XIV CONGRESSO
AMD MOLISE

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Dislipidemia Nuove LG: una reale novita'?

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

ESC
European Society of Cardiology

EAS

ESC Classes of recommendations

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	Definition	Wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended or is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	Weight of evidence/opinion is in favour of usefulness/efficacy.	Should be considered
Class IIb	Usefulness/efficacy is less well established by evidence/opinion.	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

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2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

ESC Levels of evidence

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Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/or small studies, retrospective studies, registries.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Cardiovascular risk categories (1)

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Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularisation (PCI, CABG and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis) or on carotid ultrasound. DM with target organ damage, or at least three major risk factors, or early onset of T1DM of long duration (>20 years). (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for cardiovascular imaging for risk assessment of atherosclerotic cardiovascular disease

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Recommendations	Class	Level
Arterial (carotid and/or femoral) plaque burden on ultrasonography should be considered as a risk modifier in individuals at low or moderate risk.	IIa	B
CAC score assessment with CT may be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.	IIb	B

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Cardiovascular risk categories (2)

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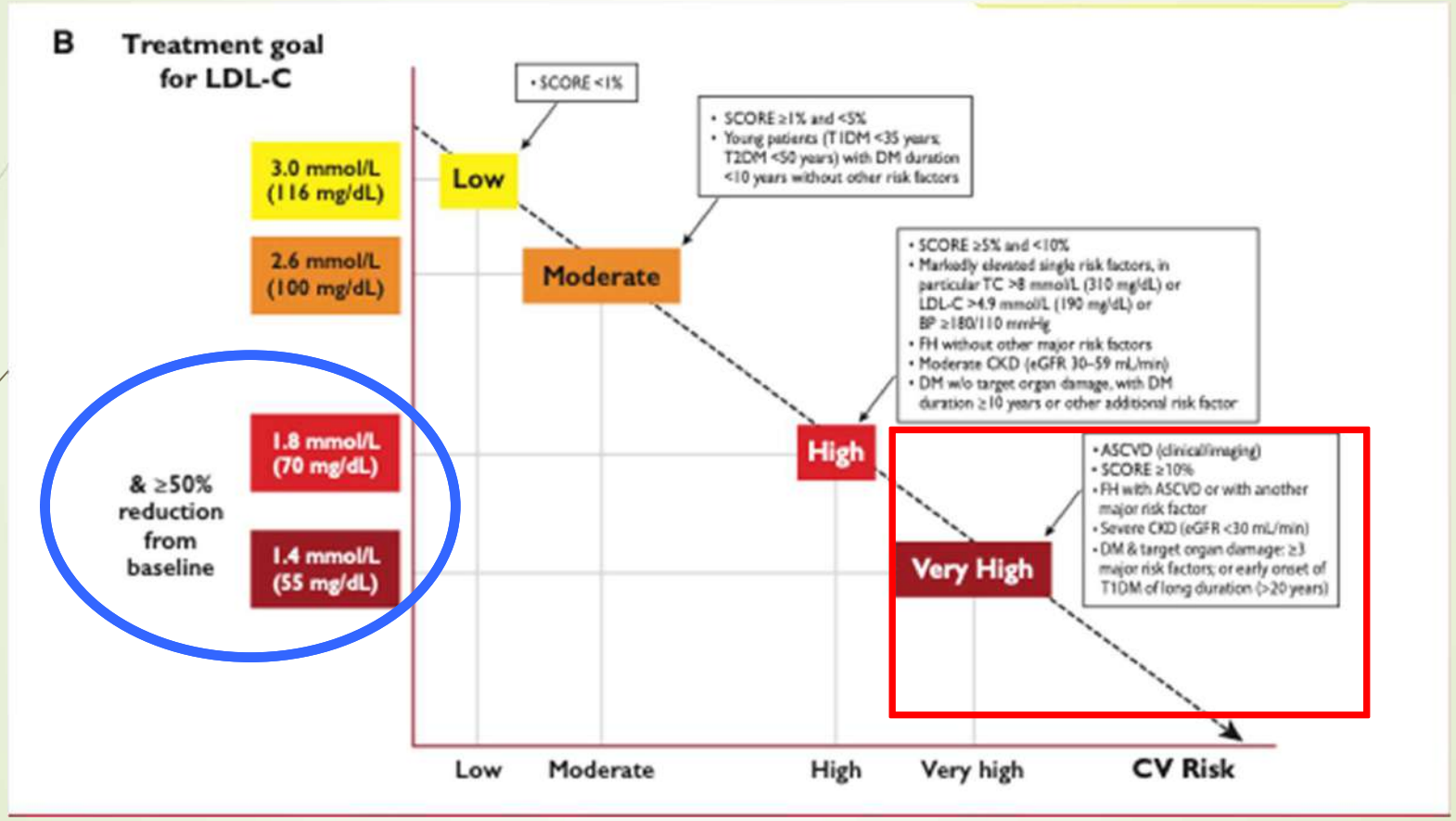
High-risk	People with: Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage*, with DM duration ≥10 years or another additional risk factors. 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.

*Target organ damage is defined as microalbuminuria, retinopathy or neuropathy

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Target colesterolo LDL



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

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	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥ 190 mg/dL)
Primary Prevention	<1 low-risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	IIa/A	IIa/A	IIa/A	IIa/A
	≥5 to <10, or high- risk	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	IIa/A	IIa/A	I/A	I/A	I/A
	≥10, or at very-high risk due to a risk condition	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/B	IIa/A	I/A	I/A	I/A	I/A
Secondary Prevention	Very-high risk	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	I/A	I/A	I/A	I/A	I/A

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2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

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

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Recommendations	Class	Level
It is recommended to prescribe a high-intensity statin up to the highest tolerated dose to reach the goals[c] set for the specific level of risk.	I	A
If the goals[c] are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.	I	B
For secondary prevention, patients at very-high risk not achieving their goal[c] on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.	I	A

Changes in recommendations (2)

EAS ESC European Society of Cardiology

2016	2019
Pharmacological LDL-C lowering	**Pharmacological LDL-C lowering**
If the LDL goal is not reached, statin combination with a cholesterol absorption inhibitor should be considered.	If the goals are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.

Classe IIa

Classe I B

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Changes in recommendations (3)

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2016	2019
Pharmacological LDL-C lowering	**Pharmacological LDL-C lowering**
In patients at very-high risk, with persistent high LDL-C despite treatment with maximal tolerated statin dose, in combination with ezetimibe or in patients with statin intolerance, a PCSK9 inhibitor may be considered.	For secondary prevention, patients at very-high risk not achieving their goal on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.
	For very-high-risk FH patients (that is, with ASCVD or with another major risk factor) who do not achieve their goals on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.

