conventional cardiovascular risk factors.

- Clinical antecedents:
  - 2020: diagnosed with Monoclonal Gammopathy of Undetermined Significance (MGUS) with abnormal monoclonal protein IgA kappa light chain that progressed to multiple myeloma in 2021.
  - He received 4 cycles of carfilzomib, lenalidomida and dexametasona, intensified with melphalan at high doses and eventually he received autologous transplant that was not effective.
  - 2022: chemotherapy related dilated cardiomyopathy. LVEF 30%
  - Medication: sacubitril/valsartan, bisoprolol, eplerenon, torasemida, dapaglifozin, lenalidomida and zolendronate, aspirin.
- **Current symptoms: dyspnea on exertion. No chest pain.**

A person with evidence of atherosclerosis on imaging

- Physical exam: BP 116/78 mmHg, HR 79 bpm, no murmurs, no signs of acute heart failure
- ECG: sinus rhythm 80 bpm, normal QRS voltage, normal QT
- Blood test:
  - Ht 34% ⇩
  - Hb 7.1 mmol/L (11.4 g/dL) ⇩
  - Glu 6.2 mmol/L (111 mg/dL) ⇧
  - Hb1Ac 6%
  - eGFR 73mL/min/1.73m²
  - Proteinuria 285 mg/24h
  - NTproBNP 88 pmol/L
  - Total Cholesterol 4.9 mmol/L (185.6 mg/dL)
  - HDL 1.2 mmol/L (46.4 mg/dL)
  - LDL 2.8 mmol/L (108.3 mg/dL)
  - Triglyc 2.1 mmol/L (186 mg/dL)

A person with evidence of atherosclerosis on imaging



- **Echocardiogram:** LVEF 30%, good RV systolic function, no MR, diastolic pattern: abnormal relaxation

New Recommendations

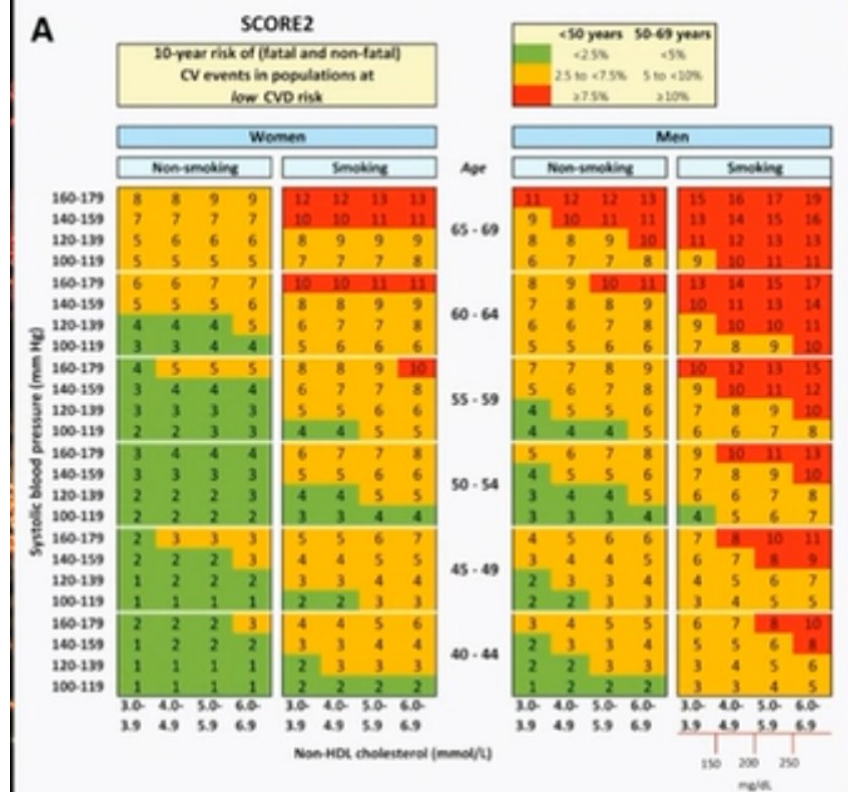
Recommendations	Class	Level
Recommendations for cardiovascular risk estimation in persons without known cardiovascular disease		
SCORE2 is recommended in apparently healthy people <70 years of age without established ASCVD, DM, CKD, genetic/rare lipid or BP disorders for estimation of 10-year fatal and non-fatal CVD risk.	I	B

Question

- **What is the cardiovascular risk category of this patient?**

A. Very high risk
B. High risk
C. Moderate risk
D. Low risk
E. Difficult to say because we cannot apply the SCORE2

SCORE2 calculator – low risk countries



What is CVD risk?

CVD risk means your risk of a fatal or non-fatal cardiovascular disease event (a composite of cardiovascular mortality, non-fatal myocardial infarction and non-fatal stroke) in the next 10 years.

Your results

Age: 60 (1/1965)

Sex: male

Systolic blood pressure: 116 mmHg

Total Cholesterol: 4,9 mmol/L

HDL-Cholesterol: 1,2 mmol/L

LDL-Cholesterol: 2,8 mmol/L

Current Smoker: No

Your 10-year risk of fatal and non-fatal CVD events is * :
4.6%

Your Risk Age: because of your risk factors, your risk is similar to a **60** year old person with low risk factors. You can reduce risk further by becoming aware of your risk factors and by changing your lifestyle.

Healthy Lifestyle Advice:
- 150 - 300 min/week of moderate intensity or 75 - 150 min/week of vigorous intensity aerobic physical activity, or an equivalent combination thereof
- Healthy diet recommendations include a Mediterranean or similar diet, replace saturated with unsaturated fats, reduce salt intake

For a person of your age, the Guidelines consider a 10-year CVD risk to be high if above:
5%

Cardiovascular risk categories (2)

High risk	People with any of the following: • 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 factor. • Moderate CKD (eGFR 30–59 mL/min/1.73 m^2). • A calculated SCORE2 or SCORE2-OP ≥10% and <20% for 10-year risk of fatal or non-fatal CVD.
Moderate risk	People with any of the following: • Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors. • **Calculated SCORE2 or SCORE2-OP ≥2% and <10% for 10-year risk of fatal or non-fatal CVD**.
Low risk	• Calculated SCORE2 or SCORE2-OP <2% for 10-year risk of fatal or non-fatal CVD.

