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Navigating Dyslipidemia: effective management and Cardiovascular protection

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Disclosure

This presentation is part of EFMS program, and all the content are evidence based and pure scientific

Presentation outlines

- Rationale for Cholesterol Screening
- Why To Treat early and reach to the control level Faster?
- Cardiovascular Disease and Dyslipidemia globally and locally
- AHA/ACC Guideline on the Management of Blood Cholesterol
- Plasma lipid management consensus in the Middle East
- EJADA guideline and Treatment Beyond LDL cholesterol
- Case discussion
- Take Home Messages

Rationale for Cholesterol Screening

- Abnormal lipid values are highly prevalent.
- Well documented relationship between total and LDL-C levels and CHD risk.
- Treatment decreases the risk of CVD events.
- Early knowledge of a lipid disorder creates the best opportunity for early intervention.

Why To Treat early and reach to the control level Faster?

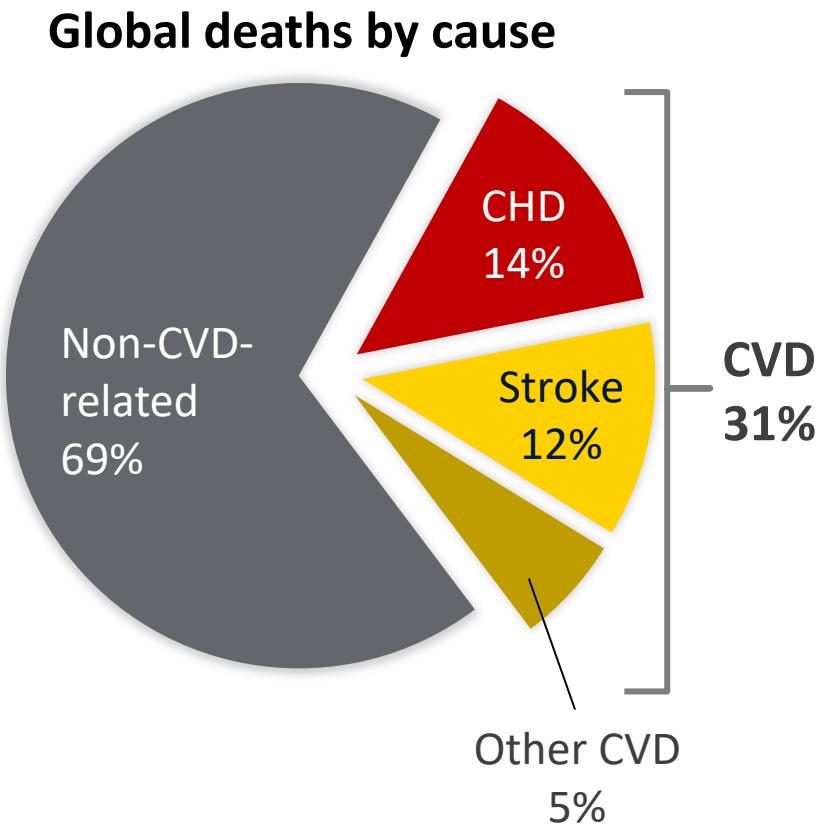
CVD remains the number 1 cause of death globally[1]

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
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

Dyslipidemia is characterized by imbalance of lipids such as cholesterol, low-density lipoprotein cholesterol, (LDL-C), triglycerides, and high-density lipoprotein (HDL)

*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.

merican Heart Association/American college of Cardiology

Circulation

Volume 140, Issue 11, 10 September 2019; Pages e596-e646
https://doi.org/10.1161/CIR.0000000000000678

ACC/AHA CLINICAL PRACTICE GUIDELINE

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Top 10 Take-Home Messages for the Primary Prevention of Cardiovascular Disease

- The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to **promote a healthy lifestyle throughout life.**
- **A team-based care approach is an effective strategy** for the prevention of cardiovascular disease. Clinicians should evaluate the social determinants of health that affect individuals to inform treatment decisions.
- Adults who are 40 to 75 years of age and are being evaluated for cardiovascular disease prevention should undergo 10-year atherosclerotic cardiovascular disease **(ASCVD) risk estimation**