Classe IIB

Classe I

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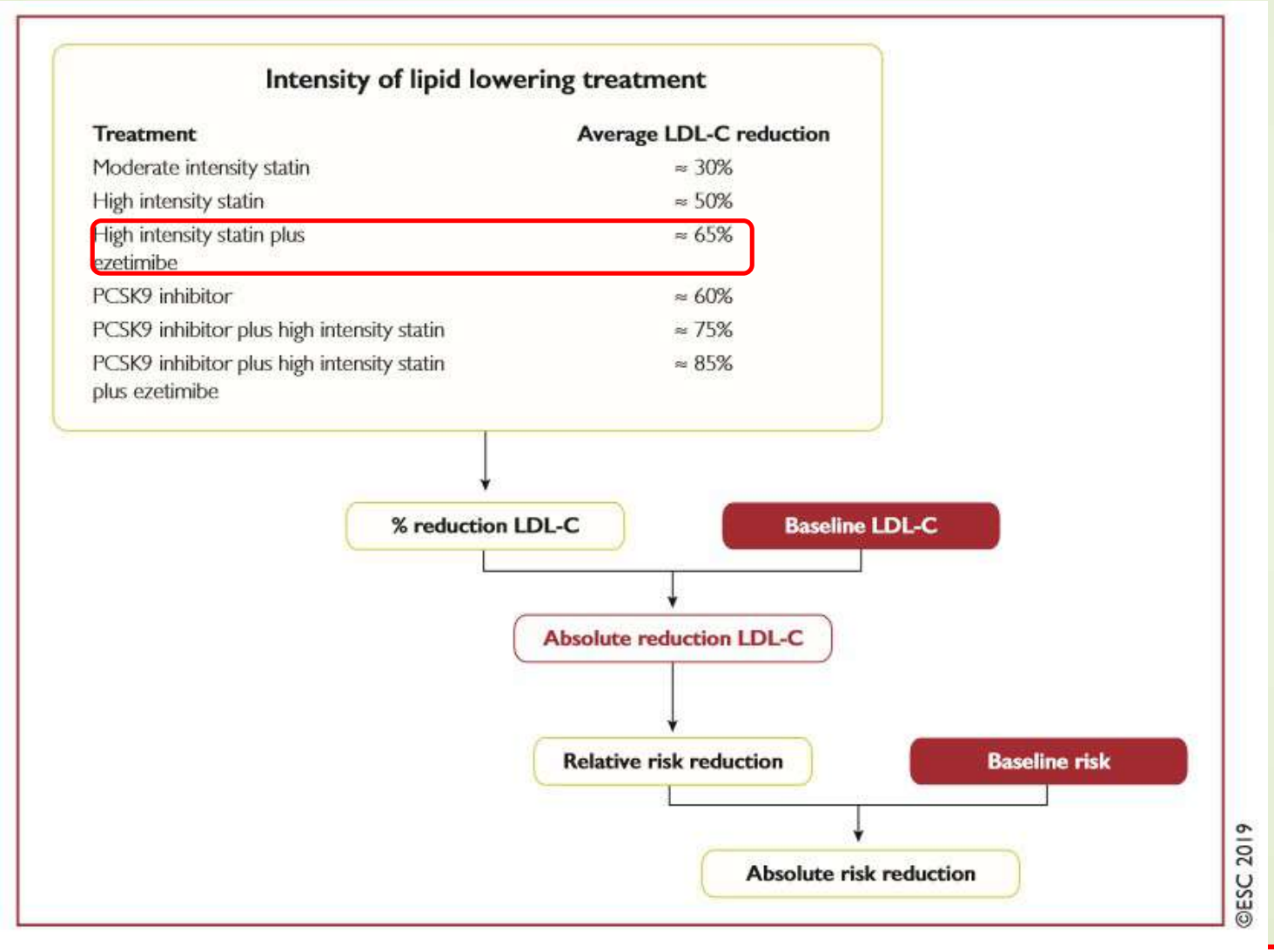
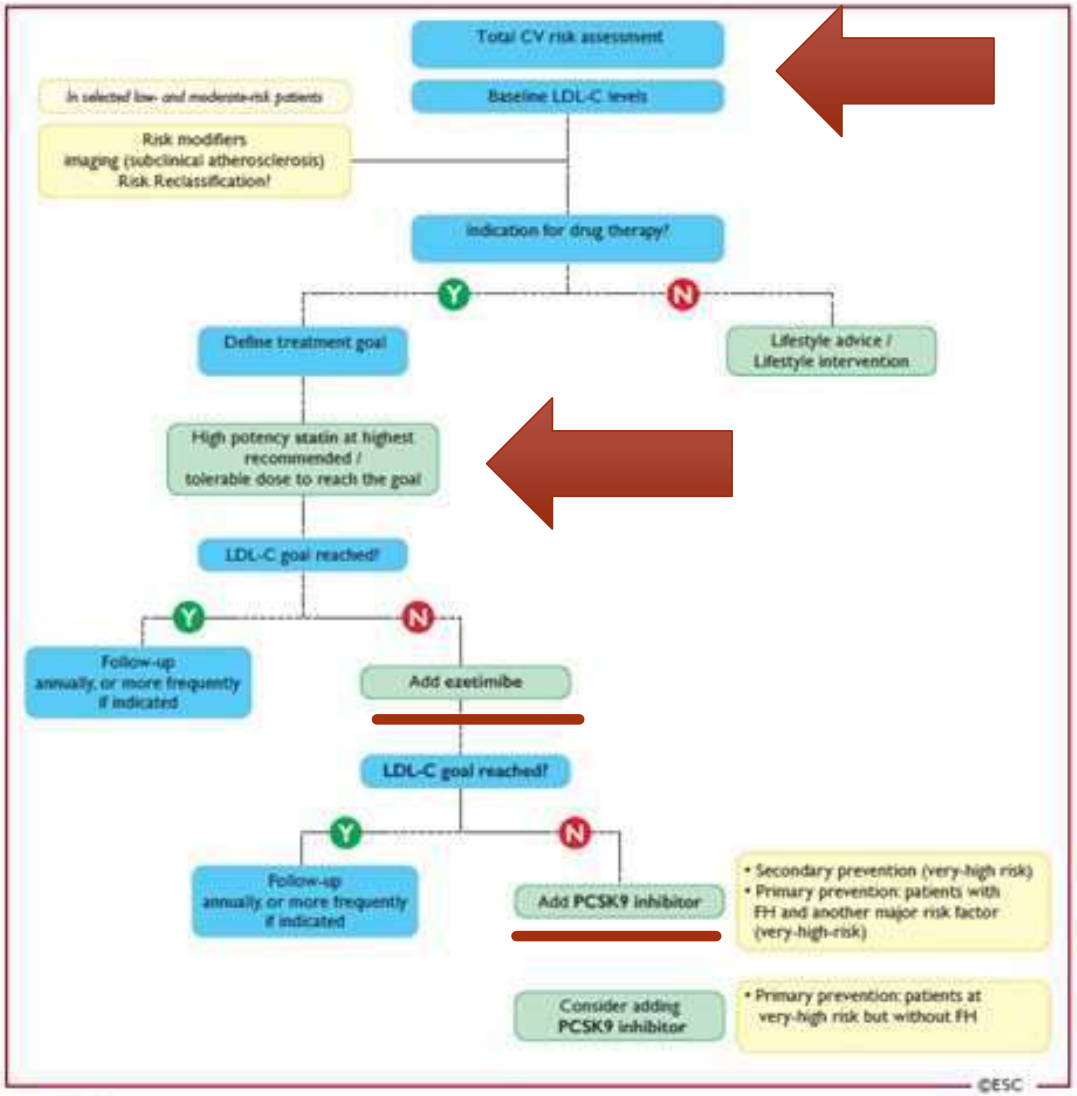
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Expected Clinical Benefits of c-LDL lowering therapies





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

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2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Target terapeutico colesterolo LDL

Recommendations for treatment goals for low-density lipoprotein cholesterol (1)

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Recommendations	Class	Level
In secondary prevention patients at very-high risk, an LDL-C reduction of at least 50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.	I	A
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

Changes in recommendations (1)