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

Demographic/clinical conditions

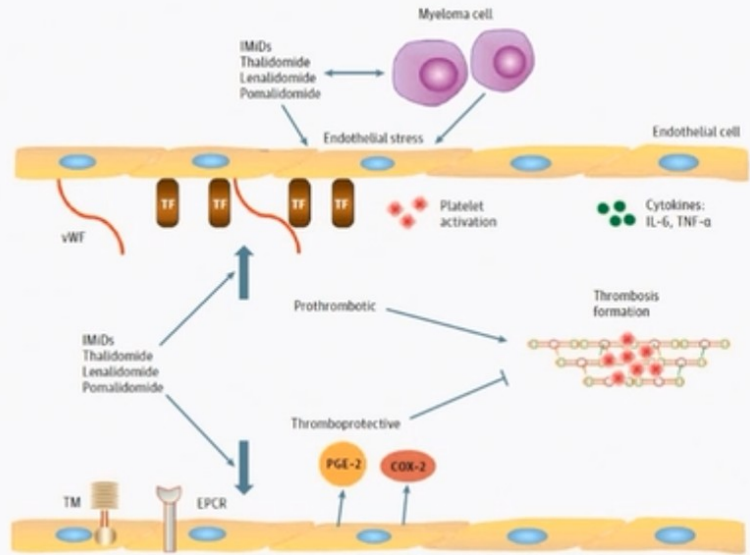
- Family history of premature CVD (men: <55 years; women: <60 years)
- High-risk (e.g. Southern Asian) ethnicity
- **Stress symptoms and psychosocial stressors**
- Social deprivation
- **Obesity**
- **Physical inactivity**
- **Chronic immune-mediated/inflammatory disorders**
- Major psychiatric disorders
- 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)]

Cardiovascular and Thrombotic Complications of Novel Multiple Myeloma Therapies

- MI or stroke account for 8% of early deaths in patients with MM while heart failure is responsible of 13% of those deaths
- Thromboembolic events are the most frequent
- Immunomodulatory drugs increase the risk of MI and stroke
- Proteasome inhibitors are associated with increased risk of heart failure, venous thromboembolism and hypertension.



doi:10.1001/jamaoncol.2016.3350

New Recommendations

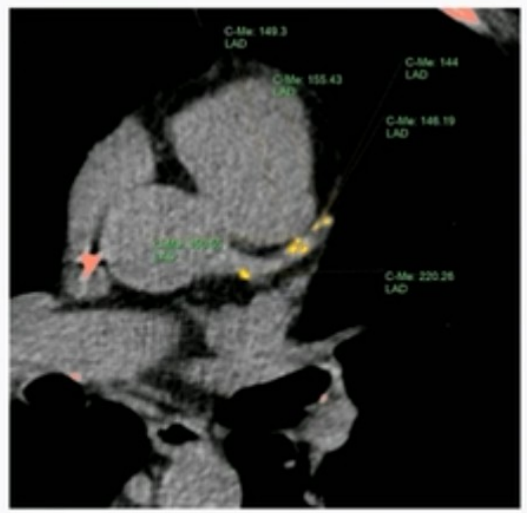
Recommendations	Class	Level
Recommendations for cardiovascular risk estimation in persons without known cardiovascular disease		
Presence of subclinical coronary atherosclerosis by imaging or increased CAC score by CT should be considered as risk modifiers in individuals at moderate risk or individuals around treatment decision thresholds to improve risk classification.	IIa	B
Risk modifiers should be considered in individuals at moderate risk or individuals around treatment decision thresholds to improve risk classification.	IIa	B

Question

- **Considering the symptoms of the patient, what would be your next test?**

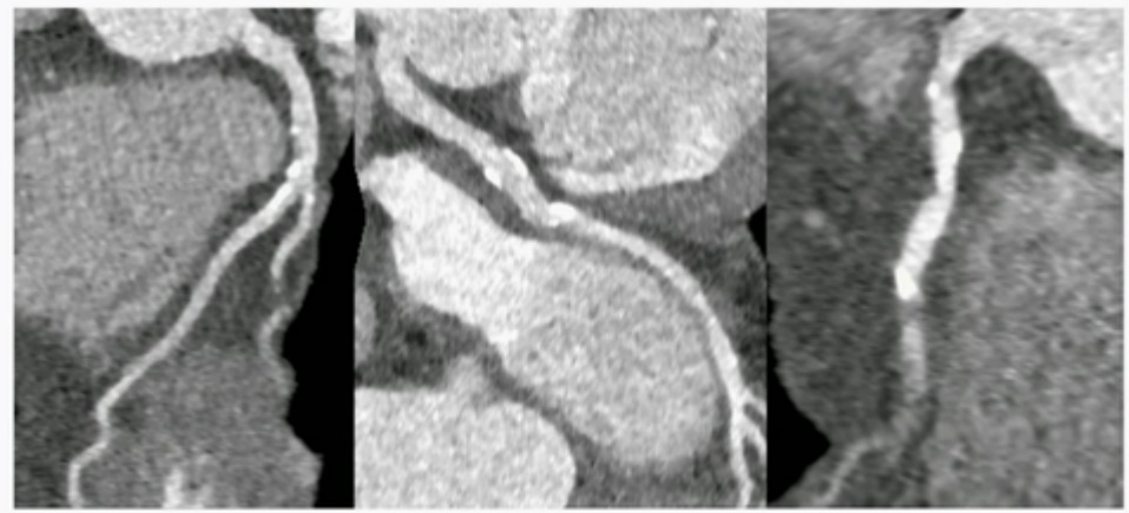
A. Exercise test
B. Dobutamine stress echocardiography
C. Stress CMR
D. CAC score
E. CTCA

CAC score and CTCA



CAC score 655

LAD Cx RCA



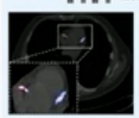
Left dominance, non-obstructive lesions, calcified plaques

Which cut-off value to use for CAC score and severity of coronary plaques

Study Population

5,678 adults with incidental coronary artery calcium (CAC) quantified on routine, non-ECG-gated chest CTs performed between 2014-2019

51% Women
18% Asian
13% Hispanic/Latin

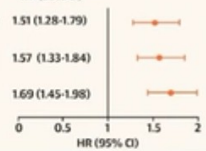


CAC >0 was identified with deep-learning algorithm (DL-CAC) in 52% of patients

Results

Multivariable-adjusted[a] hazard ratios for cardiovascular events mortality of patients with DL-CAC ≥100 compared with DL-CAC=0

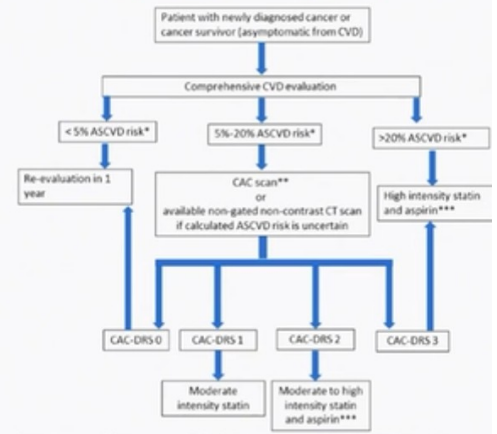
Outcome	HR (95% CI)
All-Cause Mortality	1.51 (1.28-1.79)
Death/MI/Stroke	1.57 (1.33-1.84)
Death/MI/Stroke Revascularization	1.69 (1.45-1.98)



Conclusions

- Incidental CAC ≥100, quantified on routine non-ECG-gated chest CTs using a deep-learning algorithm (DL-CAC), was associated with worse CVD and mortality outcomes, beyond traditional risk factors.
- DL-CAC is a promising, equitable tool for population-wide opportunistic screening for incidental CAC, facilitating earlier intervention by identifying millions of patients at elevated risk for cardiovascular events and mortality.

Peng AW, et al. J Am Coll Cardiol. 2023;82(12):1192–1202.