Top 10 Take-Home Messages for the Primary Prevention of Cardiovascular Disease

- All adults should consume **a healthy diet** that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and **minimizes the intake of *trans* fats**, red meat and processed red meats, refined carbohydrates, and sweetened beverages.
- Adults should engage in at least 150 minutes per week of accumulated **moderate-intensity physical** activity or 75 minutes per week of vigorous-intensity physical activity.
- or adults with type 2 diabetes mellitus, lifestyle changes, such as improving dietary habits and achieving exercise recommendations, are crucial. If medication is indicated**, metformin is first-line therapy**,

Top 10 Take-Home Messages for the Primary Prevention of Cardiovascular Disease

- All adults should be assessed at every healthcare visit for **tobacco use**, and those who use tobacco should be assisted and strongly advised to quit.
- **Aspirin should** be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.
- **Statin therapy** is first-line treatment for primary prevention of ASCVD in patients with elevated low-density lipoprotein cholesterol levels (≥190 mg/dL),
- Nonpharmacological interventions are recommended for all adults with elevated **blood pressure or hypertension**.

4 major patient groups have been defined to determine statin treatment

Based on this large and consistent body of evidence, 4 major statin benefit groups were identified for whom the ASCVD risk reduction outweighs the risk of adverse events. Individuals

1) with clinical Atherosclerotic Cardiovascular Disease*,

2) primary elevations of LDL-C >190 mg/dL,

3) diabetes aged 40 to 75 years with LDL-C 70 to189 mg/dL and without clinical ASCVD

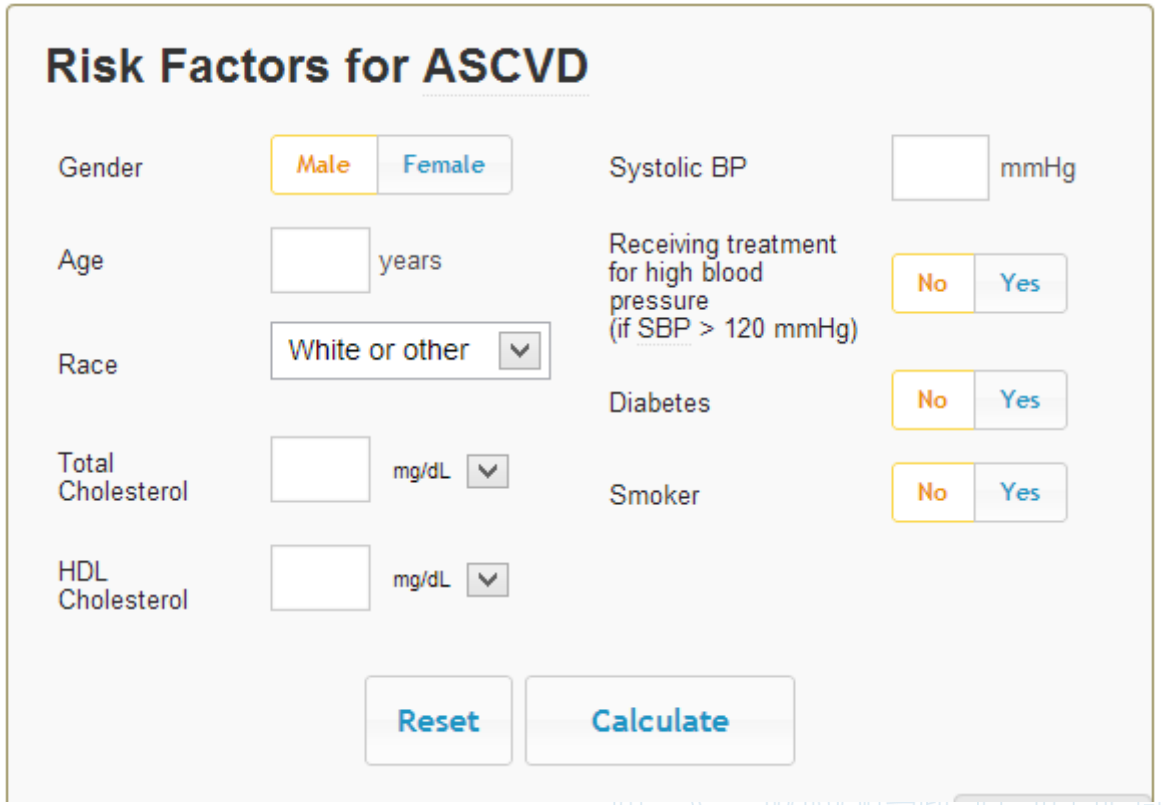
4) without clinical ASCVD or diabetes with LDL-C 70 to189 mg/dL and estimated 10-year ASCVD risk** >7.5%.