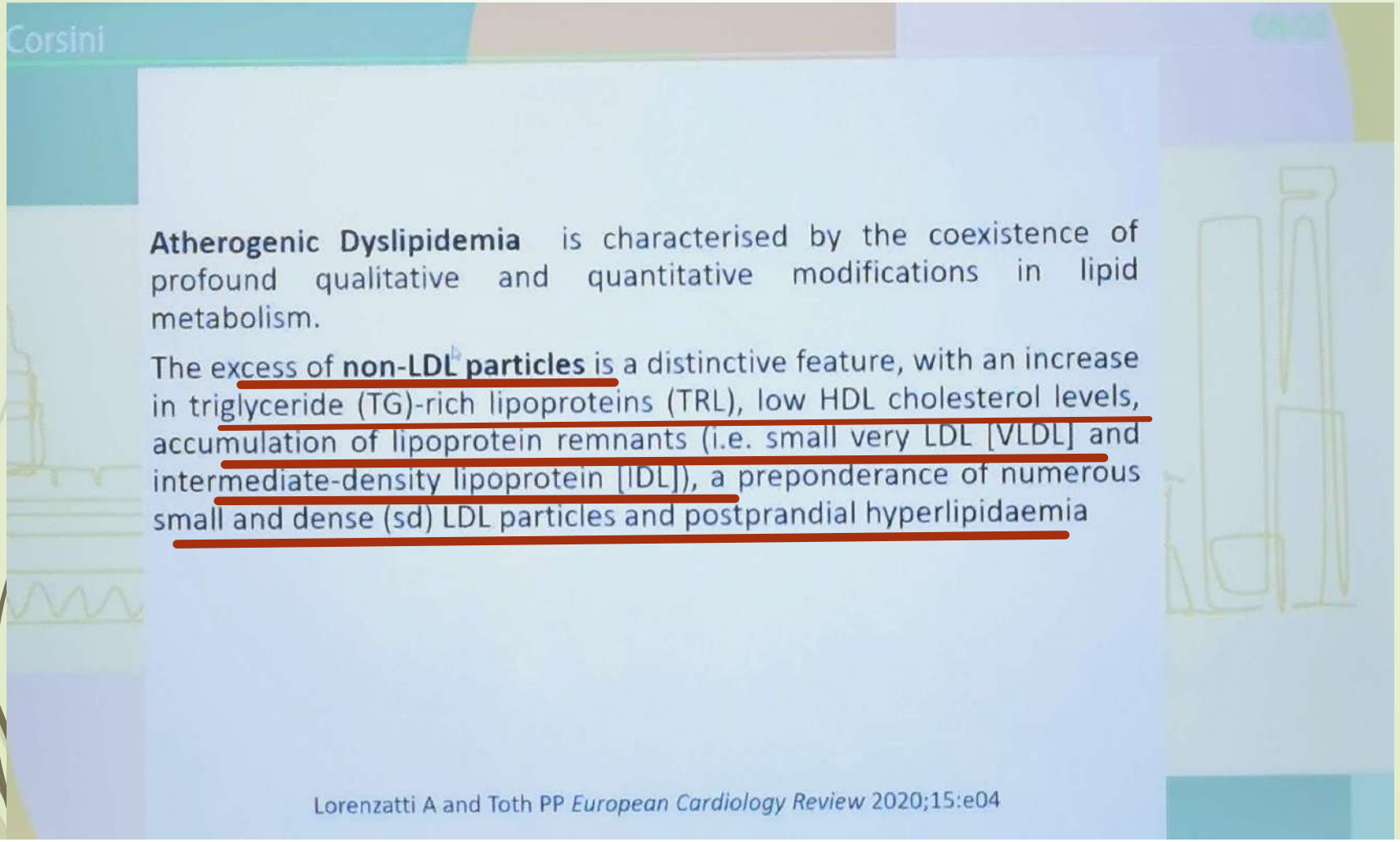
EAS ESC European Society of Cardiology

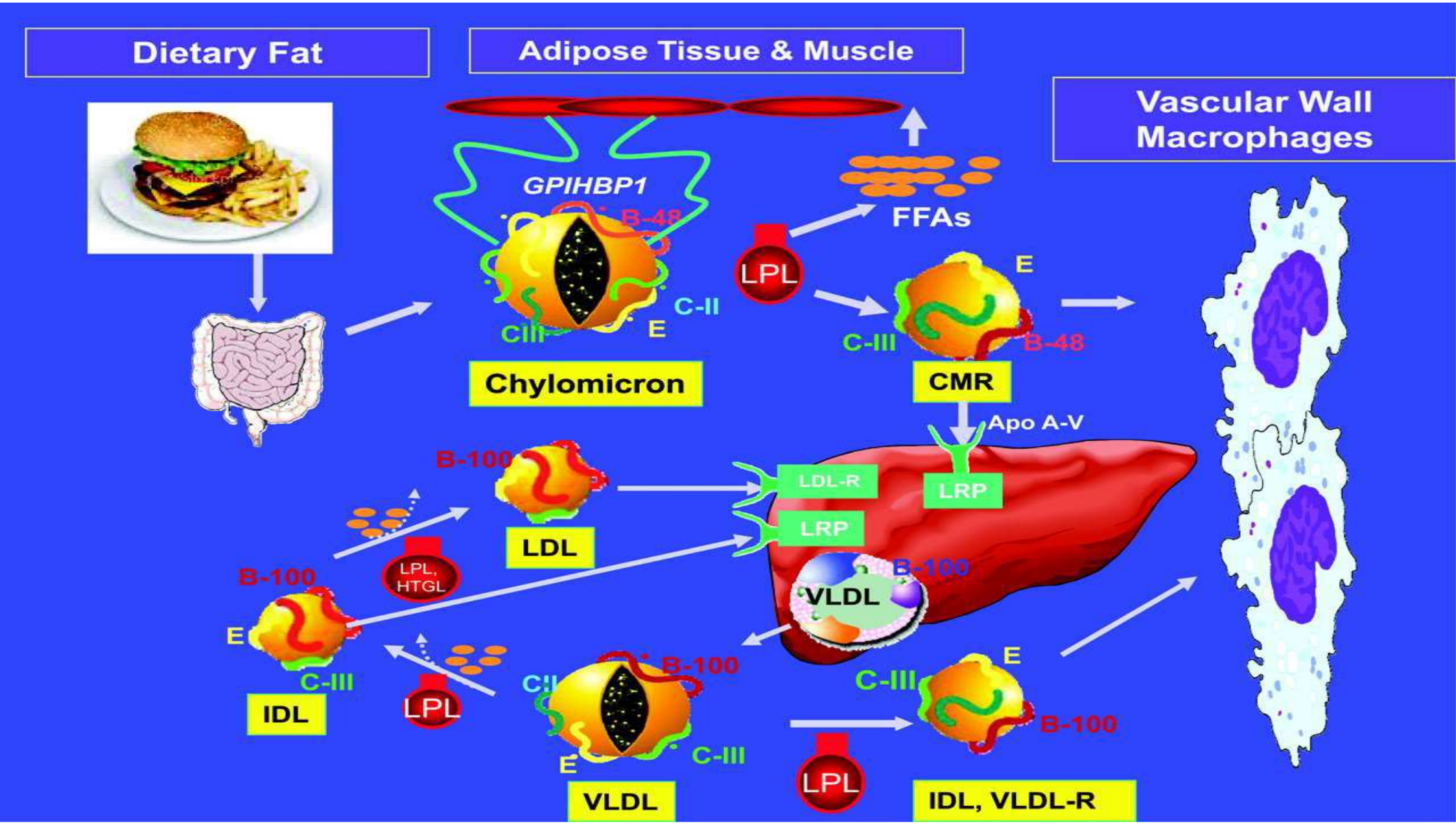
2016	2019
Lipid analyses for CVD risk estimation	**Lipid analyses for CVD risk estimation**
ApoB should be considered as an alternative risk marker whenever available, especially in individuals with high TG.	ApoB analysis is recommended for risk assessment, particularly in people with high TG, DM, obesity 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.

