Updates on Optimizing Lipid Management for Dyslipidemia patient

Dr. Mohamed Farghaly
FRCGP(UK).MRCGPI(UK).DIH(IRELAND)
DMSc(UK).MBChB(ALEX)
Professor Dubai Medical College
Consultant DHIC , DHA

Presentation outlines

- Dyslipidemia prevalence and associated risk factors in the United Arab Emirates
- LDL is the first target to address as per all guidelines
- Non-HDL Cholesterol and the Residual Risk
- 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice , Lipid modification to reduce CV risk
- Case Study
- Conclusions

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Bmj open:
Dyslipidemia prevalence and associated risk factors in the United Arab Emirates:

a population-based study

researchgate.net/publication/337097331_Dyslipidaemia_prevalence_and_associated_risk_factors_in_the_United_Arab_Emirates_a_population-based_study

- **Data From UAE**

- **Objectives: To** determine and describe the prevalence and pattern of dyslipidemia and its associated risk factors among an adult Emirati population.

- **Design** : Population-based, cross-sectional study. Setting Adults living in the Northern Emirates.

- **Participants**: 824 adult participants (51.8% men, 48.2% women, mean age 42.8—13.4 years old).

- **Primary outcome** :measures Fasting blood samples were collected, blood pressure and waist circumference were measured.

researchgate.net/publication/337097331_Dyslipidaemia_prevalence_and_associated_risk_factors_in_the_United_Arab_Emirates_a_population-based_study

Results

- The overall dyslipidemia prevalence was 72.5%,
- with 42.8% of the participants showing high total cholesterol (TC) level,
- 29% showing high triglyceride(TG) level,
- 42.5% showing low high-density lipoprotein cholesterol (HDL-C)level,
- 38.6% showing high low-density lipoprotein cholesterol (LDL-C) level
- and 72.3% showing high cholesterol ratio.

- researchgate.net/publication/337097331_Dyslipidaemia_prevalence_and_associated_risk_factors_in_the_United_Arab_Emirates_a_population-based_study

Conclusions

The prevalence of dyslipidemia was considerably high among the local adult Emiratis.

The identified dyslipidemia predictors were gender, age, smoking, central obesity and diabetes.

Further studies are recommended to assess other important risk factors and aggressive preventive measures in the United Arab Emirates.

researchgate.net/publication/337097331_Dyslipidaemia_prevalence_and_associated_risk_factors_in_the_United_Arab_Emirates_a_population-based_study

LDL is the First target to address

For well over 30 years, physicians have understood the role of LDL (low-density lipoprotein, or “bad”) cholesterol in the development of cardiovascular disease (CVD). LDL cholesterol levels are directly correlated with increasing CVD risk and lowering LDL cholesterol levels, through both lifestyle changes and medications, has been shown to reduce this risk.

Statins are the first-line choice of medications for lowering LDL cholesterol. They are widely prescribed for both primary prevention (reducing CVD risk in patients without known CVD) and secondary prevention (preventing subsequent heart attacks, strokes, and other CVD events in patients with established CVD).

health.harvard.edu/blog/are-statins-enough-when-to-consider-pcsk9-inhibitors-2020060819986

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

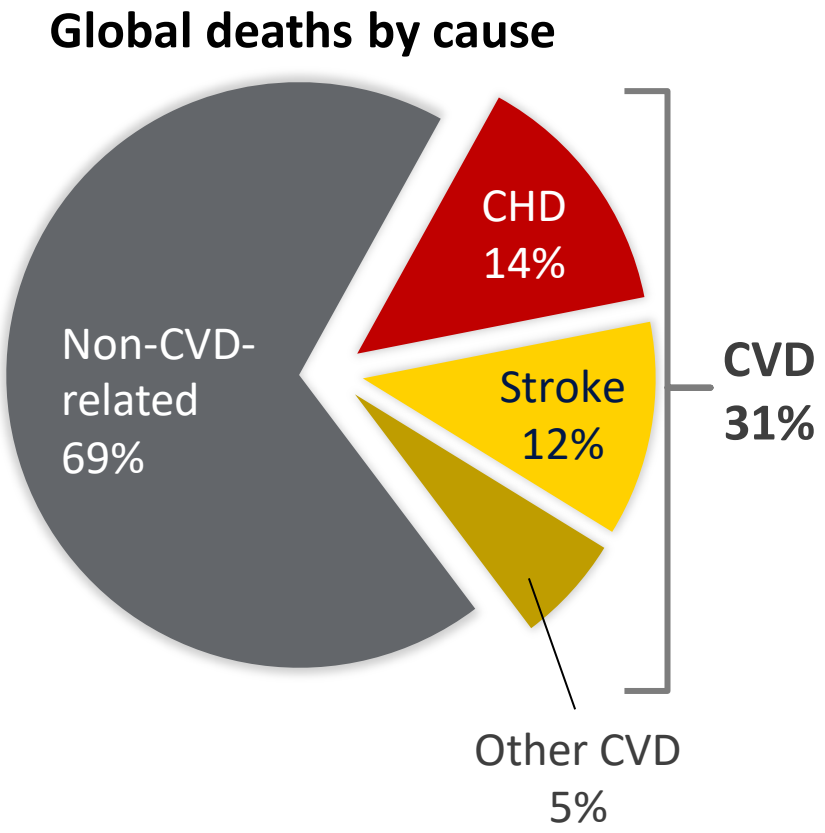
CVD remains the number 1 cause of death globally[1]

17.9 million

people die each year from CVDs, an estimated 31% of all deaths worldwide

85%

of all CVD deaths are due to heart attacks and strokes



1. Fact sheet : Cardiovascular diseases (CVDs). In: Geneva: World Health Organization. May 2017. Available at: https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)

Cardiovascular Disease and Dyslipidemia in the Gulf

In the Gulf CVD is the most common cause of deaths accounting for up to **45% of all mortalities**[1]

45 %

12

Patients that present with heart attack in the Middle East are **10 to 12 years younger** than those in western countries[2]

The increasing prevalence of **obesity** is directly associated with the increase in **lipid disorders and type 2 diabetes**

Dyslipidemia: an abnormally high concentration of lipids in the blood, is one of the **main risk factors** for the development and progression of CVD

1-Al Rasadi K et al, *Oman Med Journal*, 2015 Nov; 30(6): 403–405
European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455
2-Al Rasadi et al, Atherosclerosis 252 (2016) 182e187

CVD: cardiovascular Disease

Outcome studies have shown significantly increased risk for CAD* in the presence of dyslipidemia[1]

3 out of 4

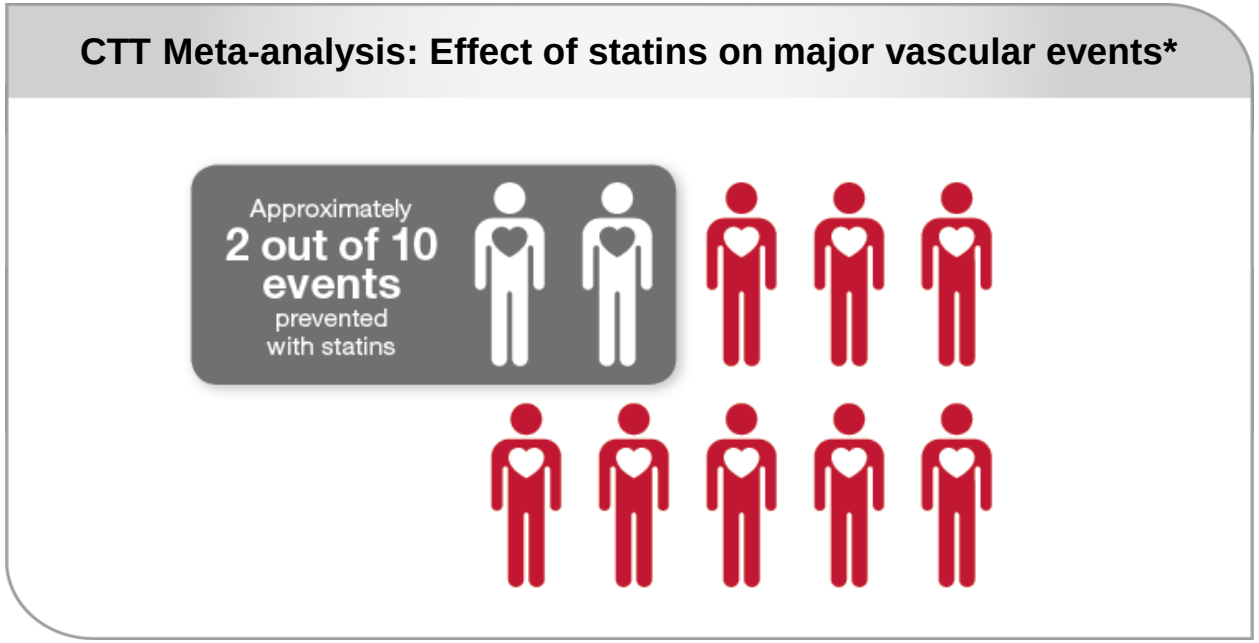
of the patients with coronary atherosclerosis had dyslipidemia.