**clinical ASCVD is defined by the inclusion criteria for the secondary prevention statin RCTs i.e. acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin.*

***The estimated absolute 10-year risk of ASCVD i.e. nonfatal MI, CHD death, nonfatal and fatal stroke, should be estimated using the Pooled Cohort Equations*

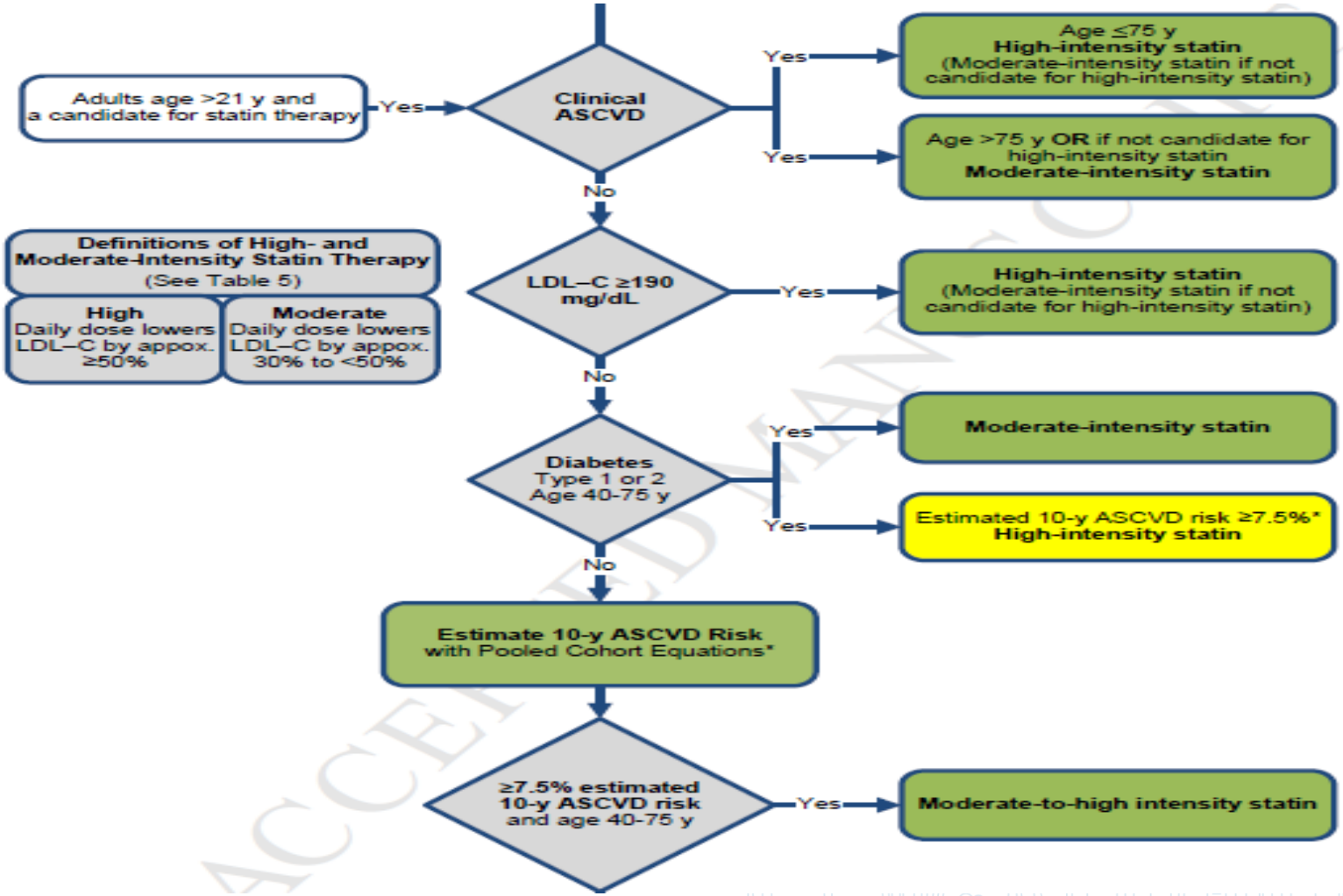
Pooled Cohort Risk Assessment Equations

Predicts 10-year risk for a first atherosclerotic cardiovascular disease (ASCVD) event



http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx

A treatment diagram has been created with 4 major patient groups and statin intensity groups