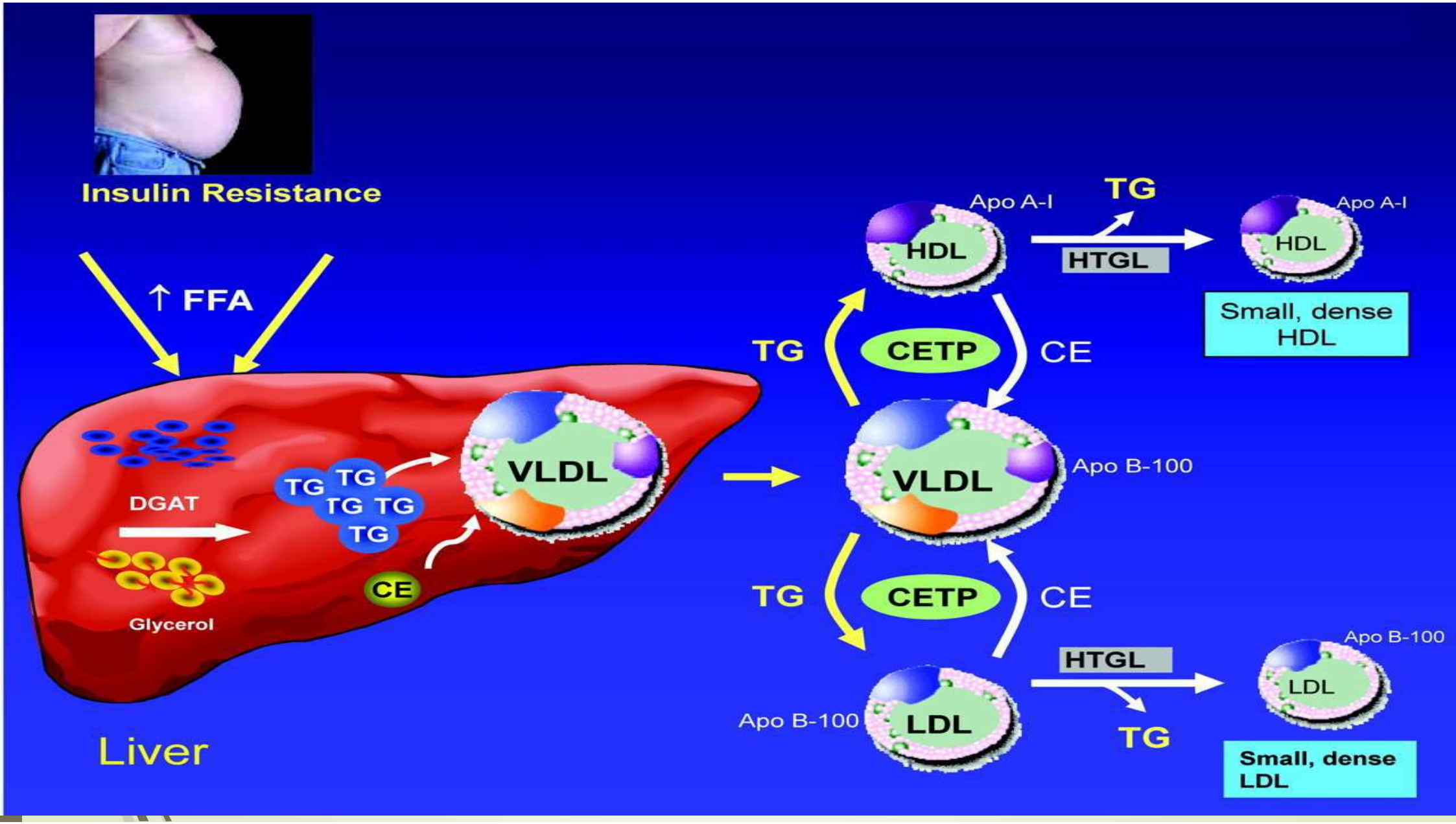
Classe IIA **Classe I C**

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Atherogenic Dyslipidemia

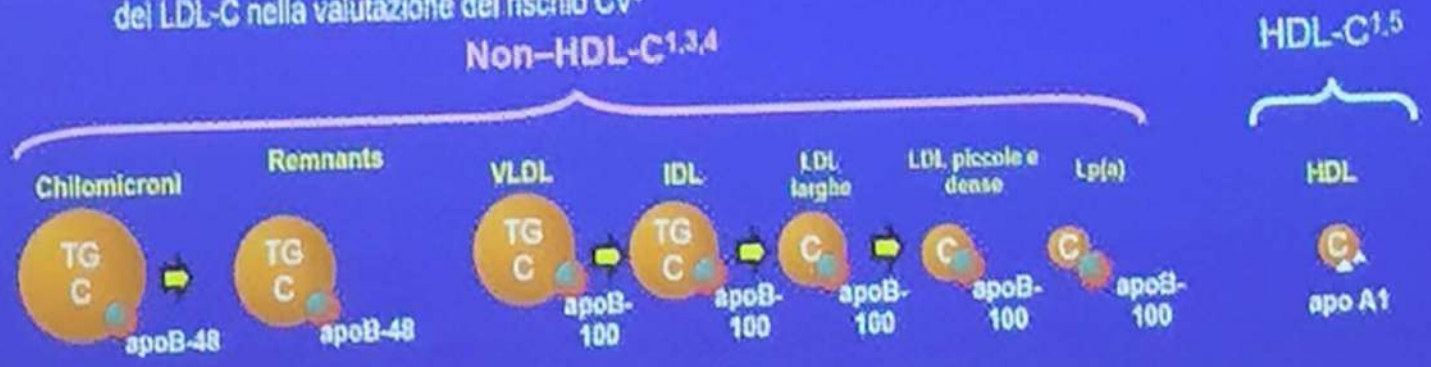



Dietary Fat
Adipose Tissue & Muscle
Vascular Wall Macrophages
GPIHBP1
B-48
C-II
CIII
E
Chylomicron
LPL
FFAs
E
C-III
B-48
CMR
Apo A-V
LRP
LDL-R
LRP
B-100
LDL
B-100
VLDL
LPL, HTGL
B-100
E
C-III
IDL
LPL
B-100
CII
E
C-III
VLDL
LPL
E
C-III
B-100
IDL, VLDL-R


Insulin Resistance
↑ FFA
DGAT
TG
TG TG
TG TG
TG
CE
VLDL
Glycerol
Liver
TG
CETP
CE
HDL
Apo A-I
TG
HTGL
HDL
Apo A-I
Small, dense HDL
VLDL
Apo B-100
TG
CETP
CE
HTGL
Apo B-100
LDL
TG
LDL
Apo B-100
Small, dense LDL

Non–HDL-C è un fattore di rischio per CHD

- Il Non–HDL-C rappresenta il contenuto di colesterolo delle lipoproteine contenenti apoB, incluse VLDL, IDL, LDL, Lp(a), chilomicroni e Remnants[1,2]
  - Non-HDL-C = colesterolo tot – HDL-C[1]
- Quando i livelli di TG sono ≥200 mg/dL, il non–HDL-C rappresenta meglio la concentrazione di lipoproteine aterogeniche del LDL-C da solo[1]
- Numerosi studi prospettici di coorte hanno dimostrato che il non–HDL-C può essere maggiormente indicativo del LDL-C nella valutazione del rischio CV[3]



Adapted with permission from Walldius G et al.[6]

Other major risk factors (beyond dyslipoproteinemia) include smoking, hypertension, and family history of premature CAD.

CHD = coronary heart disease; ApoB = apolipoprotein B; VLDL = very low-density lipoprotein; IDL = intermediate-density lipoprotein; Lp(a) = lipoprotein (a); TG = triglyceride; CV = cardiovascular; C = cholesterol; CAD = coronary artery disease.

1. NCEP ATP III Expert Panel. *Circulation*. 2002;106:3143–3421. 2. Rana JS et al. *Curr Opin Cardiol*. 2010;25:622–628. 3. Hoenig MR. *Vasc Health Risk Manag*. 2008;4:143–155.
4. Chapman M et al. *Eur Heart J Suppl*. 2004;6(suppl A):A45–A49. 5. Farter P. In: Ballantyne CM. *Clinical Lipidology: A Companion to Braunwald's Heart Disease*. Saunders, an imprint of Elsevier Inc; 2009:357–366.
6. Walldius G et al. *J Intern Med*. 2004;255:188–205.

Recommendations for lipid analyses for cardiovascular disease risk estimation (2)

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Recommendations	Class	Level
Non-HDL-C evaluation is recommended for risk assessment, particularly in people with high TG, diabetes, obesity or very low LDL-C.	I	C
ApoB analysis is recommended for risk assessment, particularly in people with high TG, diabetes, 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, diabetes, obesity or very low LDL-C.	I	C

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Recommendations for lipid analyses for cardiovascular disease risk estimation (3)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
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

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Treatment targets and goals for cardiovascular disease prevention (3)

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LDL-C	**Moderate risk:** A goal of <2.6 mmol/L (<100 mg/dL). **Low risk:** A goal of <3.0 mmol/L (<116 mg/dL)
Non-HDL-C	Non-HDL-C secondary goals are <2.2, 2.6 and 3.4 mmol/L (<85, 100 and 130 mg/dL) for very-high-, high- and moderate-risk people, respectively.
Apolipoprotein B	ApoB secondary goals are <65, 80 and 100 mg/dL for very-high-, high- and moderate-risk people, respectively.
Triglycerides	No goal but <1.7 mmol/L (<150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.
Diabetes	HbA1c: <7% (<53 mmol/mol).

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Ipertrigliceridemia

Changes in recommendations (4)

EAS ESC European Society of Cardiology

2016	2019
Drug treatments of hypertriglyceridaemia	**Drug treatments of hypertriglyceridaemia**
Statin treatment may be considered as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia.	Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia [TG >2.3 mmol/L (200 mg/dL)].

Classe IIB

Classe I B

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for drug treatments of patients with hypertriglyceridaemia (1)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia (TG >2.3 mmol/L (>200 mg/dL)).	I	B
In high-risk (or above) patients with TG between 1.5 and 5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2 x 2 g/day) should be considered in combination with statin.	IIa	B

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Pazienti con SCA

Changes in recommendations (8)

EAS ESC European Society of Cardiology

2016	2019
Lipid-lowering therapy in patients with ACS	**Lipid-lowering therapy in patients with ACS**
If the LDL-C target is not reached with the highest tolerated statin dose and/or ezetimibe, PCSK9 inhibitors may be considered on top of lipid-lowering therapy; or alone or in combination with ezetimibe in statin-intolerant patients or in whom a statin is contraindicated.	If the LDL-C goal is not achieved after 4 - 6 weeks despite maximal tolerated statin therapy and ezetimibe, addition of a PCSK9 inhibitor is recommended.

Classe II B

Classe I

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2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Diabete mellito

New recommendations (3)

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Treatment of dyslipidaemias in DM

In patients with T2DM at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55mg/dL) is recommended.

In patients with T2DM at high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) is recommended.

Statins are recommended in patients with T1DM who are at high or very-high risk.

Treatment of dyslipidaemias in DM

Intensification of statin therapy should be considered before the introduction of combination therapy.