*CAD: Coronary Artery Disease

1. Al-Shehri AM. Prevalence and pattern of lipid disorders in Saudi patients with angiographically documented coronary artery disease. J Family Community Med. 2014;21(3):166–169.

While statins reduce cardiovascular risk, a substantial residual risk remains[1]

A meta-analysis of 21 randomized clinical trials (n=129,526) revealed that statin treatment prevented approximately 2 out of 10 major vascular events* (relative risk reduction 22%, p<0.0001)

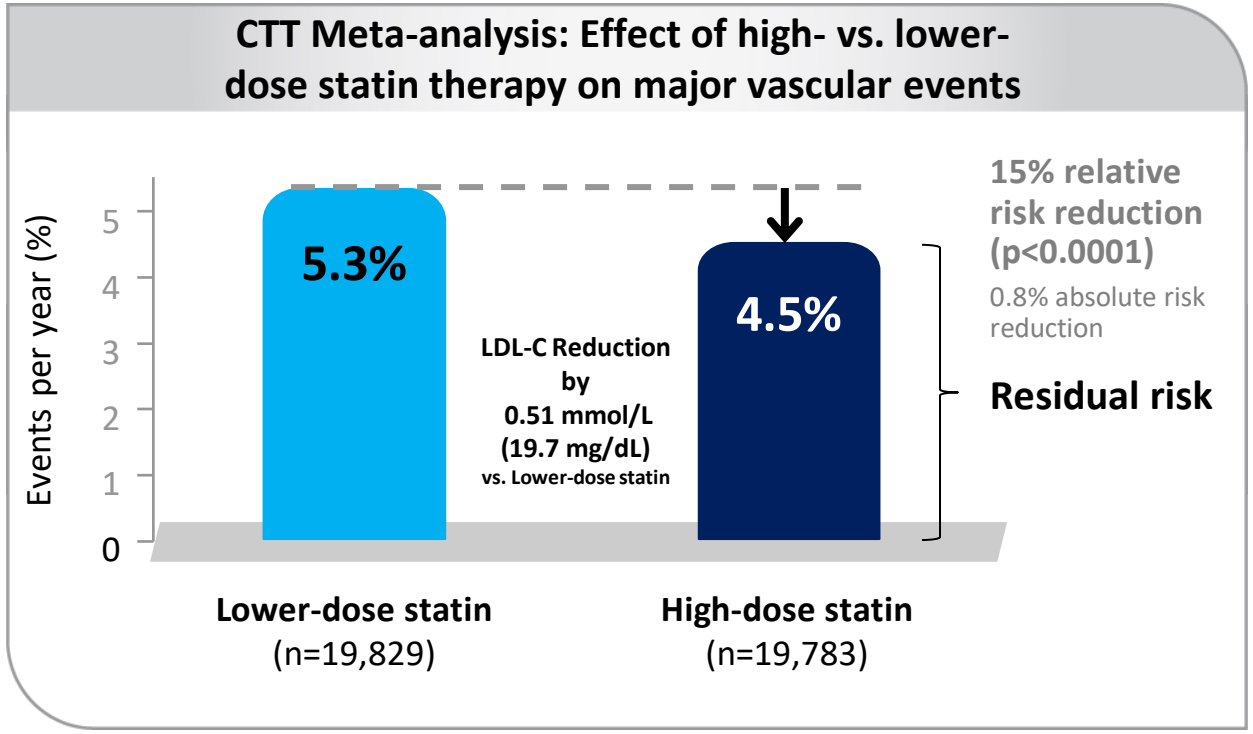


Remaining residual risk may be due to other modifiable and unmodifiable risk factors, including other lipid parameters, blood pressure, glycemic control, weight and genetic predisposition

1. Baigent C, Blackwell L, Emberson J. etal. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376:1670-81.

Increasing the statin dose can help but may not be enough[1]

In a meta-analysis of 5 clinical trials (n=39,612), high-dose statin therapy reduced the relative risk of a major vascular event by only **15%** vs. lower-dose statin therapy



1. Cholesterol Treatment Trialists' (CTT) Collaboration, Baigent C, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376:1670-81.

EXTENT OF LIPID LOWERING WITH AVAILABLE THERAPIES

Approximate reduction in LDL-C					
Statin dose mg/day	5	10	20	40	80
Fluvastatin			21%	27%	33%
Pravastatin		20%	24%	29%	
Simvastatin		27%	32%	37%	42%
Atorvastatin		37%	43%	49%	55%
Rosuvastatin	38%	43%	48%	53%	
Atorvastatin + Ezetimibe 10mg		52%	54%	57%	61%

Low intensity statins will produce an LDL-C reduction of 20-30%

Medium intensity statins will produce an LDL-C reduction of 31-40%

High intensity statins will produce an LDL-C reduction above 40%

Simvastatin 80mg is not recommended due to risk of muscle toxicity

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Diabetes medical evaluation by *laboratory tests I*

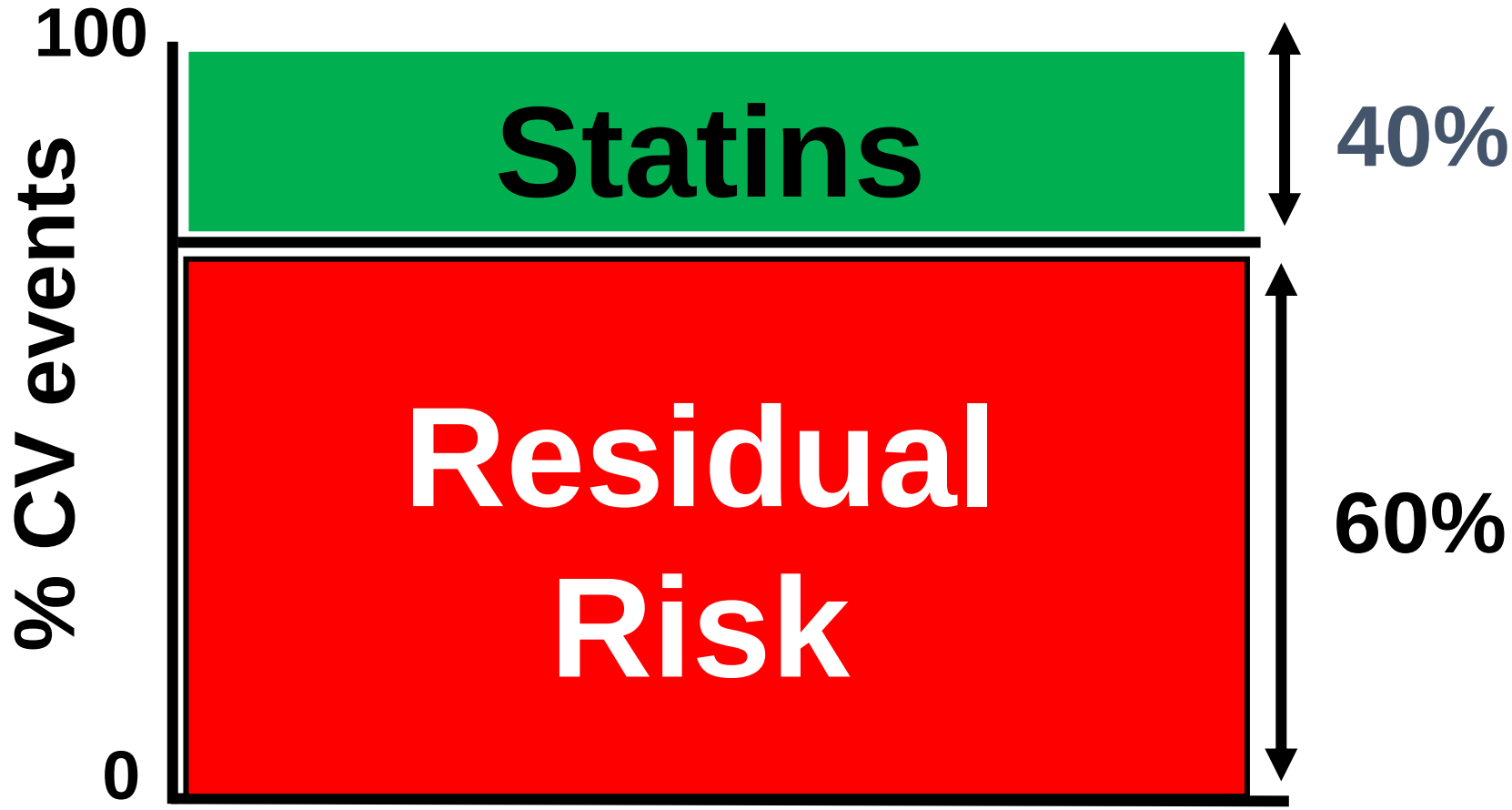
Test	Target	Initial visit	Periodic visits	Annual visit
Glycaemia				
Blood Glucose Levels	FPG 5-7 mmol/L (90 – 126 mg/dL) RBG 7-10 mmol/L (126 – 180 mg/dL)*	√	√	√
HbA1c†	≤7% (53 mmol/mol) - individual 6.5-7.5% (48-58 mmol/mol)in majority of patients*	√	√	√
Lipid profile‡				
• **Total Cholesterol**	< 4.0 mmol/L (<160 mg/dL)	√		√
• **LDL**		√		√
• **Very high risk**	< 1.4 mmol/L (<55 mg/dL)			
• **High risk**	< 1.8 mmol/L (<70 mg/dL)			
• **Moderate risk**	< 2.6 mmol/L (<100 mg/dL)			
• **Low risk**	< 3.0 mmol/L (<116 mg/dL)			
• **Triglycerides**	< 2.0 mmol/L (<178 mg/dL)	√		√