CASE

50-year-old female

Total cholesterol 180

HDL: 50

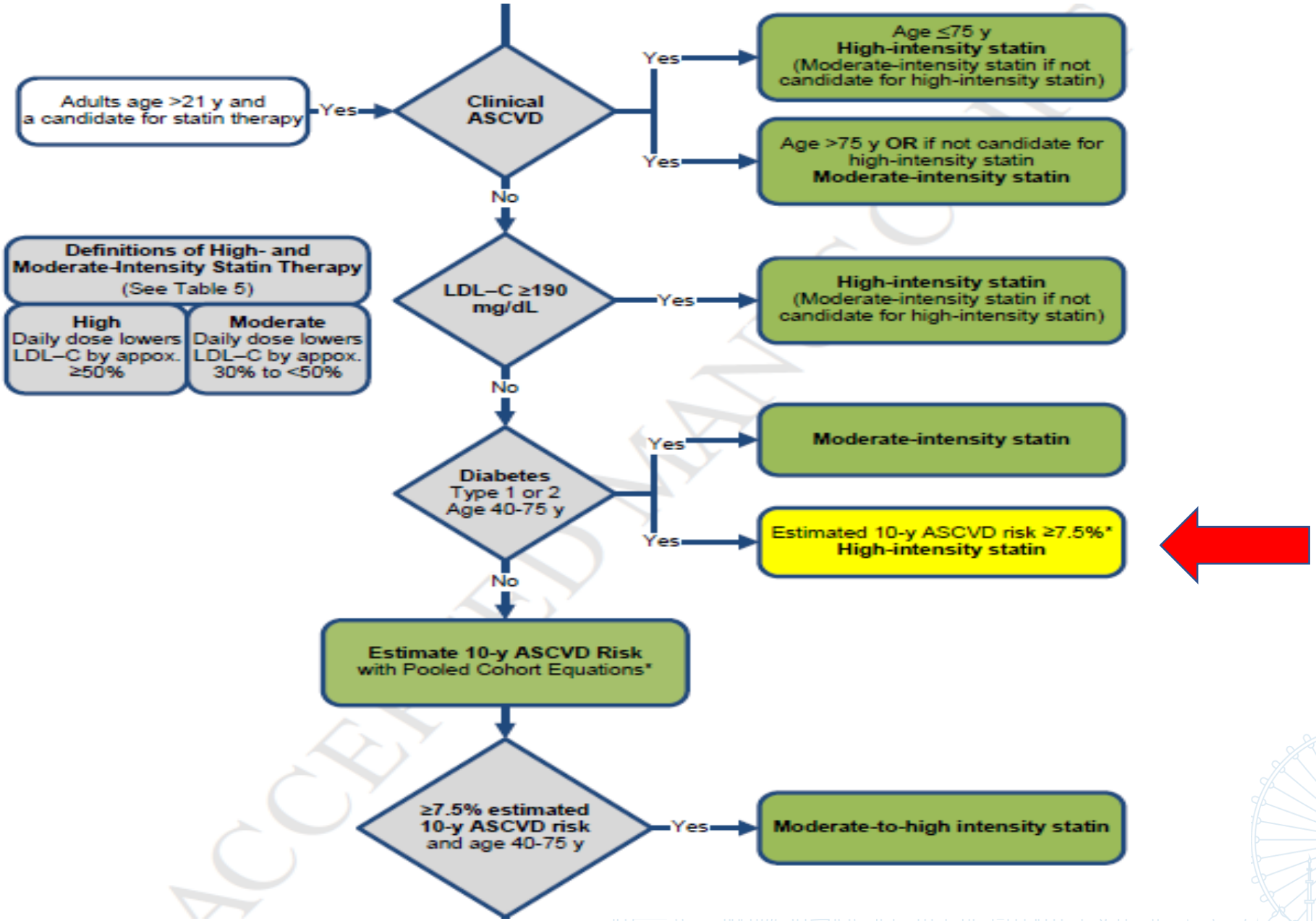
SBP: 130

taking anti-hypertension medication

+diabetic

+smoker

Calculated 10 yr. ASCVD: 9.8%


Adults age >21 y and a candidate for statin therapy
Yes
Clinical ASCVD
Yes
Age ≤75 y
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)
Yes
Age >75 y OR if not candidate for high-intensity statin
Moderate-intensity statin
No
Definitions of High- and Moderate-Intensity Statin Therapy
(See Table 5)
High
Daily dose lowers LDL–C by appox. ≥50%
Moderate
Daily dose lowers LDL–C by appox. 30% to <50%
LDL–C ≥190 mg/dL
Yes
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)
No
Diabetes