Journal of Cardiovascular Computed Tomography 17 (2023) 66–83

Quando iniziare la terapia per abbassare LDL IN PREVENZIONE PRIMARIA?

Cardiovascular risk estimation: New Recommendations (3)

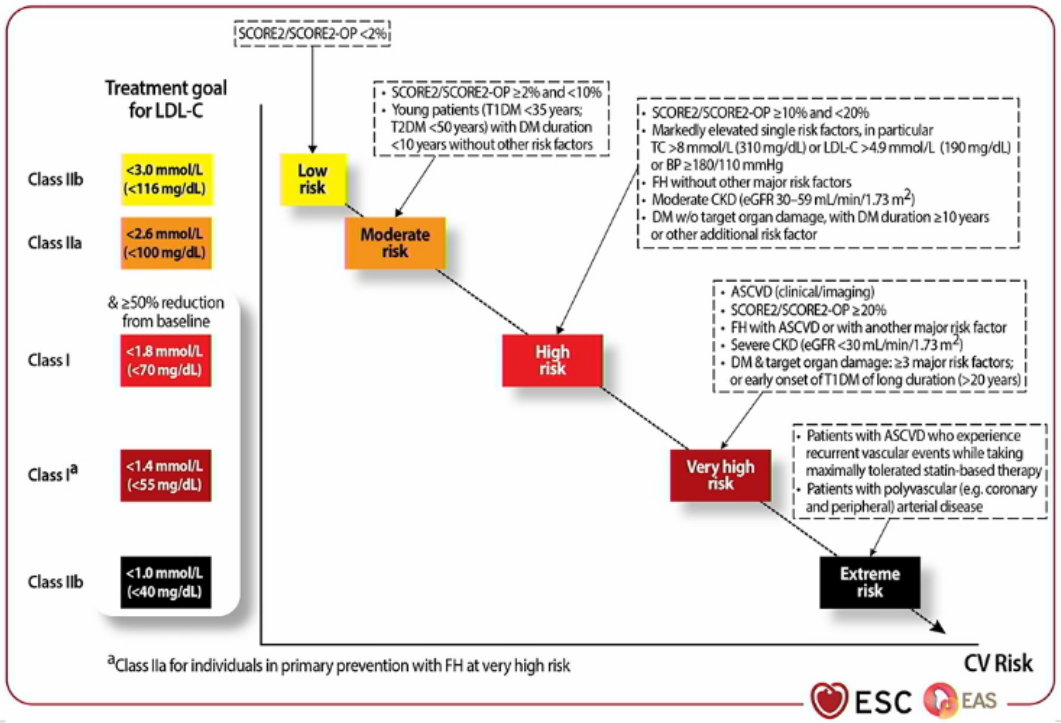
Recommendations	Class	Level
Recommendations for cardiovascular risk estimation in persons without known cardiovascular disease (Continued)		
In **primary prevention, pharmacological LDL-C-lowering therapy** is recommended in persons: • at very high risk and LDL-C ≥1.8 mmol/L (70 mg/dL), or • at high risk and LDL-C ≥2.6 mmol/L (100 mg/dL) despite optimization of non-pharmacological measures, to lower CVD risk.	I	A
In **primary prevention, pharmacological LDL-C-lowering therapy** should be considered in persons: • at very high risk and LDL-C ≥1.4 (55 mg/dL) but <1.8 mmol/L (70 mg/dL), or • at high risk and LDL-C ≥1.8 (70 mg/dL) but <2.6 mmol/L (100 mg/dL), or • at moderate risk and LDL-C ≥2.6 (100 mg/dL) but <4.9 mmol/L (190 mg/dL), or • at low risk and LDL-C ≥3.0 (116 mg/dL) but <4.9 mmol/L (190 mg/dL) despite optimization of non-pharmacological measures, to lower CVD risk.	IIa	A

New Recommendations (3)

Recommendations	Class	Level
Recommendations for pharmacological low-density lipoprotein cholesterol lowering		
Non-statin therapies with proven cardiovascular benefit, 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.	I	A
Bempedoic acid is recommended in patients who are unable to take statin therapy to achieve the LDL-C goal.	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.	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.	IIa	B

Figure 1

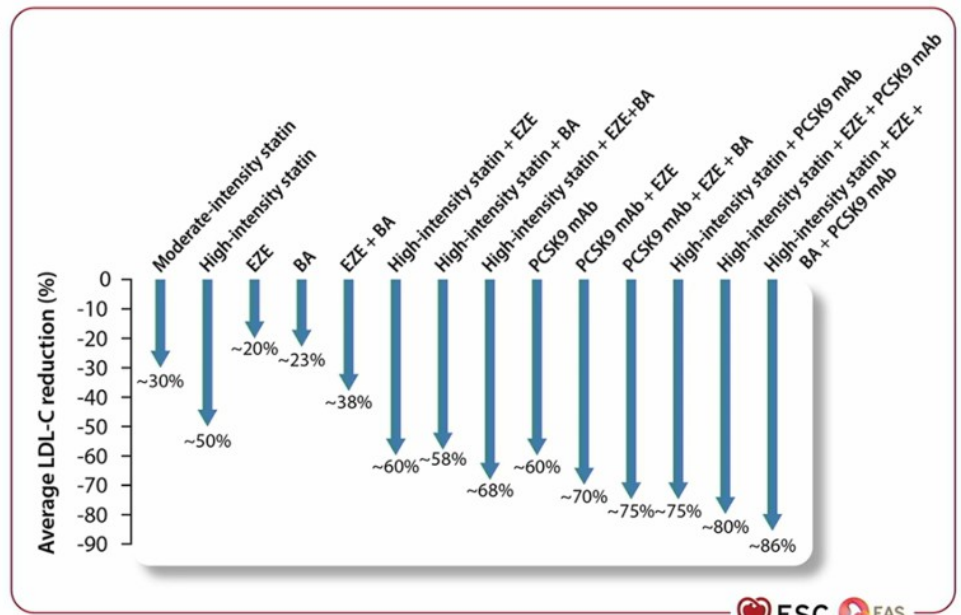
Treatment goals for low-density lipoprotein cholesterol across categories of total cardiovascular risk.