*Less stringent targets between 7.5% and 8.0% (58 to 64 mmol/mol) can be recommended for elderly, patients with short life expectancy, recurrent hypoglycaemia, and hypoglycaemia unawareness[5,6].
†The recommended frequency of HbA1c testing is 2-4 times per year[7].
‡The recommended frequency of lipids testing is 1-3 times per year. Patients without dyslipidemia and not on lipid lowing agents, testing can be less frequent.
**LDL target is based of the ESC/EASD risk categorisation mentioned in Fig 2.

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Emirates Diabetes Society Consensus Guidelines for the Management of Type 2 Diabetes 2020, 8th August 2020

Treatment of CVD: Residual Risk



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Case 1

Mr. Hassan; 40 years-old overweight, **diabetic (type 2)**

His Blood glucose level is controlled using OAD therapy

Three months ago, he was diagnosed as mixed dyslipidemia patient as well.

Currently taking **Atorvastatin 10mg** & presented with the below lipid profile :

- Total cholesterol: 232 mg/dl
- LDL: 160 mg/dl
- HDL: 40 mg/dl
- Triglycerides: 160 mg/dl
- Non HDL: 192 mg/dl

Suggested Management: **???**

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Lipid modification to reduce cardiovascular risk.

ESC
European Society of Cardiology
European Heart Journal (2021) 42, 3227–3337
doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)

Major Atherosclerotic Cardiovascular Disease Risk Factors

Major risk factors	Additional risk factors	Nontraditional risk factors
Advancing age	Obesity, abdominal obesity	⇧ Lipoprotein (a)
⇧ Total serum cholesterol level	Family history of hyperlipidemia	⇧ Clotting factors
⇧ Non–HDL-C	⇧ Small, dense LDL-C	⇧ Inflammation markers
⇧ LDL-C	⇧ Apo B	(hsCRP; Lp-PLA_2)
Low HDL-C	⇧ LDL particle concentration	⇧ Homocysteine levels
Diabetes mellitus	Fasting/postprandial	Apo E4 isoform
Hypertension	hypertriglyceridemia	⇧ Uric acid
Stage 3 or 4 chronic kidney disease	PCOS	⇧ TG-rich remnants
Cigarette smoking	Dyslipidemic triad	
Family history of ASCVD		

Abbreviations: apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; hsCRP, highly sensitive C-reactive protein; LDL, low-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; Lp-PLA2, lipoprotein-associated phospholipase; PCOS, polycystic ovary syndrome.

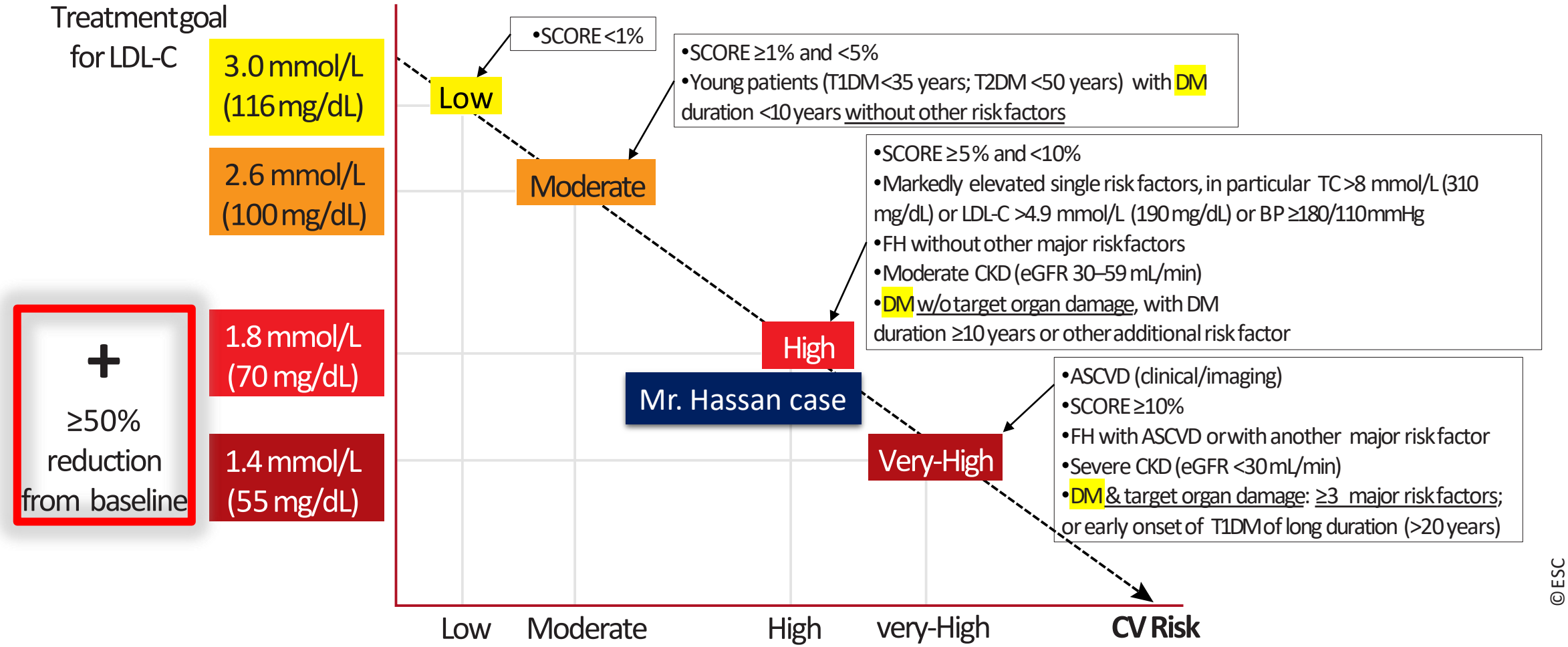
AACE POSWC. *Endocr Pract*. 2005;11:126-134; ADA. Diabetes Care. 2017;40(Suppl 1):S1-S135; Brunzell JD, et al. *Diabetes Care*. 2008;31:811-822; Cromwell WC, et al. *J Clin Lipidol.* 2007;1:583-592; Einhorn D, et al. *Endocr Pract*. 2003;9:237-252; Grundy SM, et al. *Circulation.* 1998;97:1876-1887; Jellinger P, Handelsman Y, Rosenblit P, et al. *Endocr Practice*. 2017;23(4):479-497.; Kastelein JJ, et al. *Circulation.* 2008;117:3002-3009; NCEP. NIH Publication No. 02-5215. September 2002; Neaton JD, et al. *Arch Intern Med*. 1992;152:1490-1500; NHLBI. NIH Publication No. 04-5230. August 2004; Stamler J, el al. *JAMA*. 1986;256:2823-2828; Weiner DE, et al. *J Am Soc Nephrol.* 2004;15(5):1307-1315; Yusuf S, et al. *Lancet.* 2004;364(9438):937-952.