Type 1 or 2
Age 40-75 y
Yes
Moderate-intensity statin
Yes
Estimated 10-y ASCVD risk ≥7.5%*
High-intensity statin
No
Estimate 10-y ASCVD Risk
with Pooled Cohort Equations*
≥7.5% estimated 10-y ASCVD risk
and age 40-75 y
Yes
Moderate-to-high intensity statin

- high intensity statin

Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20** *(40)* **mg**	**Atorvastatin 10** *(20)* **mg** **Rosuvastatin** (*5*) **10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40** *(80)* **mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*

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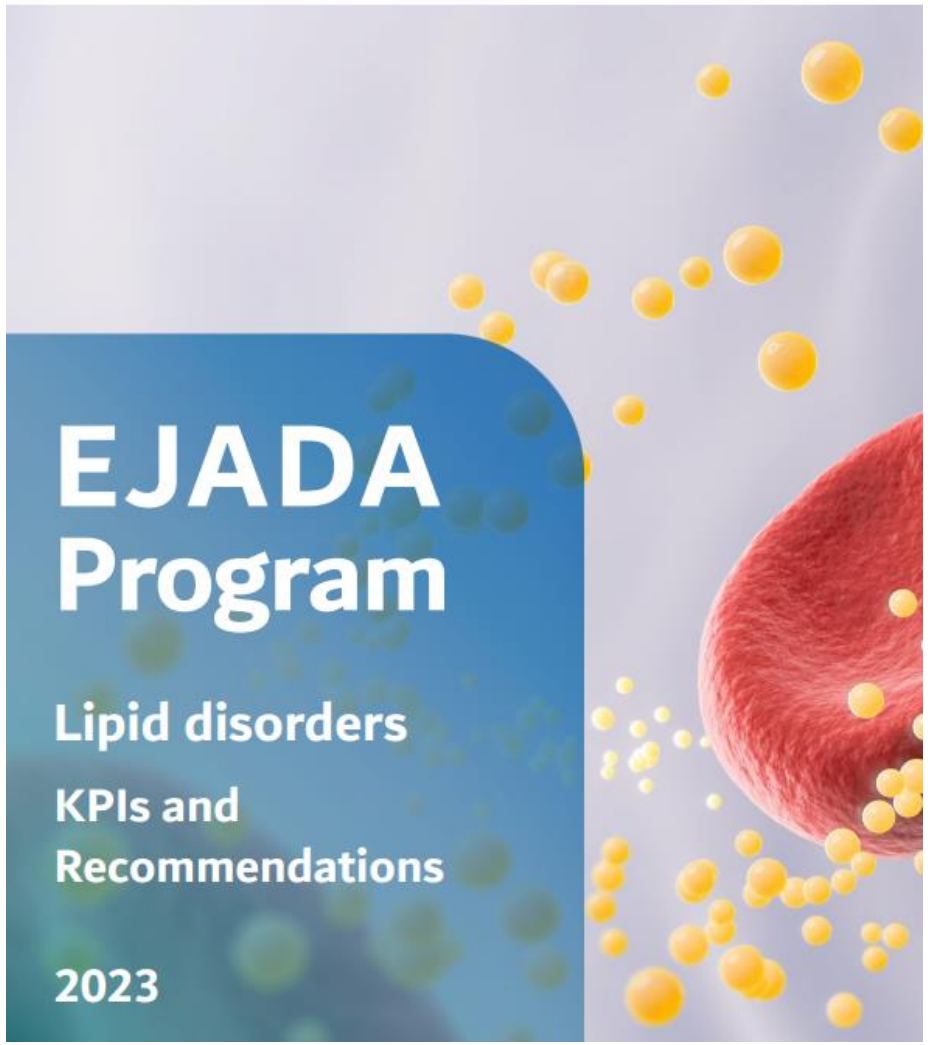
journal homepage: www.elsevier.com/locate/ijcard