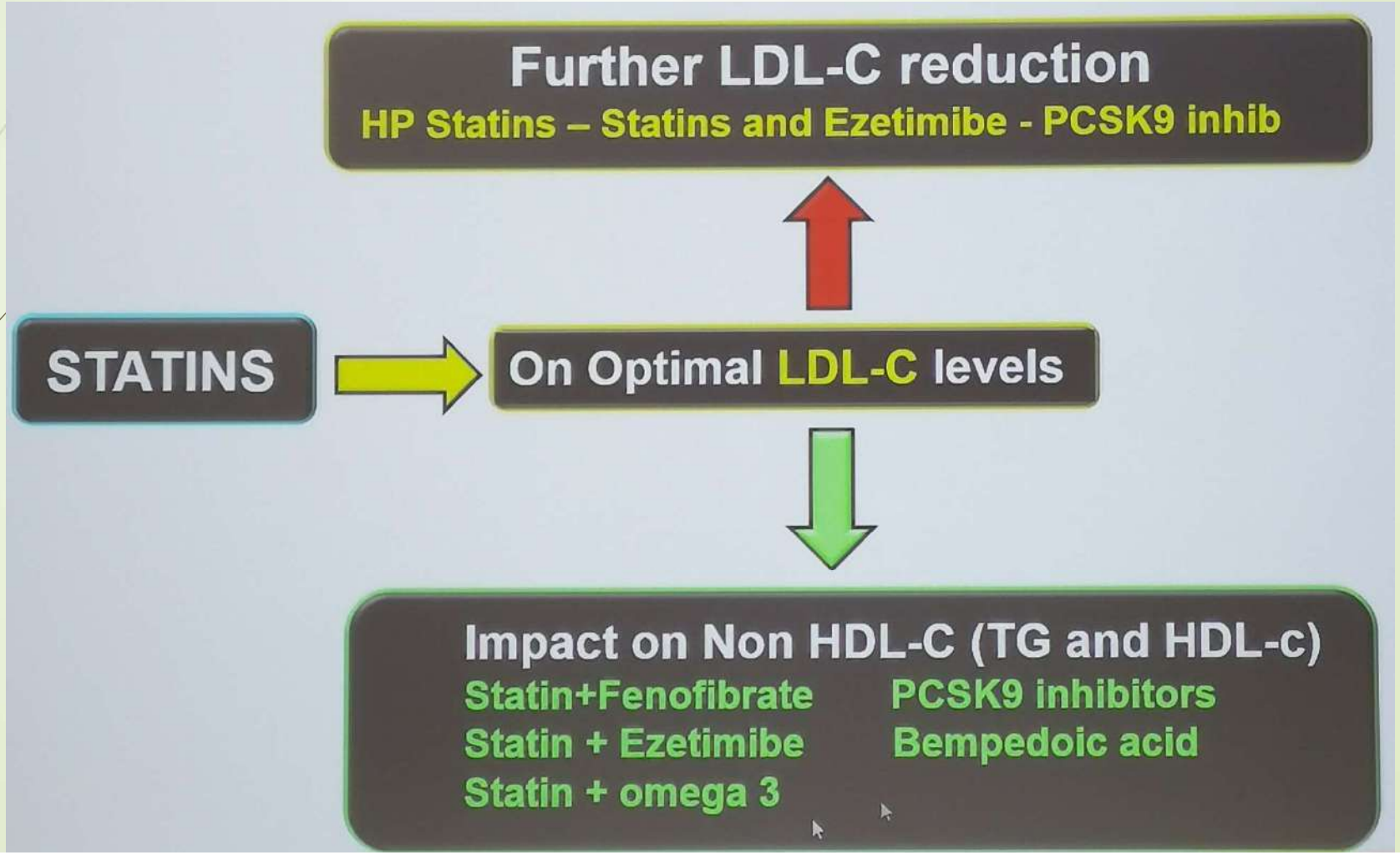
If the goal is not reached, statin combination with ezetimibe should be considered.

Treatment of dyslipidaemias in DM

Statin therapy is not recommended in pre-menopausal patients with DM who are considering pregnancy or not using adequate contraception.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Current Approaches for Macrovascular Disease Risk Prevention in Patients at CV Risk



- **New/revised concepts**

More intensive reduction of LDL-C across CV risk categories

- For secondary prevention in very-high-risk patients, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.
  - 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.
- In primary prevention, for individuals at very-high risk but without FH, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended. For individuals at very-high risk (that is, with another risk factor but without ASCVD), in primary prevention the same goals for LDL-C lowering should be considered.
- For patients at high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.
- For individuals at moderate risk, an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.
- For individuals at low risk, an LDL-C goal of <3.0 mmol/L (<116 mg/dL) may be considered.

The rationale for the revised, lower LDL-C goals across CV risk categories is discussed, based on a critical synthesis of available evidence from lipid-modifying interventions resulting in reductions in CV risk.

Pharmacological LDL-C-lowering strategies

The section on pharmacological strategies to lower LDL-C emphasizes the concept that the absolute LDL-C reduction (determined by pre-treatment LDL-C levels and the LDL-lowering efficacy of the medications) dictates the relative risk reduction, which in turn—depending on the baseline CV risk—defines the associated absolute CV risk reduction in individual patients.

http://www.escardio.org/guidelines

ESC European Society of Cardiology
European Heart Journal (2019) **00**, 1–78
doi:10.1093/eurheartj/ehz455

Take Home Messages

- Target terapeutici delle LDL sempre piu ambiziosi (in particolari categorie di pazienti Col-LDL < 40 mg/dl)

- Nella valutazione del Rischio CV Oltre il Col- LDL Colesterolo non HDL- ApoB- Lipoproteina (a)

- Terapia di associazione per migliorare aderenza ed efficacia terapeutica

GRAZIE !!

Recommendations for treatment goals for low-density lipoprotein cholesterol

Recommendations	Class[a]	Level[b]
In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]	I	A
In primary prevention for individuals at very-high risk but without FH,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[34–36]	I	C
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
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-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A

ASCVD = atherosclerotic cardiovascular disease; FH = familial hypercholesterolaemia; LDL-C = low-density lipoprotein cholesterol.
[a]Class of recommendation.
[b]Level of evidence.
[c]For definitions see *Table 4*.
[d]The term 'baseline' refers to the LDL-C level in a person not taking any LDL-C-lowering medication. In people who are taking LDL-C-lowering medication(s), the projected baseline (untreated) LDL-C levels should be estimated, based on the average LDL-C-lowering efficacy of the given medication or combination of medications.

New recommendations (1)

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Cardiovascular imaging for assessment of ASCVD risk

Assessment of arterial (carotid and/or femoral) plaque burden on arterial ultrasonography should be considered as a risk modifier in individuals at low or moderate risk.

Cardiovascular imaging for assessment of ASCVD risk

CAC score assessment with CT may be considered as a risk modifier in the CV risk assessment of asymptomatic individuals at low or moderate risk.

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.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

New recommendations (2)

EAS ESC
European Society of Cardiology

Drug treatments of patients with hypertriglyceridaemia
In high-risk (or above) patients with TG between 1.5 and 5.6 mmol/L (135 - 499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2 x 2g/day) should be considered in combination with statins.

Treatment of patients with heterozygous FH
In primary prevention, for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.

Treatment of dyslipidaemias in older people
Treatment with statins is recommended for primary prevention, according to the level of risk, in older people aged ≤75.

Treatment of dyslipidaemias in older people
Initiation of statin treatment for primary prevention in older people aged >75 may be considered, if at high risk or above.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

New recommendations (4)

EAS ESC
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Lipid-lowering therapy in patients with ACS

For patients who present with an ACS, and whose LDL-C levels are not at goal despite already taking a maximally tolerated statin dose and ezetimibe, adding a PCSK9 inhibitor early after the event (if possible, during hospitalization for the ACS event) should be considered.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Changes in recommendations (6)

EAS ESC European Society of Cardiology

2016	2019
Treatment of patients with heterozygous FH	**Treatment of patients with heterozygous FH**
Treatment with a PCSK9 antibody should be considered in FH patients with CVD or with other factors putting them at very-high risk for CHD, such as other CV risk factors, family history, high Lp(a), or statin intolerance.	Treatment with a PCSK9 inhibitor is recommended in very-high-risk FH patients if the treatment goal is not achieved on maximal tolerated statin plus ezetimibe.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

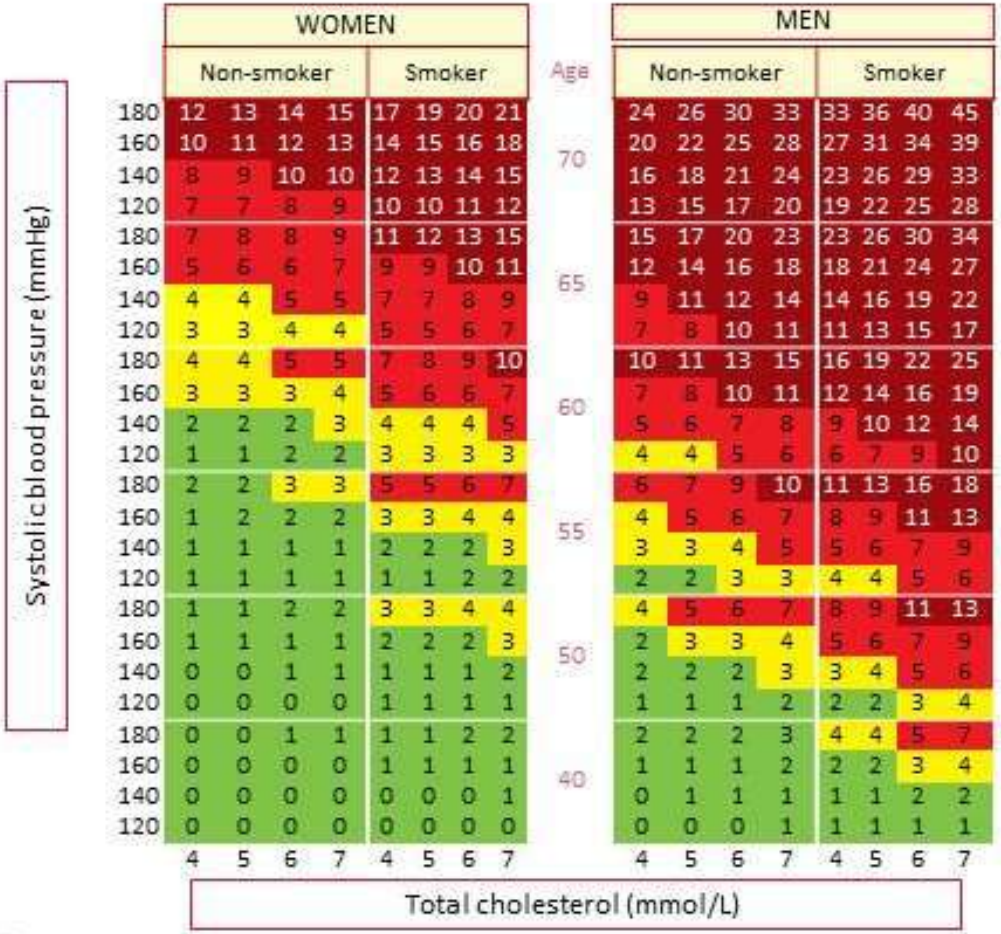
Changes in recommendations (5)