Risk Category ESC/EAS 2019 - 2021

NEW

Risk category: CVD PREVENTION	LDL-c	Non-HDL-c	Apo B
Very High • ASCVD (clinical/imaging) • SCORE ≥10% • FH with ASCVD or with another major risk factor • Severe CKD (eGFR <30 mL/min) • DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)	<55mg/dL	<85mg/dL	<65 mg/dL
High Mr. Hassan case • SCORE ≥5% and <10% • Markedly elevated single risk factors, in particular TC >8 mmol/L (310 mg/dL) or LDL-C >4.9 mmol/L (190 mg/dL) or BP ≥180/110 mmHg • FH without other major risk factors • Moderate CKD (eGFR 30–59 mL/min) • DM w/o target organ damage, with DM duration ≥10 years or other additional risk factor	<70 mg/dL	<100 mg/dL	<80 mg/dL
Moderate • SCORE ≥1% and <5% • Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years without other risk factors	<100 mg/dL	<130 mg/dL	<100 mg/dL
Low • SCORE <1%	<115 mg/dl	<145 mg/dL	<90 mg/dL

Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk



European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Recommendations for lipid analyses for cardiovascular disease risk estimation (1)

Recommendations	Class	Level
TC is to be used for the estimation of total CV risk by means of the SCORE system.	I	C
HDL-C analysis is recommended to further refine risk estimation using the online SCORE system.	I	C
LDL-C analysis is recommended as the primary lipid analysis for screening, diagnosis and management.	I	C
TG analysis is recommended as a part of the routine lipid analysis.	I	C

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

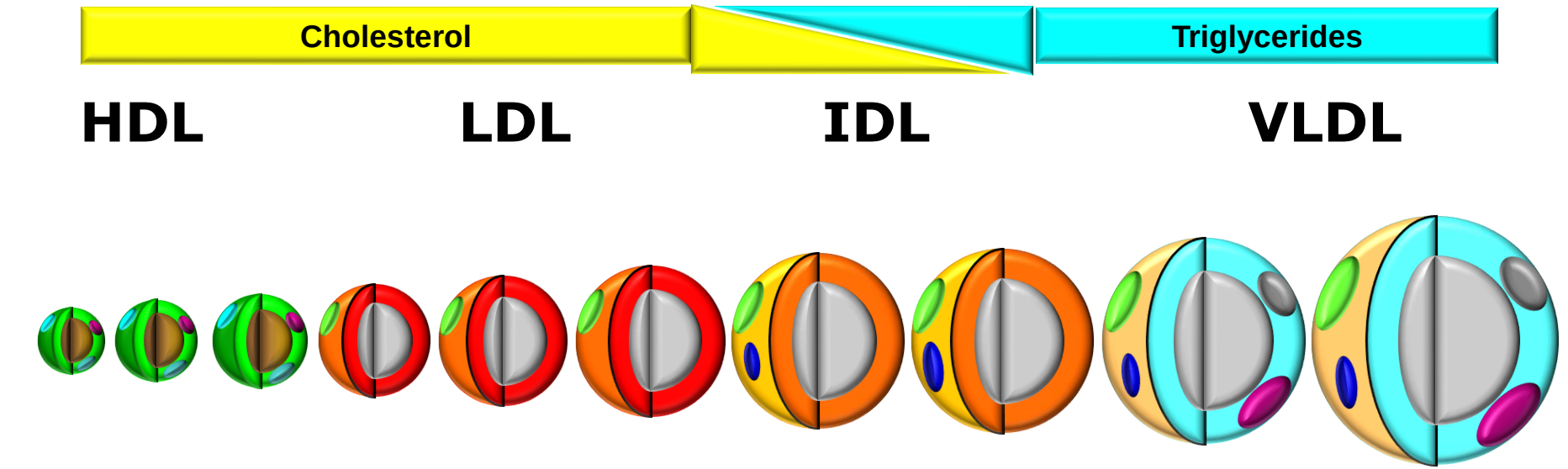
Recommendations for lipid analyses for cardiovascular disease risk estimation (2)

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

- Non-high-density lipoprotein cholesterol (HDL-C) encompasses all atherogenic (apo-B-containing) lipoproteins, and is calculated as: total cholesterol — HDL-C = non-HDL-C. The relationship between non-HDL-C and CV risk is at least as strong as the relationship with LDL-C. Non-HDL-C levels contain, in essence, the same information as a measurement of apo-B plasma concentration.[23,24] Non-HDL-C is used as an input in the Systemic Coronary Risk Estimation 2 (SCORE2) and SCORE2-Older Persons (SCORE2-OP) risk algorithms.

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Non-HDL Cholesterol



Anti Atherogenic Lipoproteins

Atherogenic Lipoproteins

Non HDL-C: Total Cholesterol minus HDL-C

Very easy to calculate, No extra cost!

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Consensuss Clinical Recommendations for the management of Plasma lipid disorders in the Middle East – 2021 update

ELSEVIER

Atherosclerosis

Volume 343, February 2022, Pages 28-50

Consensus clinical recommendations for the management of plasma lipid disorders in the Middle East: 2021 update

Nasreen Alsayed [a], Wael Almahmeed [b], Fahad Alnouri [c, 1], Khalid Al-Waili [d], Hani Sabbour [e], Kadhim Sulaiman [f], Mohammad Zubaid [g], Kausik K. Ray [h, 1], Khalid Al-Rasadi [i, 1]

In several population studies, an elevated TG level is associated with an increased risk of ASCVD [68]. A post hoc analysis from the Treating to New Targets (TNT) trial [69] suggested that triglyceride-rich lipoprotein-cholesterol is not only a cardiovascular risk marker, but also a potential target for therapeutic intervention. The AACE guidelines report patients with TG levels ≥200 mg/dL to have a greatly increased ASCVD risk [15]. Consequently, elevated plasma TG should be considered as an indication for more aggressive LDL-C lowering therapy to reduce this risk.

The lack of robust, consistent evidence from RCTs does not allow to set a goal for TG levels in CVD prevention, but levels of <150 mg/dL (1.7 mmol/L) are desirable, and higher levels indicate a need to look for other risk factors [13].

European Heart Journal, ehz455, https://doi.org/10.10

Nasreen A. Sayed et al. Consensus clinical recommendations for the management of plasma lipid disorders in the middle East: 2021 update, Atherosclerosis 343 (2022) 28–50

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5.2. *Primary treatment target: non-HDL-C levels*

A number of authors and international guidelines report non-HDL-C levels (Table 5) to be more predictive of ASCVD risk than are LDL-C levels [16,29,65]. Reductions in non-HDL-C levels by a range of lipid-lowering drug classes are associated with decreased ASCVD events, and CHD reduction [66]. The new ESC/EAS guidelines classify non-HDL-C as a secondary goal because it has not been extensively studied in RCTs. However, non-HDL-C levels are a particularly useful measure in people with hypertriglyceridaemia, diabetes, CKD or MetS, where this value may provide a more accurate indication of ASCVD risk than is provided by the level of LDL-C alone [13]. Therefore, non-HDL-C levels may be of particular clinical relevance in Middle Eastern populations. We recommend non-HDL-C as a primary treatment target, alongside LDL-C. Treatment goals should be non-HDL-C levels 0.8 mmol/L (30 mg/dL) higher than LDL-C targets for all patients (Table 5)