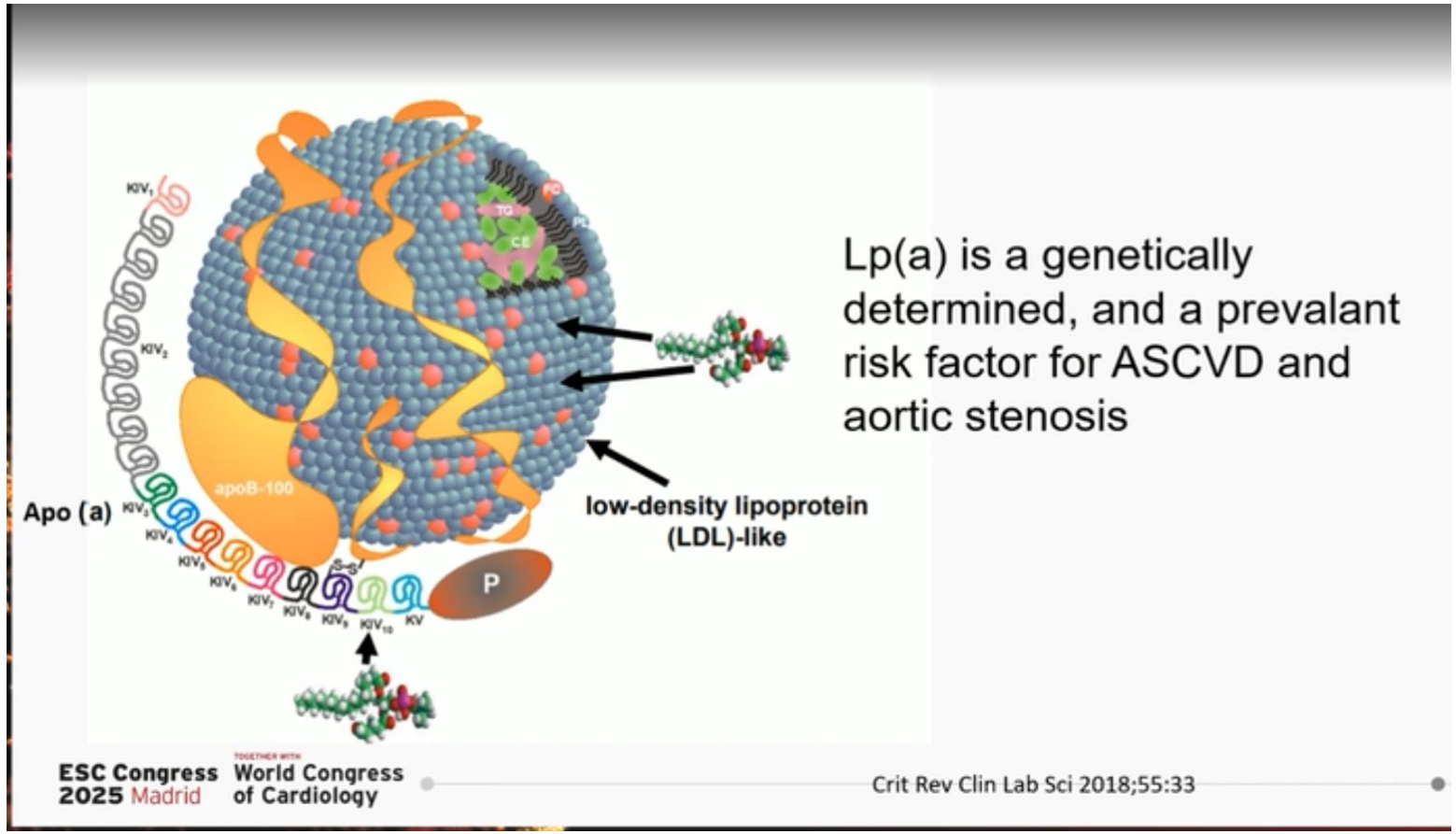
2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias
(European Heart Journal; doi: 10.1093/eurheartj/ehaf190)

Figure 2

Average reduction in low-density lipoprotein cholesterol levels with different pharmacological therapies with proven cardiovascular benefit.



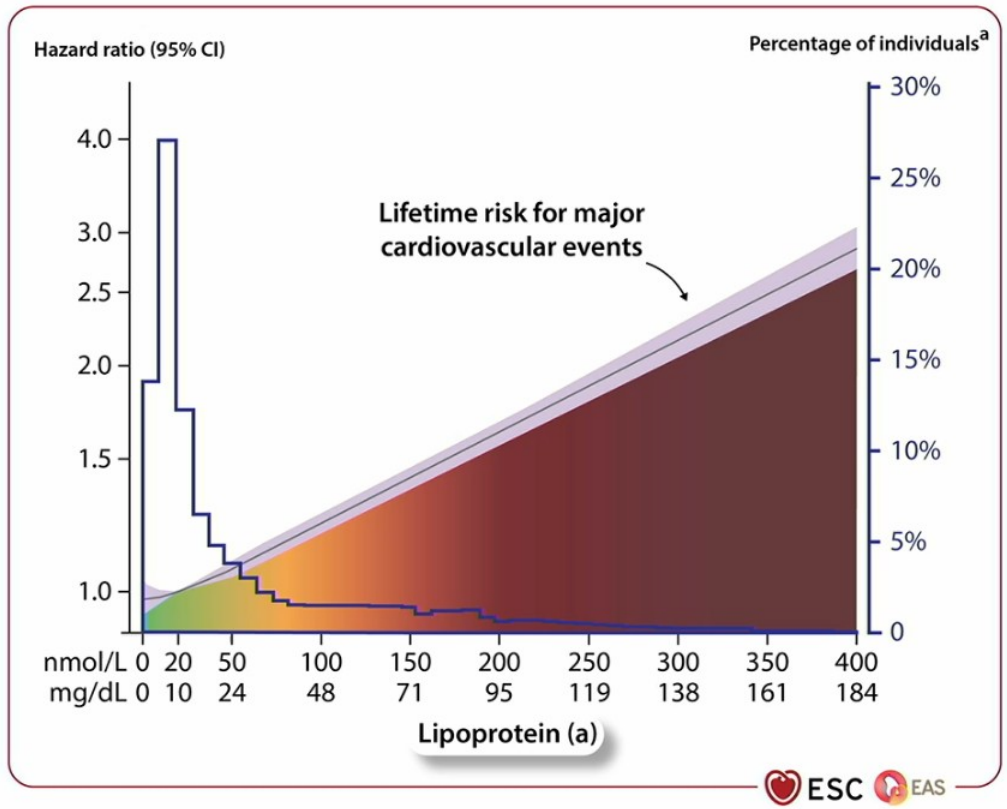
2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias
(European Heart Journal; doi: 10.1093/eurheartj/ehaf190)


Lp(a) is a genetically determined, and a prevalant risk factor for ASCVD and aortic stenosis
Apo (a)
apoB-100
low-density lipoprotein (LDL)-like
P
TG
CE
FC
PL
ESC Congress 2025 Madrid
TOGETHER WITH
World Congress of Cardiology
Crit Rev Clin Lab Sci 2018;55:33

Estimated prevalence of elevated Lp(a) globally

Figure 3

Association between Lp(a) levels and lifetime risk of major cardiovascular events.