EAS ESC European Society of Cardiology

2016	2019
Treatment of patients with heterozygous FH	**Treatment of patients with heterozygous FH**
Treatment should be considered to aim at reaching an LDL-C <2.6 mmol/L (<100 mg/dL) or in the presence of CVD <1.8 mmol/L (<70 mg/dL). If targets cannot be reached, maximal reduction of LDL-C should be considered using appropriate drug combinations.	For FH patients with ASCVD who are at very-high risk, treatment to achieve at least a 50% reduction from baseline and an LDL-C <1.4 mmol/L (<55 mg/dL) is recommended. If goals cannot be achieved, a drug combination is recommended.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

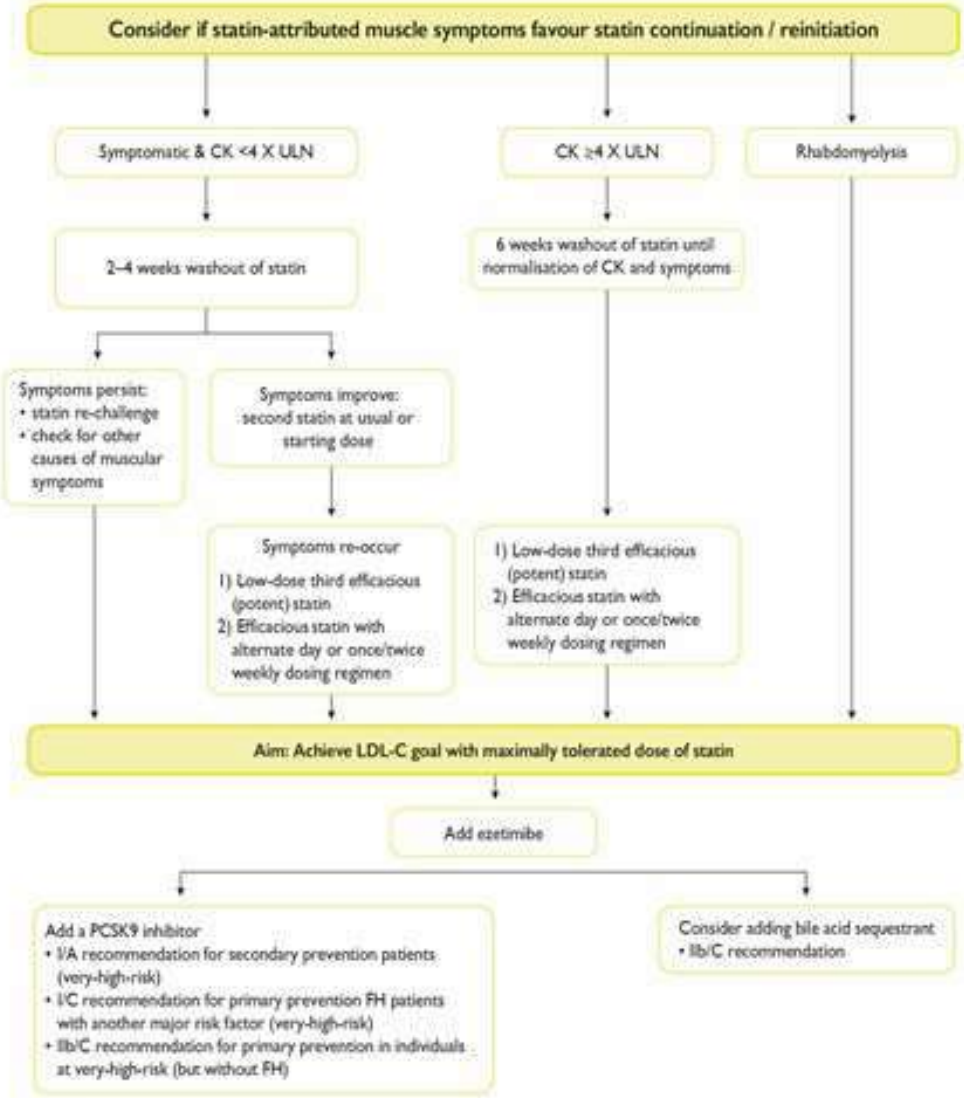
SCORE Cardiovascular Risk Chart
10-year risk of fatal CVD
High-risk regions of Europe



SCORE chart for European populations at high cardiovascular disease risk

www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)



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Algorithm for treatment of muscular symptoms during statin treatment

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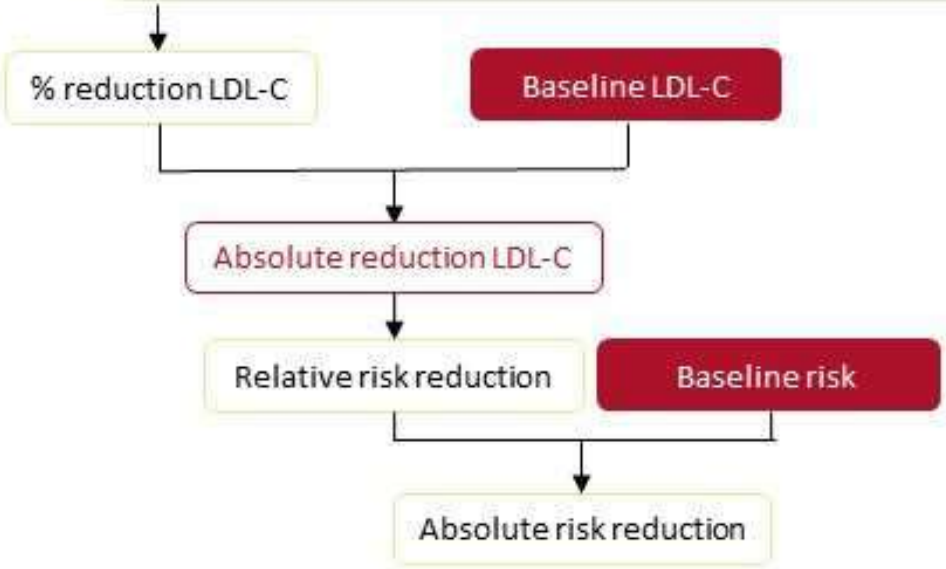
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

EAS ESC
European Society of Cardiology

Expected clinical benefit of low-density lipoprotein cholesterol lowering therapies

Intensity of lipid lowering treatment

Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%



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

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Recommendations for treatment goals for low-density lipoprotein cholesterol

Recommendations	Class[a]	Level[b]
In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]	I	A
In primary prevention for individuals at very-high risk but without FH,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[34–36]	I	C
In primary prevention for individuals with FH at very-high risk, an LDL-C reduction of ≥50% from baseline and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) should be considered.	IIa	C
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-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B
In patients at high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL) are recommended.[34,35]	I	A
In individuals at moderate risk,[c] an LDL-C goal of <2.6 mmol/L (<100 mg/dL) should be considered.[34]	IIa	A
In individuals at low risk,[c] an LDL-C goal <3.0 mmol/L (<116 mg/dL) may be considered.[36]	IIb	A

ASCVD = atherosclerotic cardiovascular disease; FH = familial hypercholesterolaemia; LDL-C = low-density lipoprotein cholesterol.
[a]Class of recommendation.
[b]Level of evidence.
[c]For definitions see *Table 4*.
[d]The term 'baseline' refers to the LDL-C level in a person not taking any LDL-C-lowering medication. In people who are taking LDL-C-lowering medication(s), the projected baseline (untreated) LDL-C levels should be estimated, based on the average LDL-C-lowering efficacy of the given medication or combination of medications.