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

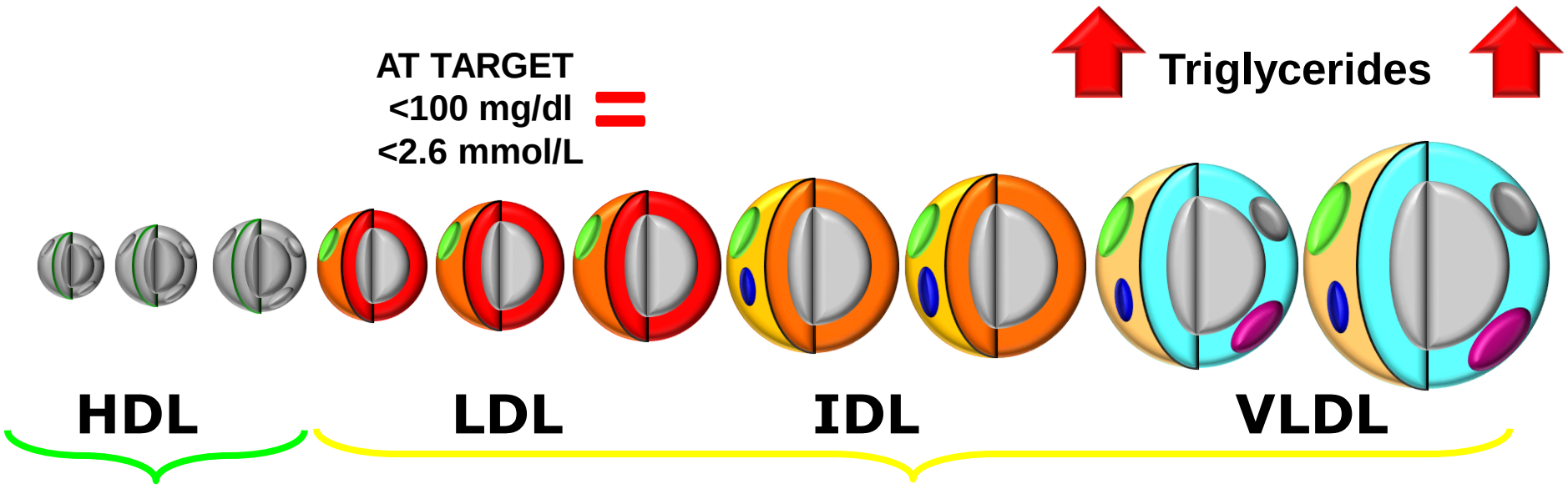
Nasreen A. Sayed et al. Consensus clinical recommendations for the management of plasma lipid disorders in the middle East: 2021 update, Atherosclerosis 343 (2022) 28–50

Recommendations for drug treatments of patients with hypertriglyceridaemia (1)

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

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Non-HDL Cholesterol



Anti Atherogenic Lipoproteins

Non HDL-C ≥130 mg/dl or 3.4 mmol/L NOT AT TARGET

Atherogenic Lipoproteins

Non-HDL cholesterol: Emerging # 1 TARGET for treatment of (Residual) Cardiovascular Risk

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Case 1

Mr. Hassan; 40 years-old overweight, **diabetic (type 2)**

His Blood glucose level is controlled using OAD therapy

Three months ago, he was diagnosed as mixed dyslipidemia patient as well.

Currently taking **Atorvastatin 10mg** & presented with the below lipid profile :

- Total cholesterol: 232 mg/dl
- LDL: 160 mg/dl (GOAL LEVEL <70 mg/dL)
- HDL: 40 mg/dl
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- Non HDL: 192 mg/dl (GOAL LEVEL <100 mg/dL)

Suggested Management: ???

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Suggested Management: (achieve LDL & Non-HDL GOALs)

- Increase Atorvastatin dose to 20mg daily, 1 tablet at night. **OR**
- Add Ezetimibe once daily with 10mg of Atorvastatin at night.

Diabetes, Hypertension & Dyslipidemia are chronic diseases **need life-long treatment**

Case 2

Mr. ADAM; 57 years-old overweight, controlled hypertensive, **diabetic (type 2) with hypercholesterolemia**

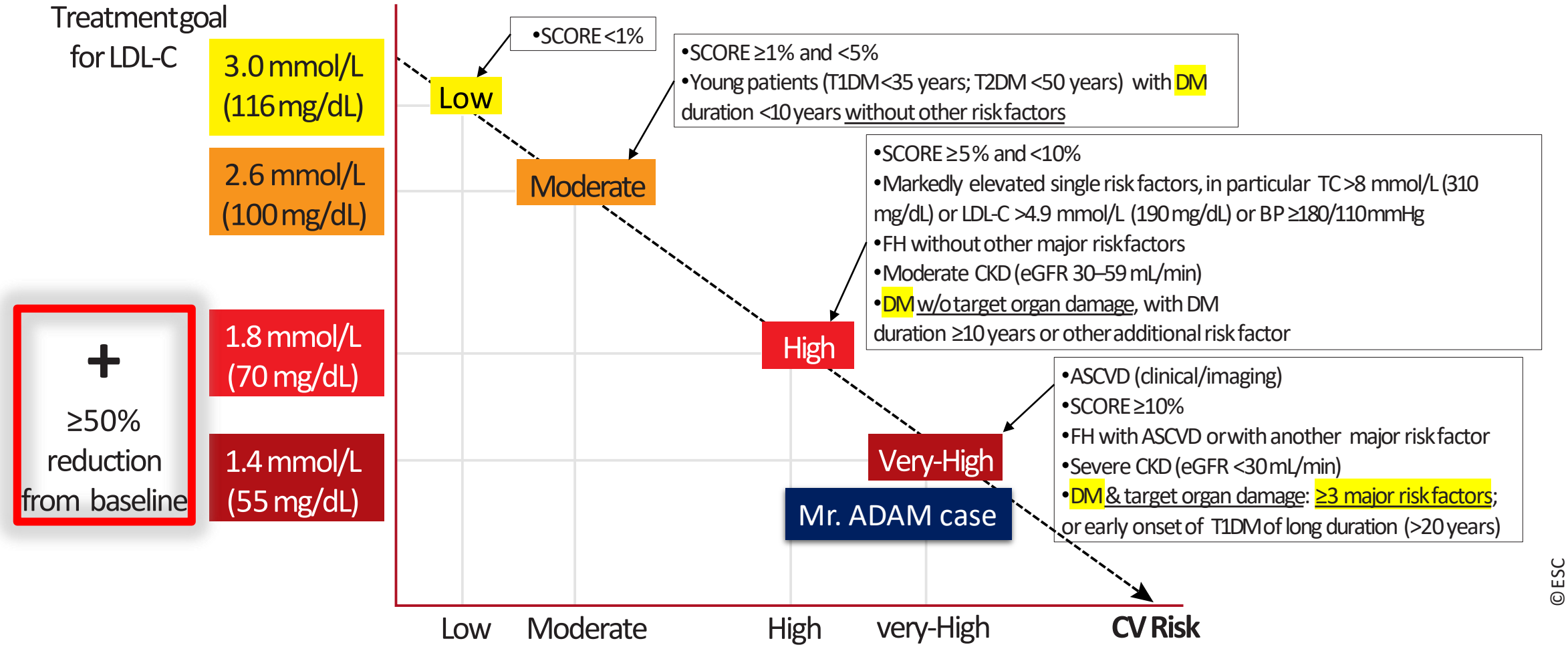
His Blood glucose level& BP are controlled using OAD & antihypertensive therapies

Currently taking Rosuvastatin 20mg & presented with the below lipid profile :

- Total cholesterol: 143 mg/dl
- LDL: 54 mg/dl
- HDL: 33 mg/dl
- Triglycerides: 280 mg/dl
- Non HDL: 125 mg/dl

Suggested Management: **???**

Treatment goals for low-density lipoprotein cholesterol (LDL-C) across categories of total cardiovascular disease risk



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Low • SCORE <1%	<115 mg/dl	<145 mg/dL	<90 mg/dL

Case 2

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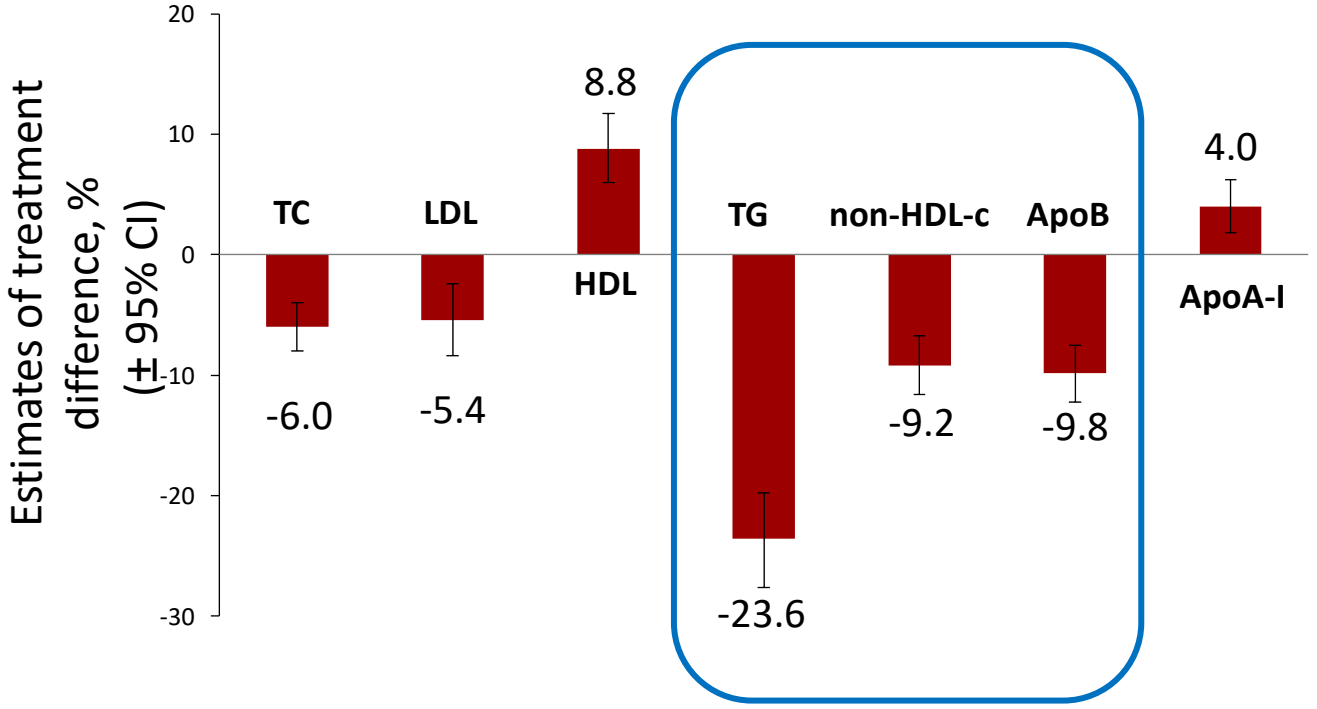
- Non HDL: 125 mg/dl (GOAL LEVEL <85 mg/dL)