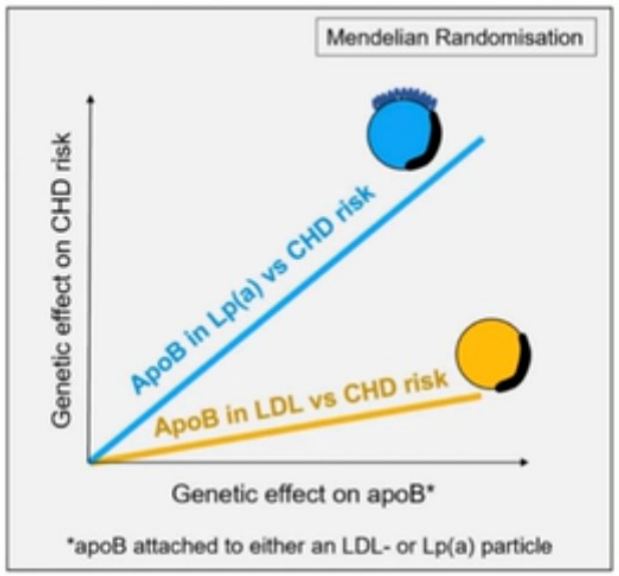


2025 Focused Update of the 2019 ESC/EAS Guidelines for the management of dyslipidaemias
(European Heart Journal; doi: 10.1093/eurheartj/ehaf190)

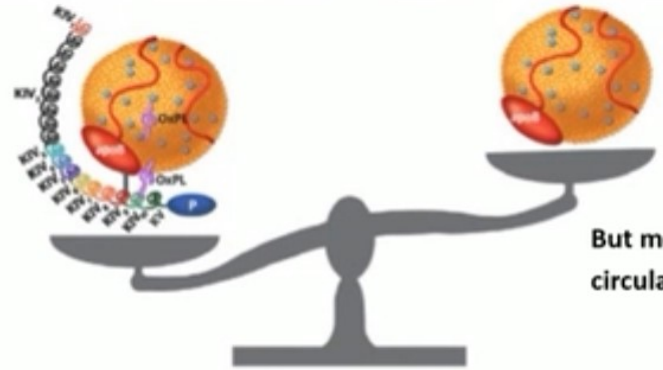
New Recommendations (5)

Recommendations	Class	Level
Recommendation for measurement of lipoprotein(a)		
Lp(a) levels above 50 mg/dL (105 nmol/L) should be considered in all adults as a CV risk-enhancing factor, with higher Lp(a) levels associated with a greater increase in risk.	IIa	B

Is Lp(a) more atherogenic than LDL-C ?

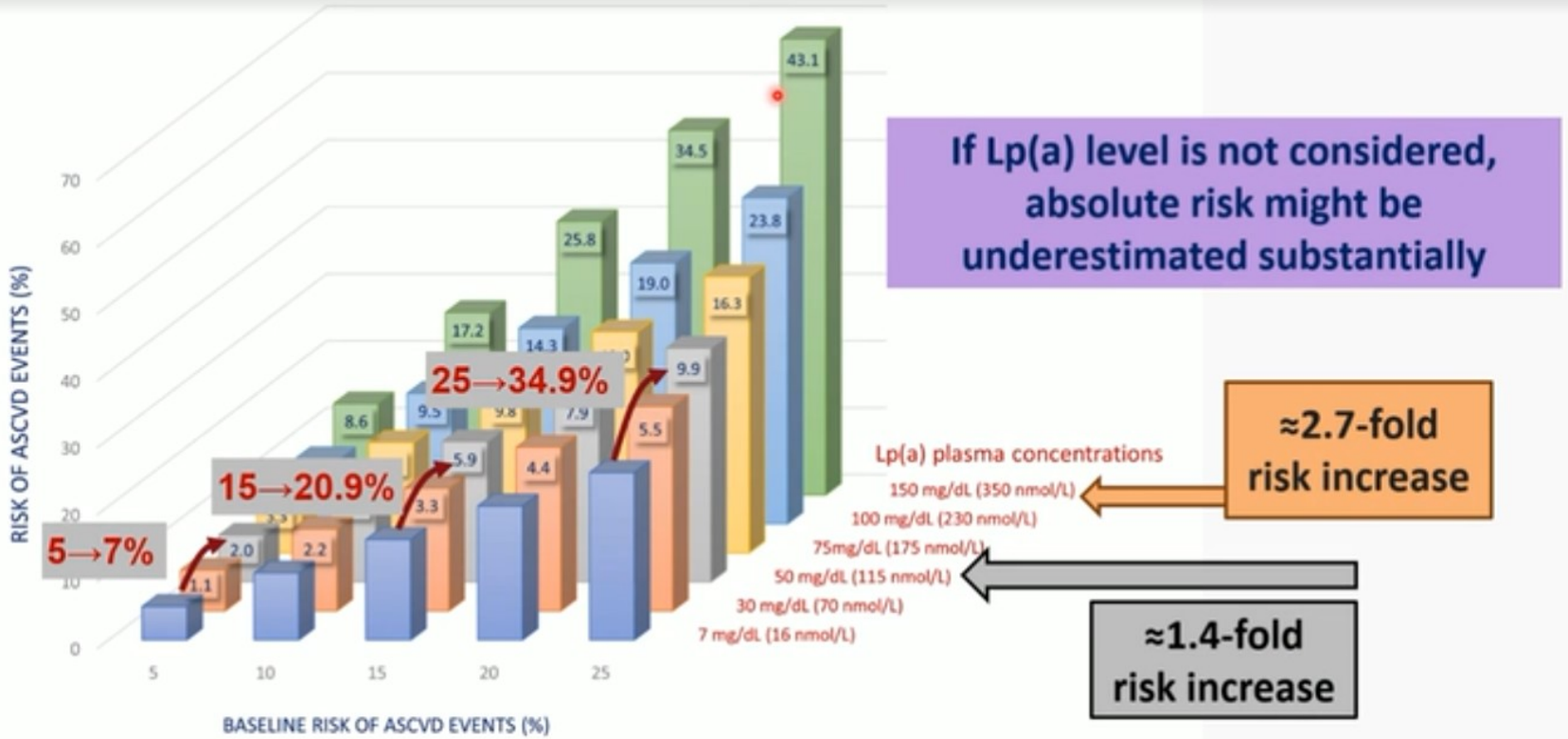


Lp(a)-apoB - 250 nmol/L	LDL-apoB - 250 nmol/L
• Proinflammatory OxPL • Proinflammatory proteome • Smaller, more dense • Antifibrinolytic	• Not inflammatory unless oxidized • More benign proteome • Larger, less dense • Not antifibrinolytic



But more circulating LDL-C

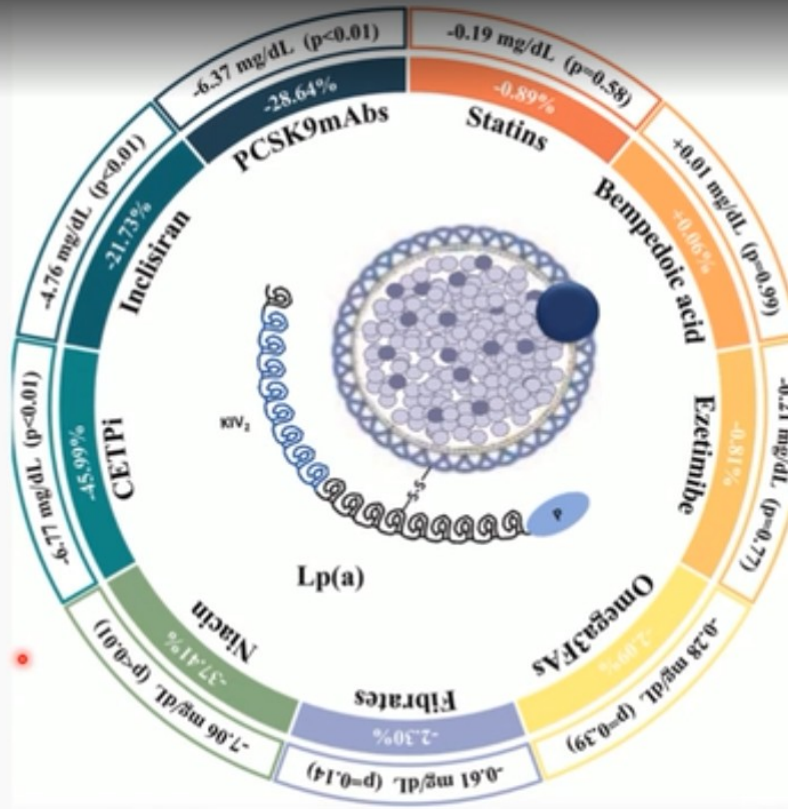
Incremental increase in absolute risk caused by a Lp(a) level



Effect of LLT on Lp(a)

Lifestyle: No change
High-intensity statin: no change
Ezetimibe, Bempedoic acid : no change
PCSK9 inhibitor: decrease by 25%
Niacin: decrease by 25% but no clinical benefit
Obicetrapib: decrease by 30-50 % ?