Review

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

Nasreen Al Sayed [a,*], Khalid Al Waili [b], Fatheya Alawadi [c], Saeed Al-Ghamdi [d], Wael Al Mahmeed [e], Fahad Al-Nouri [f], Mona Al Rukhaimi [g], Khalid Al-Rasadi [h], Zuhier Awan [i], Mohamed Farghaly [j], Mohamed Hassanein [k], Hani Sabbour [l], Mohammad Zubaid [m], Philip Barter [n]



The Ejada KPIs are quality indicators and ratings for physicians, facilities and insurance companies based on information collected by DHA systems from providers, payers and patients.

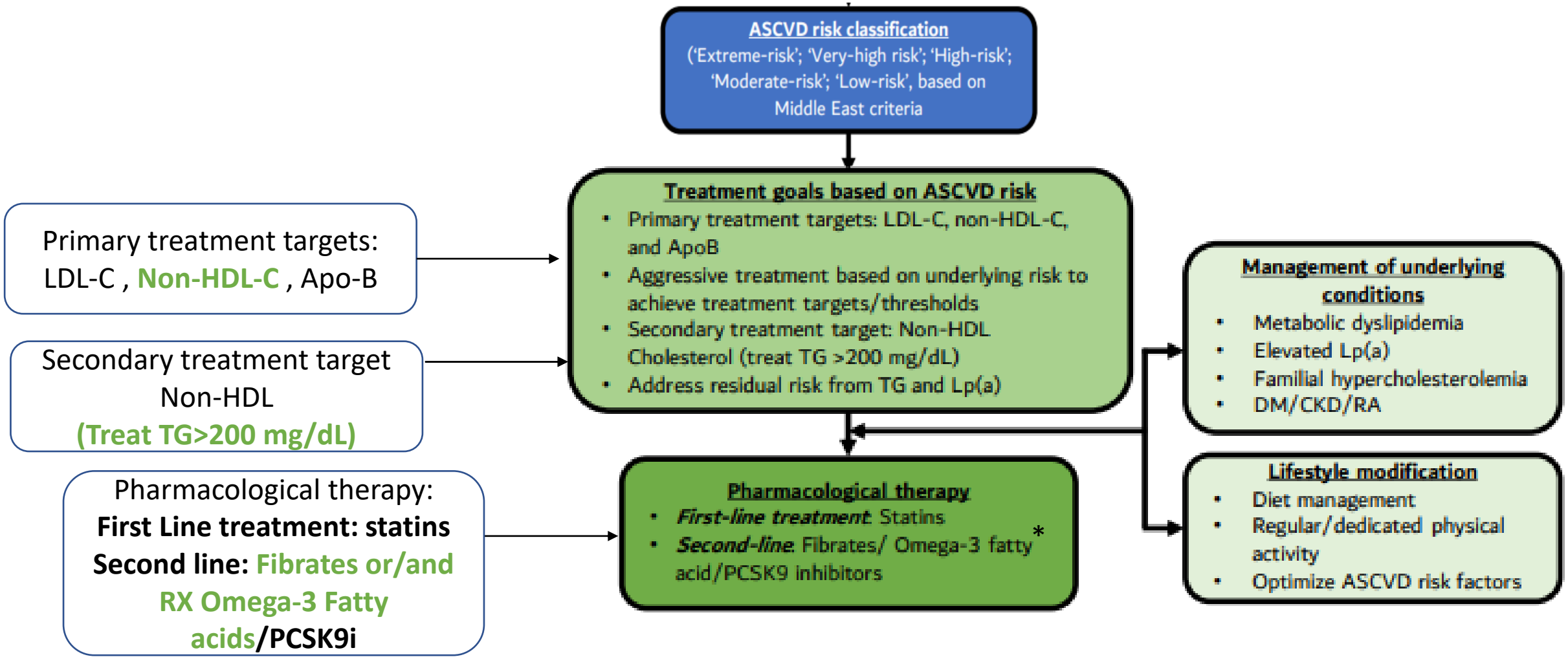
The dyslipidemia KPIs and recommendations are based on UAE and international guidelines. The KPIs are designed for healthcare practitioners and providers to follow international best practices in the management of dyslipidemia patients.