Suggested Management:

- Add Fibrate OR/AND
- Add OMEGA-3

Fenofibrate-statin Combination improves complete lipid profile

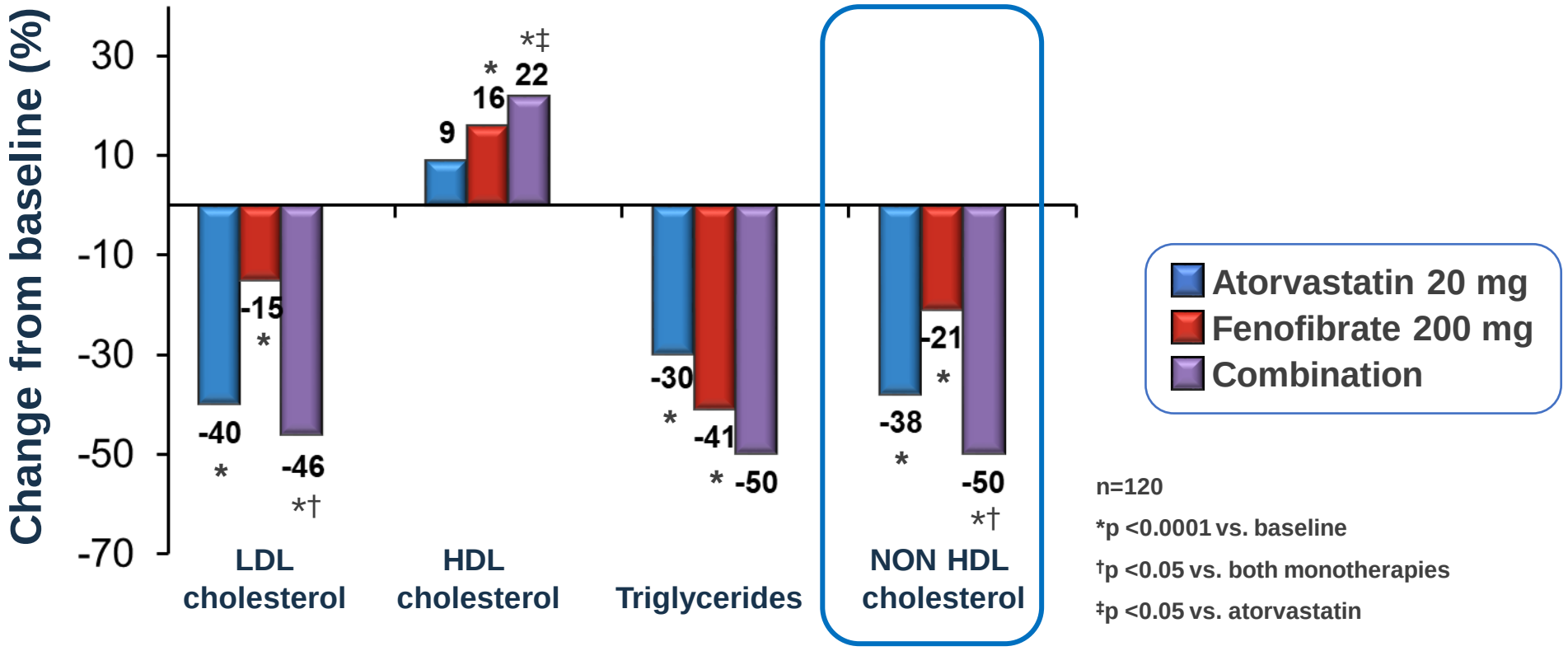
Treatment differences in lipid parameters for fenofibrate–simvastatin *versus* simvastatin



p<0.001 for all parameters

Grundy SM et al. *Am J Cardiol* **2005**;95:462

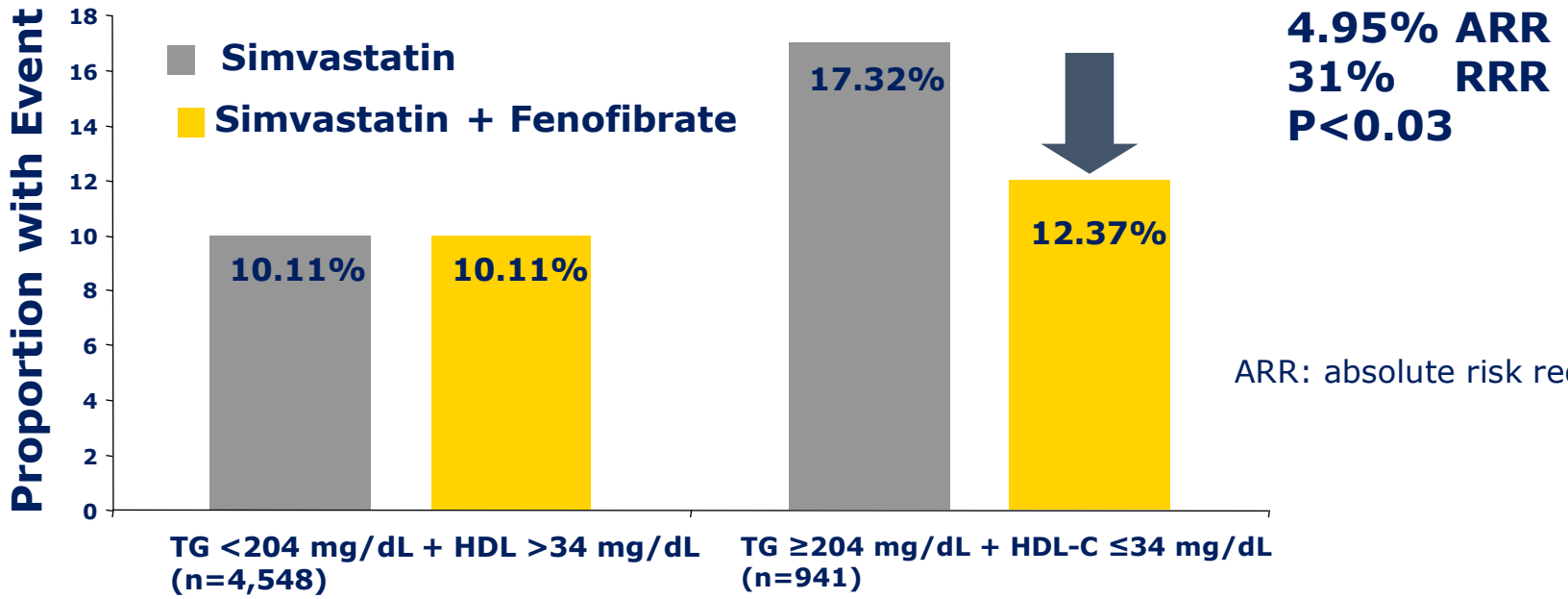
Atorvastatin and Fenofibrate Alone or in Combination in Patients With Type 2 Diabetes



Adapted from Athyros VG et al. Diabetes Care 2002; 25: 1198-202

Fenofibrate reduced events in T2D patients with elevated TG and low HDL-C

70% ↑ CV events in Patients in dyslipidaemia subgroup vs others despite mean LDL-C <80 mg/dL



4.95% ARR
31% RRR
P<0.03

ARR: absolute risk reduction

ACCORD Study Group. N Engl J Med. 2010. Epub.