Apheresis: decrease up to 70 %
Specific Lp(a) lowering therapies awaited



Le ipertrigliceridemie

The NEW ENGLAND JOURNAL of MEDICINE

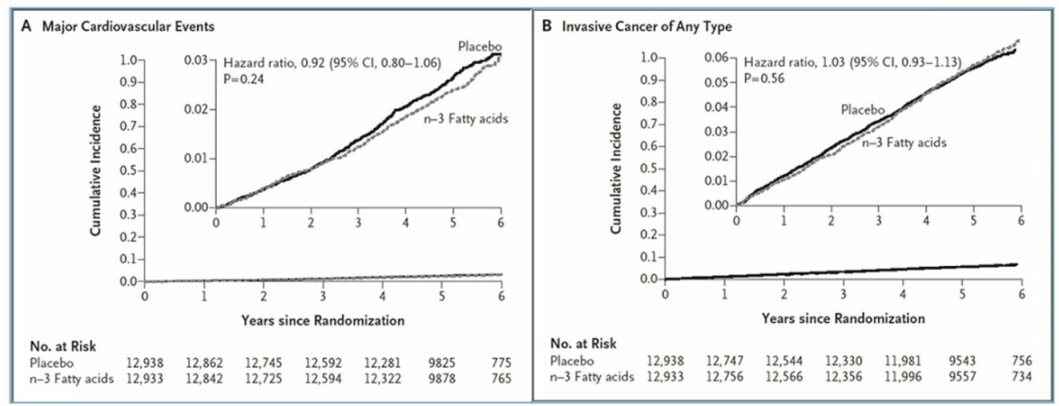
ORIGINAL ARTICLE

Marine n–3 Fatty Acids and Prevention of Cardiovascular Disease and Cancer

JoAnn E. Manson, M.D., Dr.P.H., Nancy R. Cook, Sc.D., I-Min Lee, M.B., B.S., Sc.D., William Christen, Sc.D., Shari S. Bassuk, Sc.D., Samia Mora, M.D., M.H.S., Heike Gibson, Ph.D., Christine M. Albert, M.D., M.P.H., David Gordon, M.A.T., Trisha Copeland, M.S., R.D., Denise D'Agostino, B.S., Georgina Friedenberg, M.P.H., Claire Ridge, M.P.H., Vadim Bubes, Ph.D., Edward L. Giovannucci, M.D., Sc.D., Walter C. Willett, M.D., Dr.P.H., and Julie E. Buring, Sc.D., for the VITAL Research Group*

Primary Prevention

25871 patients in the United States:
- men ≥50 years
- women ≥55 years
N-3 PUFA: 1 g daily *vs* placebo
Median follow-up of 5.3 years



N Engl J Med 2019;380:23-32.

Linee Guida ESC/EAS: Raccomandazioni sulle Analisi Lipidiche per la Stima del Rischio di CVD

Raccomandazioni	Classe	Livello
TC deve essere utilizzato per la stima del rischio CV totale mediante il sistema SCORE.	I	C
È raccomandata l'analisi di HDL-C per perfezionare ulteriormente la stima del rischio mediante il sistema SCORE online.	I	C
L'analisi del colesterolo LDL è raccomandata come metodo principale di analisi dei lipidi per lo screening, la diagnosi e la gestione.	I	C
L'analisi dei TG è raccomandata come parte del processo di analisi dei lipidi di routine.	I	C
È raccomandata la valutazione del colesterolo non-HDL per la valutazione del rischio, in particolare nelle persone con alti livelli di TG, DM, obesità o livelli molto bassi di LDL-C.	I	C
È raccomandata l'analisi di ApoB per la valutazione del rischio, in particolare nelle persone con alti livelli di TG, DM, obesità, sindrome metabolica o livelli molto bassi di LDL-C. Può essere usata in alternativa a LDL-C, se disponibile, come misuria primaria per lo screening, la diagnosi e la gestione, inoltre può essere preferita al non-HDL-C in persone con alti livelli di TG, DM, obesità, livelli LDL-C molto bassi.	I	C
La misurazione Lp(a) dovrebbe essere considerata almeno una volta nella vita di ogni persona adulta per identificare gli individui con livelli ereditari di Lp(a) molto elevati >180 mg/dL (>430 nmol/L), che possono presentare un rischio di malattia cardiovascolare aterosclerotica equivalente al rischio associato all'ipercolesterolemia familiare eterozigote.	IIa	C
La Lp(a) dovrebbe essere considerata in pazienti selezionati con una storia familiare di malattie cardiovascolari premature e per la riclassificazione in persone borderline tra il rischio moderato e alto.	IIa	C

APO=apolipoproteina; CV=cardiovascolare; CVD=malattia cardiovascolare; DM=diabete mellito; HDLC=colesterolo lipoproteico ad alta densità; LDL-C=colesterolo lipoproteico a bassa densità; Lp(a)=lipoproteina (a); SCORE=Stima sistematica del rischio coronarico; TC=colesterolo totale; TG=trigliceridi.

1. Mach F, et al., 2020

Terapie ipolipemizzanti di vecchia generazione: nessuna evidenza di benefici CV

Agenti Riduttori dei TG	Studi Chiave*	Riscontro 1° endpoint MACE?
Fibrati	ACCORD[1] FIELD[2] PROMINENT[11]	✕
Niacina	AIM-HIGH[3] HPS2-THRIVE[4]	✕
Prescrizione e integratori, miscele EPA + DHA	RISK & PREVENTION,[5] ORIGIN,[6] OMEGA,[7] ASCEND,[8] VITAL,[9] STRENGTH[10]	✕

*ACCORD: Action to Control Cardiovascular Risk in Diabetes; ASCEND: A Study of Cardiovascular Events in Diabetes; FIELD: Fenofibrate Intervention and Event Lowering in Diabetes; OMEGA: Effect of Omega-3 Fatty Acids on the Reduction of Sudden Cardiac Death After Myocardial Infarction; ORIGIN: Outcome Reduction with an Initial Glargine Intervention; STRENGTH: Statin Residual Risk with Epanova in High Cardiovascular Risk Patients with Hypertriglyceridemia;
VITAL: Vitamin D and Omega-3 Trial.