Categorie di rischio

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

ESC European Society of Cardiology
EAS

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularisation (PCI, CABG and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis) or on carotid ultrasound. DM with target organ damage, or at least three major risk factors, or early onset of T1DM of long duration (>20 years). (>20 years).Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.

Changes in recommendations

2016	2019
Pharmacological LDL-C lowering	**Pharmacological LDL-C lowering**
In patients at very-high risk, with persistent high LDL-C despite treatment with maximal tolerated statin dose, in combination with ezetimibe or in patients with statin intolerance, a PCSK9 inhibitor may be considered.	For secondary prevention, patients at very-high risk not achieving their goal on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.
	For very-high-risk FH patients (that is, with ASCVD or with another major risk factor) who do not achieve their goals on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.

http://www.escardio.org/guidelines

ESC European Society of Cardiology
European Heart Journal (2019) 00, 1–78
doi:10.1093/eurheartj/ehz455

Changes in recommendations

2016	2019
Pharmacological LDL-C lowering	**Pharmacological LDL-C lowering**
If the LDL goal is not reached, statin combination with a cholesterol absorption inhibitor should be considered.	If the goals are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.

http://www.escardio.org/guidelines

ESC European Society of Cardiology
European Heart Journal (2019) 00, 1–78
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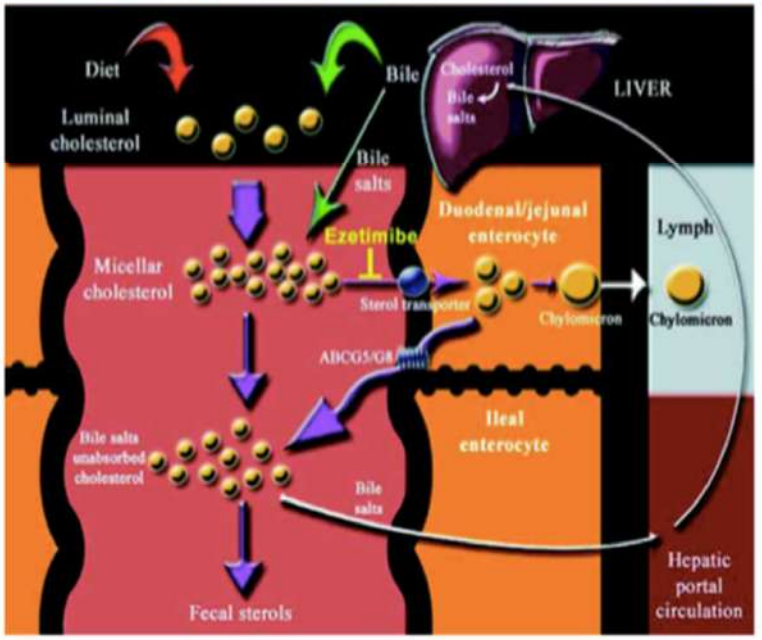
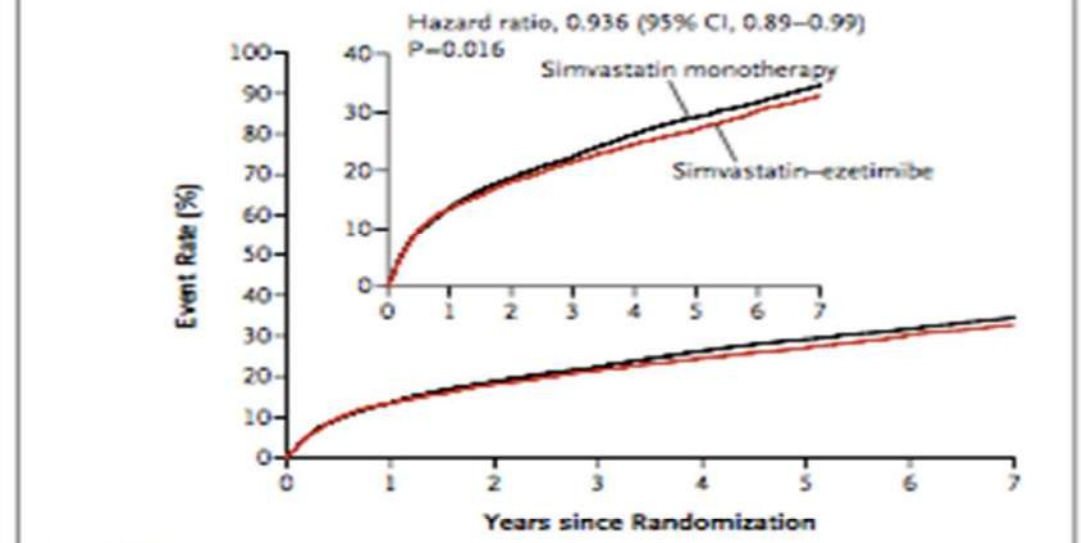
Ezetimibe

When added to statin, produces ~20% further reduction in LDL-C

Two recent human genetic analyses have correlated polymorphisms in NPC1L1 with lower levels of LDL-C and lower risk of CV events

- Ezetimibe inhibits Niemann-Pick C1-like 1 (NPC1L1) protein
  - located primarily on the epithelial brush border of the GI tract
  - resulting in reduced cholesterol absorption



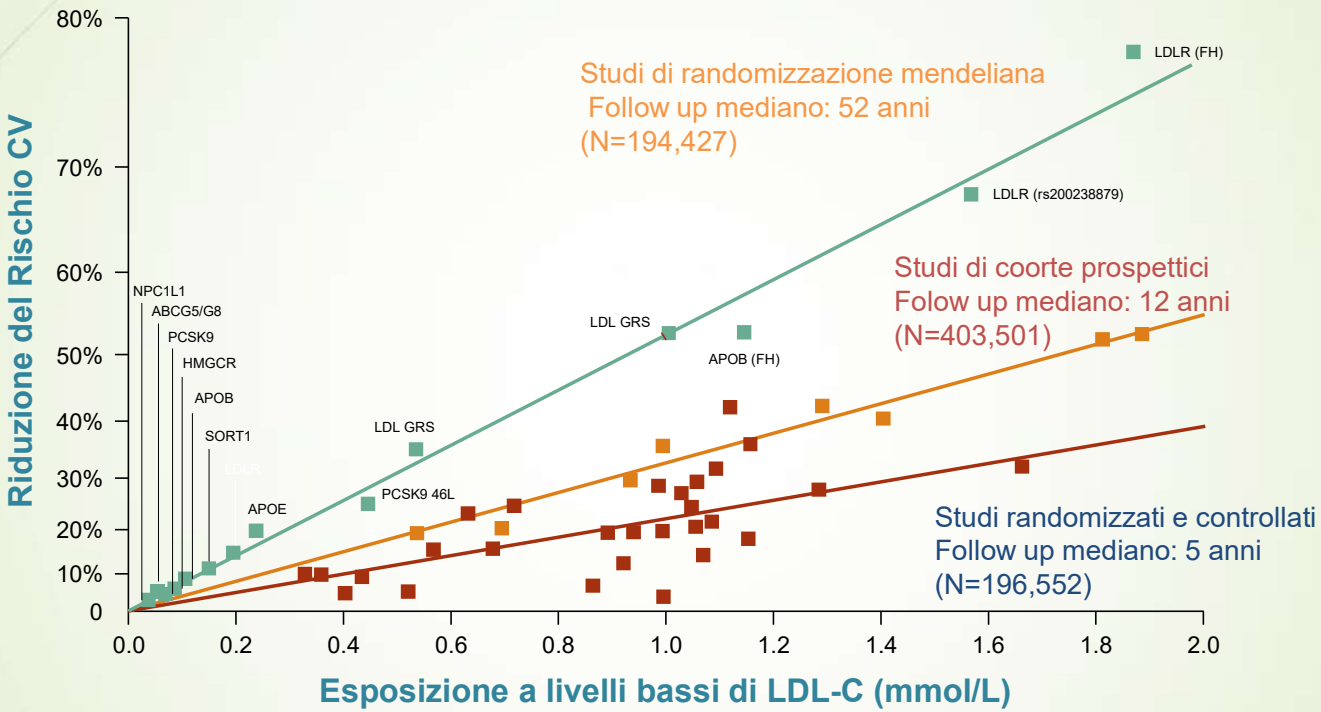


No. at Risk								
Simvastatin–ezetimibe	9067	7371	6801	6375	5839	4284	3301	1906
Simvastatin	9077	7455	6799	6327	5729	4206	3284	1857

Figure 1. Kaplan–Meier Curves for the Primary Efficacy End Point.