The dyslipidemia KPIs cover the following aspects of dyslipidemia management:

- Assessment of risk of dyslipidemia/atherosclerotic cardiovascular disease
- Pharmacological management of dyslipidemia
- Treatment for dyslipidemia in special clinical situations patients such as pregnant women
- Hospitalization and referrals of dyslipidemia patients

The KPIs and recommendations have been reviewed by leading experts in the country.

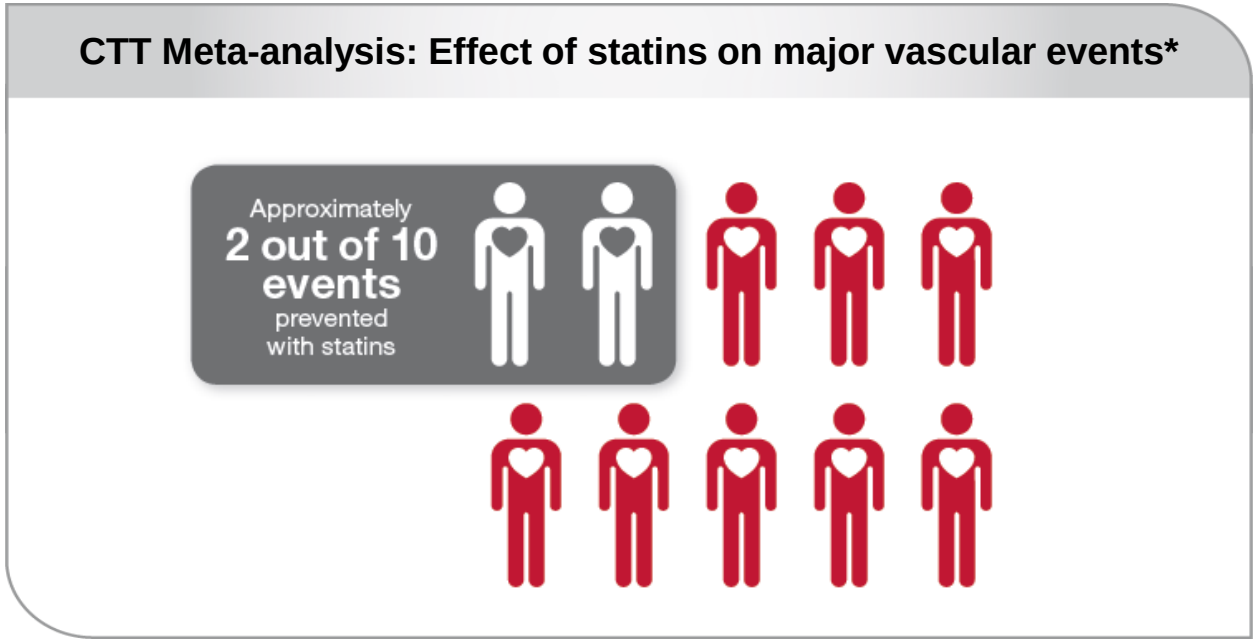
Assessment and management of patients with suspected dyslipidemia