CV, cardiovascolare; DHA, acido docosaesaenoico; EPA, acido eicosapentaenoico; MACE, evento cardiovascolare avverso maggiore; TG, trigliceridi.

68. ACCORD Study Group, 2010; 69. FIELD Study Investigators. 2005; 70. Risk and Prevention Study Collaborative Group, 2013; 71. ORIGIN Trial Investigators, 2012; 72. OMEGA Study Group, 2010; 73. ASCEND Study Collaborative Group, 2018; 74. Manson JE, et al., 2019; 75. Nicholls SJ et al., 2020; 11 https://www.prnewswire.com/news-releases/kowa-to-discontinue-k-877-pemafibrate-prominent-cardiovascular-outcomes-study-301520956.html

Reduction of Cardiovascular Events with Icosapent Ethyl Intervention Trial

reduce-it

The NEW ENGLAND JOURNAL of MEDICINE

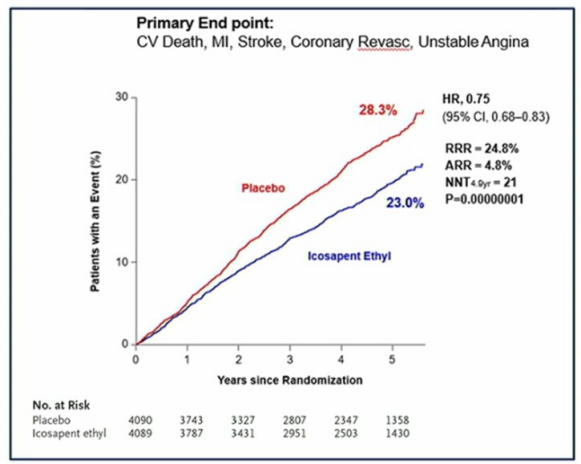
ORIGINAL ARTICLE

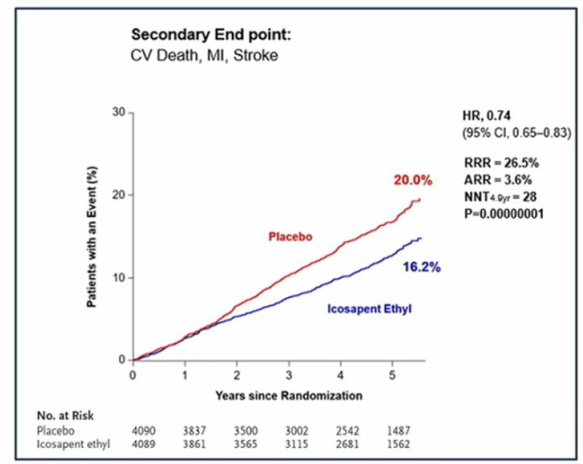
N Engl J Med. 2019 Jan 3;380(1):11-22.

Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia

Deepak L. Bhatt, M.D., M.P.H., P. Gabriel Steg, M.D., Michael Miller, M.D., Eliot A. Brinton, M.D., Terry A. Jacobson, M.D., Steven B. Ketchum, Ph.D., Ralph T. Doyle, Jr., B.A., Rebecca A. Juliano, Ph.D., Lixia Jiao, Ph.D., Craig Granowitz, M.D., Ph.D., Jean-Claude Tardif, M.D., and Christie M. Ballantyne, M.D., for the REDUCE-IT Investigators*

Primary and key secondary endpoints



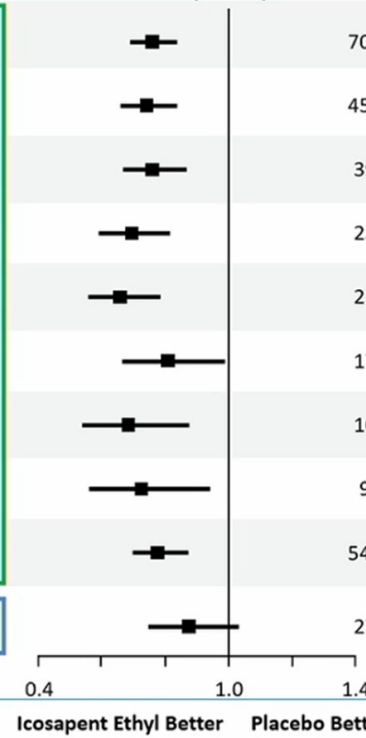


ARR, absolute risk reduction; HR, hazard ratio; MACE, major adverse cardiovascular event; NNT, number needed to treat; RRR, relative risk reduction.

N Engl J Med. 2019 Jan 3;380(1):11-22.

REDUCE-IT: PRE-SPECIFIED HIERARCHICAL TESTING OF ENDPOINTS

Endpoint	Icosapent Ethyl n/N (%)	Placebo n/N (%)	Hazard Ratio (95% CI)	RRR	P-value
Primary Composite (ITT)	705/4089 (17.2%)	901/4090 (22.0%)	0.75 (0.68–0.83)	↓ 25%	<0.001
Key Secondary Composite (ITT)	459/4089 (11.2%)	606/4090 (14.8%)	0.74 (0.65–0.83)	↓ 26%	<0.001
Cardiovascular Death or Nonfatal Myocardial Infarction	392/4089 (9.6%)	507/4090 (12.4%)	0.75 (0.66–0.86)	↓ 25%	<0.001
Fatal or Nonfatal Myocardial Infarction	250/4089 (6.1%)	355/4090 (8.7%)	0.69 (0.58–0.81)	↓ 31%	<0.001
Urgent or Emergent Revascularization	216/4089 (5.3%)	321/4090 (7.8%)	0.65 (0.55–0.78)	↓ 35%	<0.001
Cardiovascular Death	174/4089 (4.3%)	213/4090 (5.2%)	0.80 (0.66–0.98)	↓ 20%	0.03
Hospitalization for Unstable Angina	108/4089 (2.6%)	157/4090 (3.8%)	0.68 (0.53–0.87)	↓ 32%	0.002
Fatal or Nonfatal Stroke	98/4089 (2.4%)	134/4090 (3.3%)	0.72 (0.55–0.93)	↓ 28%	0.01
Total Mortality, Nonfatal Myocardial Infarction, or Nonfatal Stroke	549/4089 (13.4%)	690/4090 (16.9%)	0.77 (0.69–0.86)	↓ 23%	<0.001
Total Mortality	274/4089 (6.7%)	310/4090 (7.6%)	0.87 (0.74–1.02)	↓ 13%	0.09



Centro Studi ANMCO
Fondazione per il Tuo cuore

N Engl J Med. 2019 Jan 3;380(1):11-22.