Safety profile of Fenofibrate

Fibrates are generally well tolerated with mild adverse effects, GI disturbances being reported in <5% of patients, and skin rashes in 2%.[319] In general, myopathy, liver enzyme elevations, and cholelithiasis represent the most well-known adverse effects associated with fibrate therapy.[319] The risk of myopathy has been reported to be 5.5-fold greater with fibrate monotherapy (mainly with gemfibrozil) compared with a statin, and it varies with different fibrates and statins used in combination. This is explained by the pharmacological interactions between the metabolism of different fibrates and pathways of glucuronidation of statins. Gemfibrozil inhibits the metabolism of statins via the glucuronidation pathway, which leads to marked increases in plasma concentrations of statins.[320] As fenofibrate does not share the same pharmacokinetic pathways as gemfibrozil, the risk of myopathy is much less with this combination therapy.[319]

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Fenofibrate + Statins combination

4.6.4. Important groups

Recommendations for drug treatments of patients with hypertriglyceridaemia.

Recommendations	Class[a]	Level[b]
Statin treatment is recommended as the first drug of choice for reducing CVD risk in high-risk individuals with hypertriglyceridaemia [triglycerides >2.3 mmol/L (200 mg/dL)].[533]	I	A
In patients taking statins who are at LDL-C goal with triglycerides >2.3 mmol/L (200 mg/dL), fenofibrate or bezafibrate may be considered.[534–536]	IIb	B
In high-risk (or above) patients with triglycerides >1.5 mmol/L (135 mg/dL) despite statin treatment and lifestyle measures, n-3 PUFAs (icosapent ethyl 2 × 2 g/day) may be considered in combination with a statin.[84]	IIb	B

CVD = cardiovascular disease; LDL-C = low-density lipoprotein cholesterol; PUFA = polyunsaturated fatty acid.
[a]Class of recommendation.
[b]Level of evidence.
Adapted from [3]

Consensuss Clinical Recommendations for the management of Plasma lipid disorders in the Middle East – 2021 update

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Nasreen Alsayed [a], Wael Almahmeed [b], Fahad Alnouri [c, 1], Khalid Al-Waili [d], Hani Sabbour [e], Kadhim Sulaiman [f], Mohammad Zubaid [g], Kausik K. Ray [h, 1], Khalid Al-Rasadi [i, 1]

7.3.6. Fibrates

The addition of a fibrate to a statin may benefit some patients with type 2 diabetes with both high TG and low HDL-C dyslipidaemia pattern, particularly those with microvascular complications. When used as an add-on therapy to statins, fibrates are associated with greater reductions in TG levels, and a greater increase in HDL-C (compared with either used as a monotherapy) [132]. The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study demonstrated that fibrates decrease ASCVD events in subjects with type 2 diabetes with elevated levels of plasma TG and low levels of HDL-C [133]. Furthermore, in the ACCORD-Lipid trial, participants with the combination of significant hypertriglyceridaemia and low HDL-C experienced a 31% lower CVD event rate with statin-fibrate combined treatment [134]. Fibrates are safe and generally well tolerated.

[136]. The use of fibrates in addition to statins in patients with metabolic dyslipidaemia may lower TG levels, increase HDL-C, and lower the risk of ASCVD events [132–134]. Fibrates are generally well tolerated.

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Case 2

Mr. ADAM; 45 years-old overweight, controlled hypertensive, **diabetic (type 2) with hypercholesterolemia**

His Blood glucose level& BP are controlled using OAD & antihypertensive therapies

Currently taking Rosuvastatin 20mg & presented with the below lipid profile :

- Total cholesterol: 143 mg/dl
- LDL: 54 mg/dl (GOAL LEVEL <55 mg/dL)
- HDL: 33 mg/dl
- Triglycerides: 280 mg/dl (GOAL LEVEL <150 mg/dL)*
- Non HDL: 125 mg/dl (GOAL LEVEL <85 mg/dL)

Suggested Management:

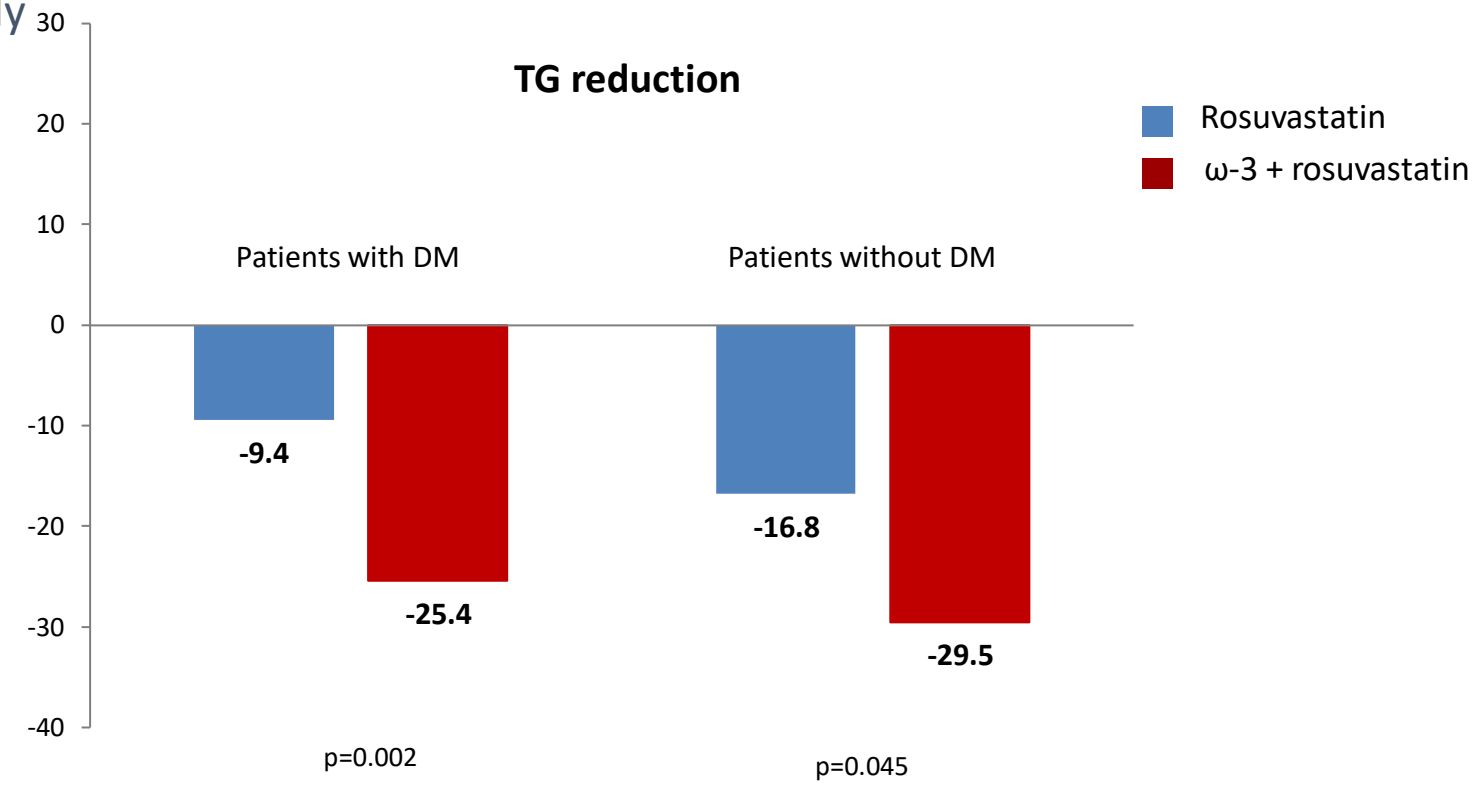
- Add Fibrate OR/AND
- Add OMEGA-3

Omega-3 – Rosuvastatin combination

The most important treatment in patients with dyslipidemia is **statins,** which mainly **lowers LDL-C**

However, statins do not control TG levels effectively

The combination group had a greater reduction in TG levels after 8 weeks compared with the rosuvastatin group regardless of the presence of DM



Hypertriglyceridemia is known as an independent risk factor associated with cardiovascular event [1-3]

1- Freiberg JJ,et al. JAMA. 2008;300:2142–2152.
2- Labreuche J et alAtherosclerosis. 2009;203:331–345.
3- Sarwar N et al. Circulation. 2007;115:450–458.