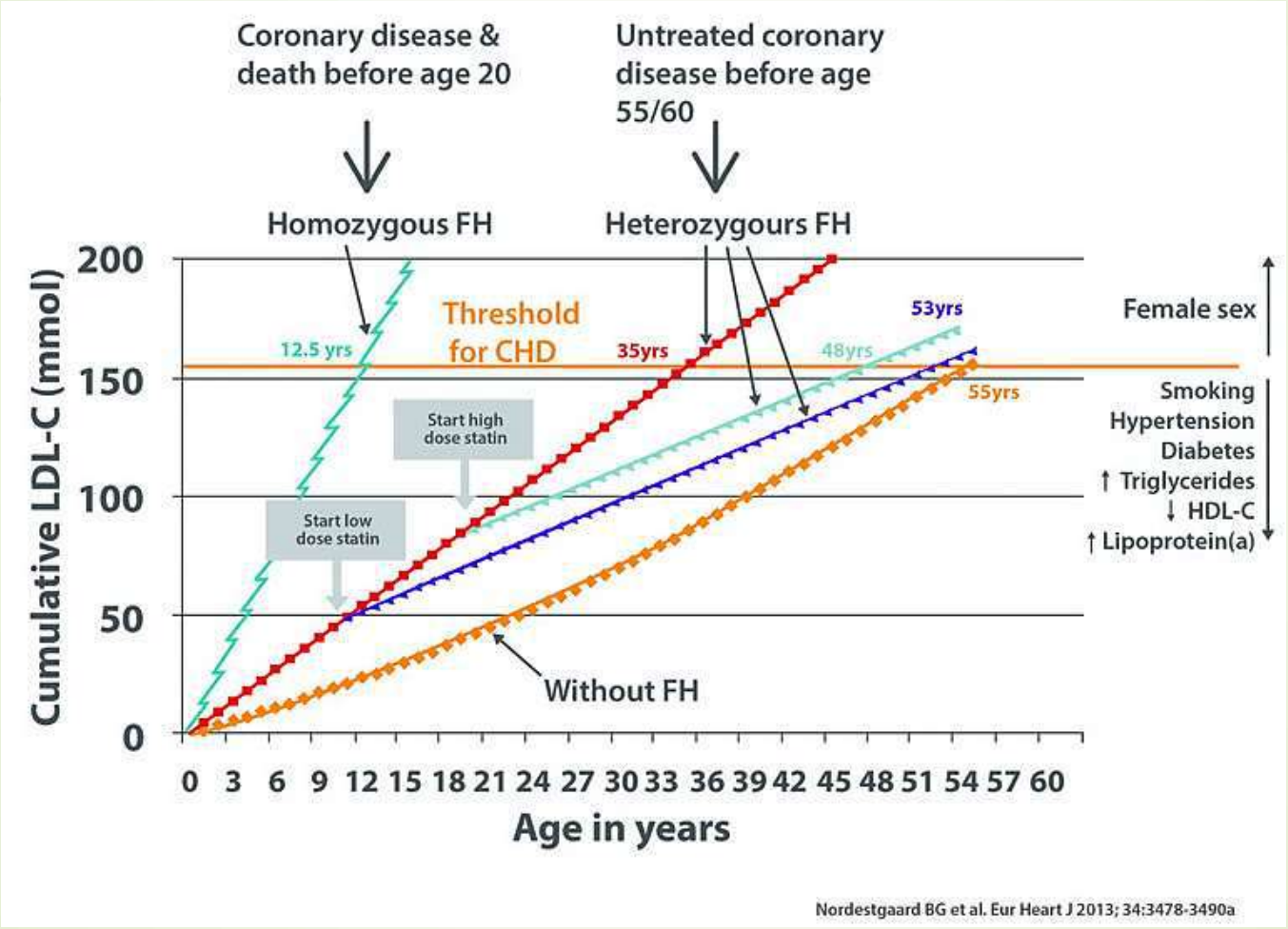
Shown are the cumulative event rates for the primary composite end point of death from cardiovascular disease, a major coronary event (nonfatal myocardial infarction, documented unstable angina requiring hospital admission, or coronary revascularization occurring at least 30 days after randomization), or nonfatal stroke in the intention-to-treat population during the overall study period (i.e., beginning from the time of randomization to the day of the first occurrence of a primary end-point event, the day of the last office or phone visit, or the day of death during follow-up). The inset shows the same data on an enlarged y axis.

Associazione dei livelli LDL con il rischio CV



Ference BA et al. Eur Heart J. 2017.

Importanza di un trattamento precoce ed efficace



Nordestgaard BG et al. Eur Heart J 2013; 34:3478-3490a

CV RISK CATEGORIES

2019

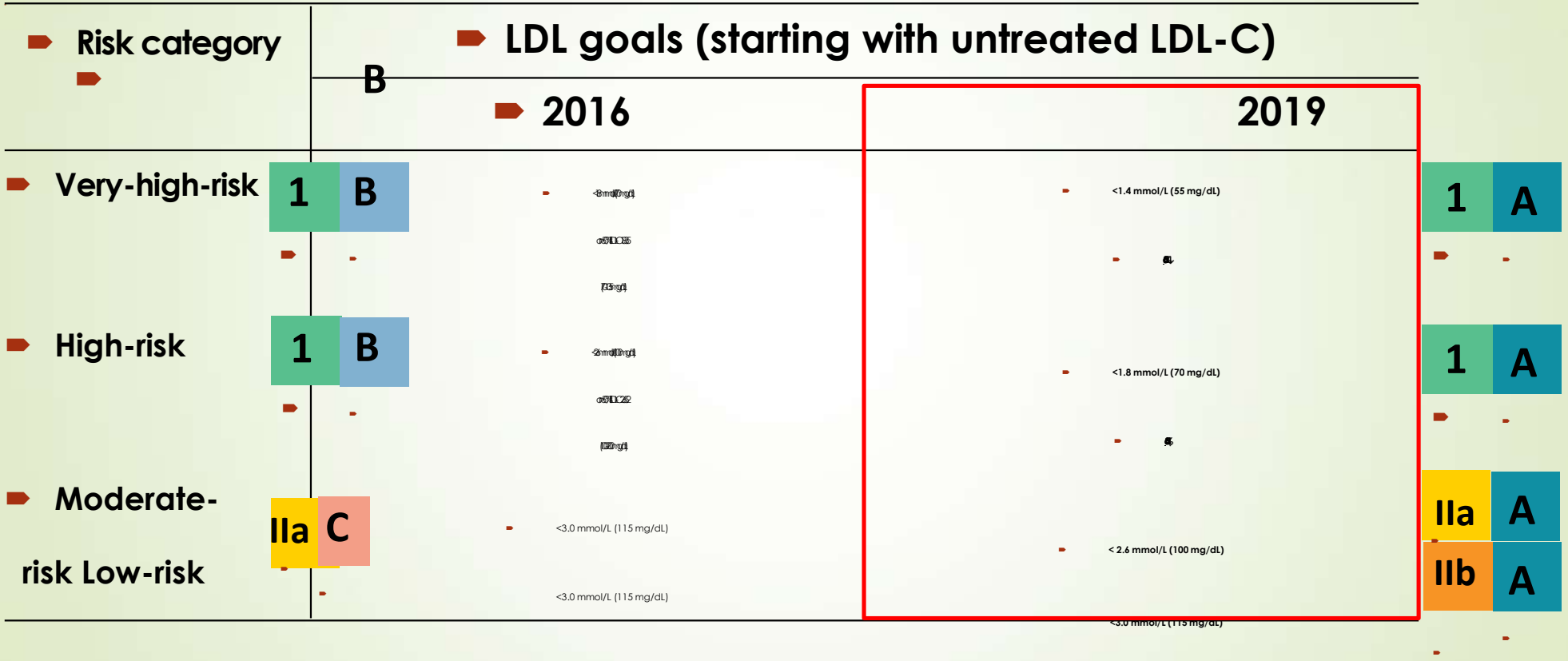
Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral 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.

2016

Very high-risk	Subjects with any of the following: • Documented cardiovascular disease (CVD), clinical or unequivocal on imaging. Documented CVD includes previous myocardial infarction (MI), acute coronary syndrome (ACS), coronary revascularisation (percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG)) and other arterial revascularization procedures, stroke and transient ischaemic attack (TIA), and peripheral arterial disease (PAD). Unequivocally documented CVD on imaging is what has been shown to be strongly predisposed to clinical events, such as significant plaque on coronary angiography or carotid ultrasound. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking, hypertension or dyslipidaemia. • Severe CKD (GFR <30 mL/min/1.73 m^2). • A calculated SCORE ≥10% for 10-year risk of fatal CVD.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

RECOMMENDED TREATMENT GOALS FOR LDL-LOWERING THERAPY : MAIN CHANGES FROM 2016 to 2019



2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)