REDUCE-IT evaluated statin-treated patients with well-controlled LDL-C and multiple CV risk factors[1,2]

reduce-it

PATIENTS	AT RISK FOR	RANDOMISATION
8179 Patients… ▪ Men and women aged ≥45 years on stable statin therapy +/- ezetimibe ▪ LDL-C 40 – 100 mg/dl ; median at baseline 74 mg/dl	**At High Risk for CV Events due to:** **Mild to moderate TG elevation** ▪ TG 135 –500 mg/dl; median at baseline 216 mg/dl **- AND -** ▪ Established CVD (secondary prevention cohort) **- OR -** ▪ Diabetes mellitus + age ≥50 years + at least 1 risk factor for CVD (primary prevention cohort)	Randomisation 1:1 **Study Treatment** ▪ Stable statin + IPE 4 g/day (2 g twice daily with meals) **- OR -** ▪ Stable statin + placebo

1. Bhatt DL, et al. Clin Cardiol. 2017;40(3). 2. Bhatt DL, et al. N Engl J Med. 2019;380(1).

New Recommendations (6)

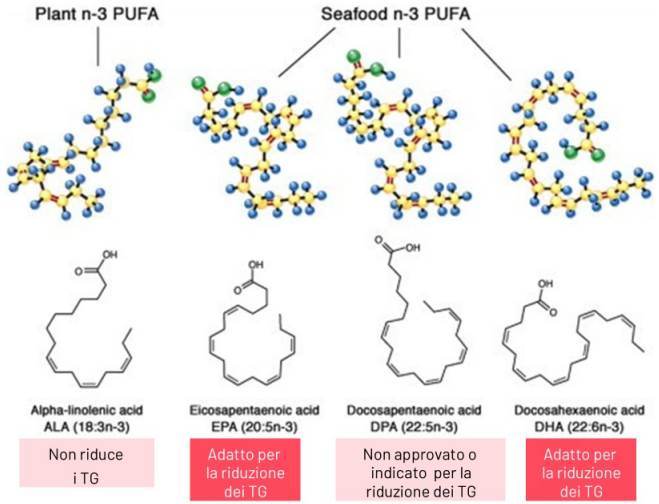
Recommendations	Class	Level
Recommendations for drug treatment of patients with hypertriglyceridaemia		
High-dose icosapent ethyl (2 x 2 g/day) should be considered in combination with a statin in high-risk or very high-risk patients with elevated triglyceride levels (fasting triglyceride levels 135–499 mg/dL or 1.52–5.63 mmol/L) to reduce the risk of cardiovascular events.	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.	IIa	B

Rimborsabilità e prescrizione da SSN

La determinazione di Agenzia Italiana del Farmaco (AIFA) del 14 dicembre 2024 stabilisce che **icosapent etile** viene classificato in **classe A**, con rimborsabilità da parte del SSN nella seguente condizione: gazzettaufficiale.biz

- Età: 18-80 anni
- Malattia cardiovascolare accertata
- BMI ≥ 27 kg/m²
- Trattamento con statina ad alta potenza **alla massima dose tollerata** + ezetimibe
- LDL-C < 70 mg/dL
- Trigliceridi residui (TG ≥ 200 mg/dL) non spiegabili da altre cause e confermati in almeno 3 determinazioni nonostante buona aderenza dietetica.

Struttura degli Acidi Grassi Polinsaturi n-3 PUFA (Omega-3)



AHA reccomanda 2 porzioni di pesce alla settimana (soprattutto pesce grasso).
I pesci grassi come il salmone, lo sgombro, l'aringa, la trota, le sardine e il tonno sono ricche di n-3PUFA.

Tarterburn LM et al. *Am J Clin Nutr.* 2006;83:1467S-76S. Graphic with permission from Mozaffarian D, Wu JH. *J Am Coll Cardiol.* 2011;58:2047-67. PUFA=polyunsaturated fatty acid; Rimm EB, et al. *Circulation.* 2018 Jul 3; 138(1): e35-e47. Holub BJ. Clinical nutrition: 4. Omega-3 fatty acids in cardiovascular care. CMAJ 2002; 166: 608-615;

Le formulazioni a base di solo EPA hanno dimostrato un significativo beneficio CV, mentre le formulazioni EPA+DHA non hanno mostrato alcun beneficio CV

Riassunto delle caratteristiche del prodotto

Indicazioni terapeutiche

(Icosapent Etile) è indicato per ridurre il rischio di eventi cardiovascolari in pazienti adulti in trattamento con statine ad elevato rischio cardiovascolare e con trigliceridi elevati (≥ 150 mg/dL [≥ 1,7 mmol/L]) e

- **malattia cardiovascolare accertata o**
- **diabete e almeno un altro fattore di rischio cardiovascolare.**

Posologia e modo di somministrazione

La dose orale giornaliera raccomandata è di 4 capsule, da assumere in due capsule da 998 mg due volte al giorno. In caso di dimenticanza di una dose, i pazienti devono assumerla non appena se ne ricordano. Tuttavia, se dimenticano una dose giornaliera, non devono raddoppiare la dose successiva.

Non è necessario alcun adattamento della dose in base all'età, compromissione renale o compromissione epatica.

deve essere assunto ai pasti o dopo i pasti.

Per accertarsi che venga assunta l'intera dose, i pazienti devono essere avvisati di ingerire le capsule intere e di non spezzarle, frantumarle, scioglierle o masticarle.

Due popolazioni specifiche che possono o devono essere trattate con terapia ipolipemizzante INDIPENDENTEMENTE DAL LIVELLO DI LDL :

Cancer IIb

HIV I a

New Recommendations (8)

Recommendations	Class	Level
Recommendation for statin therapy in patients receiving cancer therapy		
Statins should be considered in adult patients at high or very high risk of developing chemotherapy-related cardiovascular toxicity to reduce the risk of anthracycline-induced cardiac dysfunction.	IIa	B

Reduction of MACE by Statin Therapy in HIV Infection

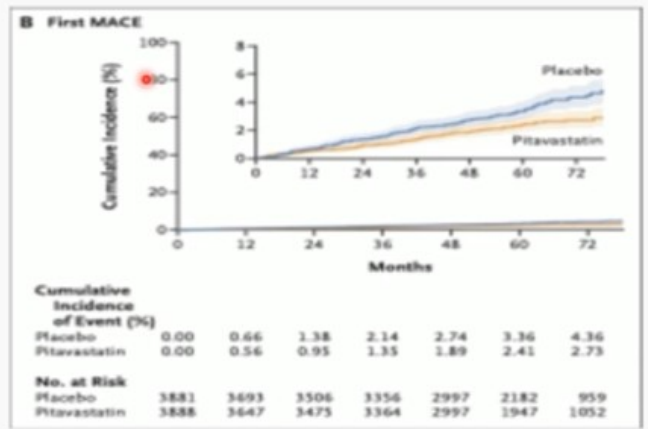
The NEW ENGLAND JOURNAL of MEDICINE

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

Pitavastatin to Prevent Cardiovascular Disease in HIV Infection

REPRIEVE Study:

7769 participants with HIV infection (receiving antiretro-viral therapy) with low-to-moderate CVD risk - pitavastatin (4 mg) vs. placebo.



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

New recommendations

Recommendations	Class	Level
Recommendation for statin therapy in primary prevention for people with human immunodeficiency virus infection		
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.	I	B

La terapia con statine è raccomandata in prevenzione primaria in classe I
livello di evidenza B
nei soggetti >40 anni con HIV

indipendentemente dal livello di LDL?

in base al livello di LDL ?

in base al livello di rischio secondo le tabelle SCORE?

solo se diabetici?


THANK YOU
For Advancing Medical Research