European Heart Journal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

*1. Kim CH et al. Clin Ther **2018**;40:83*

DM= Diabetes Mellitus, ω-3 = Omega-3, LDL-C = Low Density Lipoprotein Cholesterol, TG = Triglycerides

Supplement fish oil vs Prescription Omega-3

Not regulated by FDA	FDA approved
Fish oil supplements	**Prescription Omega-3**
Contain up to 30% EPA +DHA	1 capsule contains 90% EPA +DHA
EPA & DHA as Triacylglycerols	EPA & DHA as Ethyl Esters
Rapidly degraded in the duodenum	Sustained release absorbed more slowly
Short acting	Covering 24 hours
May contain toxins such as lead or mercury	Highly purified
Oxidation products exceed maximum levels for international standards of quality	Highly regulated to meet international standards of quality

AACE 2020 : Over-the-counter fish oil dietary supplements are not FDA-approved for lowering triglycerides and are not recommended for this purpose because they contain very low amounts of polyunsaturated omega-3 fatty acids as well as trans fatty acids and saturated fat.

E ournal, ehz455, https://doi.org/10.1093/eurheartj/ehz455

Jellinger P, Handelsman Y, Rosenblit P, et al. Endocr Practice. 2020

Question: How are different drugs used to treat dyslipidemia?

omega-3 fish oil, combination therapy

Recommendations associated with this question:

Omega-3 Fish Oil

- **R63.** Prescription omega-3 oil, 2 to 4 g daily, should be used to treat hypertriglyceridemia (TG >200 mg/dL) **(Grade A, BEL 1)**.
- Dietary supplements are not FDA-approved for treatment of hypertriglyceridemia and generally are not recommended for this purpose **(Grade A, BEL 1)**.

Combination Therapy

- **R71.** Combination therapy of lipid-lowering agents should be considered when the LDL-C/non-HDL-C level is markedly increased and monotherapy (usually with a statin) does not achieve the therapeutic goal **(Grade A; BEL 1)**.

Abbreviations: apo, apolipoprotein; FDA, Food and Drug Administration; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides.

Jellinger P, Handelsman Y, Rosenblit P, et al. *Endocr Practice.* 2017;23(4):479-497.

ESC 2021 Guidelines!

4.6.3.2 Strategies to control plasma triglycerides

Although CVD risk is increased when fasting triglycerides are >1.7 mmol/L (150 mg/dL),[531] the use of drugs to lower triglyceride levels may only be considered in high-risk patients when triglycerides are >2.3 mmol/L (200 mg/dL) and triglycerides cannot be lowered by life-style measures. The available pharmacological interventions include statins, fibrates, PCSK9 inhibitors, and n-3 PUFAs (in particular icosa-pent ethyl in doses of 2—4 g/day; see *section 4.3.2.4.4*).

In high-risk (or above) patients with triglycerides >1.5 mmol/L (135 mg/dL) despite statin treat-ment and lifestyle measures, n-3 PUFAs (icosa-pent ethyl 2 × 2 g/day) may be considered in combination with a statin.[84]	IIb	B

There is price difference between the two approaches

AHA SCIENCE ADVISORY

Omega-3 Fatty Acids for the Management of Hypertriglyceridemia

A Science Advisory From the American Heart Association

https://www.ahajournals.org/journal/circ

Table 5. Summary Statements About the Effects of n-3 FA in Managing HTG

	Summary Statements
Triglycerides 200–499 mg/dL	≈20%–30% reduction in triglycerides and no LDL-C increase with 4 g/d prescription n-3 FA
Triglycerides ≥500 mg/dL	≥30% reduction in triglycerides with 4 g/d prescription n-3 FA, LDL-C increase with DHA-containing agents
Use with other lipid therapy	Safe and apparently additive triglyceride reduction with statin therapy; apparently safe with fibrates or niacin but more research needed to evaluate efficacy
Prescription n-3 FA agent	On the basis of available data, all prescription agents appear comparably effective, but head-to-head comparisons are lacking

DHA indicates docosahexaenoic acid; HTG, high triglycerides; LDL-C, low-density lipoprotein cholesterol; and n-3 FA, omega-3 fatty acid.

2020. We conclude that prescription n-3 FAs (EPA+DHA or EPA-only) at a dose of 4 g/d (>3 g/d total EPA+DHA) are an effective and safe option for reducing triglycerides as monotherapy or as an adjunct to other lipid-lowering agents.

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7.3.5. Omega-3 fatty acids

Omega-3 fatty acids have proven effective at reducing TGs by up to 45% when administered at pharmacological doses (2–4 g/day)

In addition to statins, fibrates and lifestyle modifications, there is some evidence that n−3 fatty acids may have utility in patients with high levels of plasma TG and low levels of HDL-C – with up to 25–30% dose-dependent decreases reported in fasting and post-prandial TGs [13, 138]. Recent evidence suggests that n-3 fatty acids significantly lower ASCVD risk in patients with elevated TG levels, despite the use of statins

Nasreen A. Sayed et al. Consensus clinical recommendations for the management of plasma lipid disorders in the middle East: 2021 update, Atherosclerosis 343 (2022) 28–50

Case 3

Mrs. RANA; 43 years-old overweight, smoker and **hypertensive**

Her BP is controlled using oral antihypertensive therapies

Currently presented with the below lipid profile :

- Total cholesterol: 206 mg/dl
- LDL: 64 mg/dl (GOAL LEVEL <100 mg/dL)
- HDL: 26 mg/dl
- Triglycerides: 580 mg/dl (GOAL LEVEL <150 mg/dL)*
- Non HDL: 180 mg/dl (GOAL LEVEL <85 mg/dL)

Suggested Management:

- Add Fibrate AND
- Add OMEGA-3

Isolated hypertriglyceridemia should be addressed to avoid risk of pancreatitis

AACE 2020- Dyslipidemia guidelines

To reduce the risk of **acute pancreatitis**, **a fibrate, prescription-grade omega-3 fatty acid (IPE, EPA, or EPA-DHA formulation),** and/or niacin should be given to all patients with severe hypertriglyceridemia (>500 mg/dL), with the goal of reducing triglycerides to well below 500 mg/dL

Alan J. Garber, Yehuda Handelsman,, George Grunberger et al. consensus statement by the American Association of Clinical Endocrinologists and American college of endocrinology on the comprehensive type 2 diabetes management algorithm – 2020 executive summary, ENDOCRINE PRACTICE Vol 26 No. 1 January 2020

How do PCSK9 inhibitors work?

in 2003, researchers found a genetic mutation that caused some people to develop very high LDL cholesterol levels and CVD at a young age. This laid the groundwork for understanding the PCSK9 pathway, and ultimately the medications now known as PCSK9 inhibitors.

Our liver makes PCSK9 protein, and this protein breaks down LDL receptors, which remove LDL cholesterol from our bloodstream. So the more PCSK9 protein in our bodies, the fewer LDL receptors in our liver, and the higher our LDL cholesterol levels. PCSK9 inhibitors are monoclonal antibodies that block the PCSK9 protein from working. As a result, levels of LDL receptors increase, and LDL cholesterol levels fall. PCSK9 inhibitors work via a pathway different from statin medications, and may be used together.

health.harvard.edu/blog/are-statins-enough-when-to-consider-pcsk9-inhibitors-2020060819986

Who could benefit from PCSK9 inhibitors?

A 2019 study published in JAMA Cardiology asked the question: does adding a PCSK9 inhibitor to a statin, in patients with stable CVD and LDL cholesterol levels above goal (greater than 70 mg/dl), prevent future CVD events?

For this study, patients fitting this profile were randomized to receive either the PCSK9 inhibitor evolocumab or a placebo.

All patients in the study continued to take their statin medication.

Researchers looked at the occurrence of CVD events (heart attack, stroke, or hospitalization for heart-related reasons) during the average two-year follow-up period.

They found a significant reduction in cardiac events in patients receiving the PCSK9 inhibitor plus a statin, compared to study subjects taking statin plus a placebo.

health.harvard.edu/blog/are-statins-enough-when-to-consider-pcsk9-inhibitors-202006819986

Side effects and cost of PCSK9 inhibitors

PCSK9 inhibitors are usually well tolerated. Some people experience flulike symptoms with fatigue, feeling cold, and back pain. Muscle aches and pains have also been reported. The most common side effect is pain at the injection site.

health.harvard.edu/blog/are-statins-enough-when-to-consider-pcsk9-inhibitors-2020060819986

Thank you