ADAPTED & MODIFIED FROM: Consensus clinical recommendations for the management of plasma lipid disorders in the Middle East - 2021 update https://doi.org/10.1016/j.atherosclerosis.2021.11.022; A Modern Approach to Dyslipidemia. Endocrine Reviews, Volume 43, Issue 4, August 2022, Pages 611-653, https://doi.org/10.1210/endrev/bnab037

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)

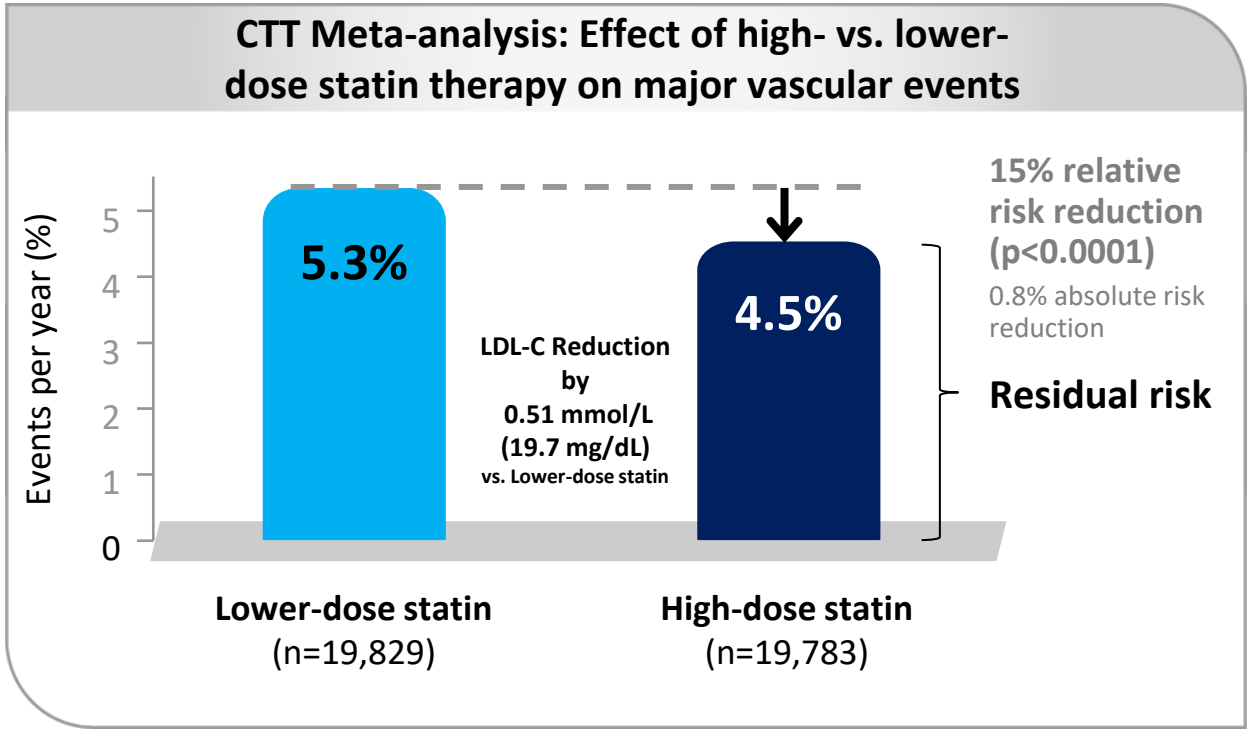


Remaining residual risk may be due to other modifiable and unmodifiable risk factors, including other lipid parameters, blood pressure, glycemic control, weight and genetic predisposition

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.

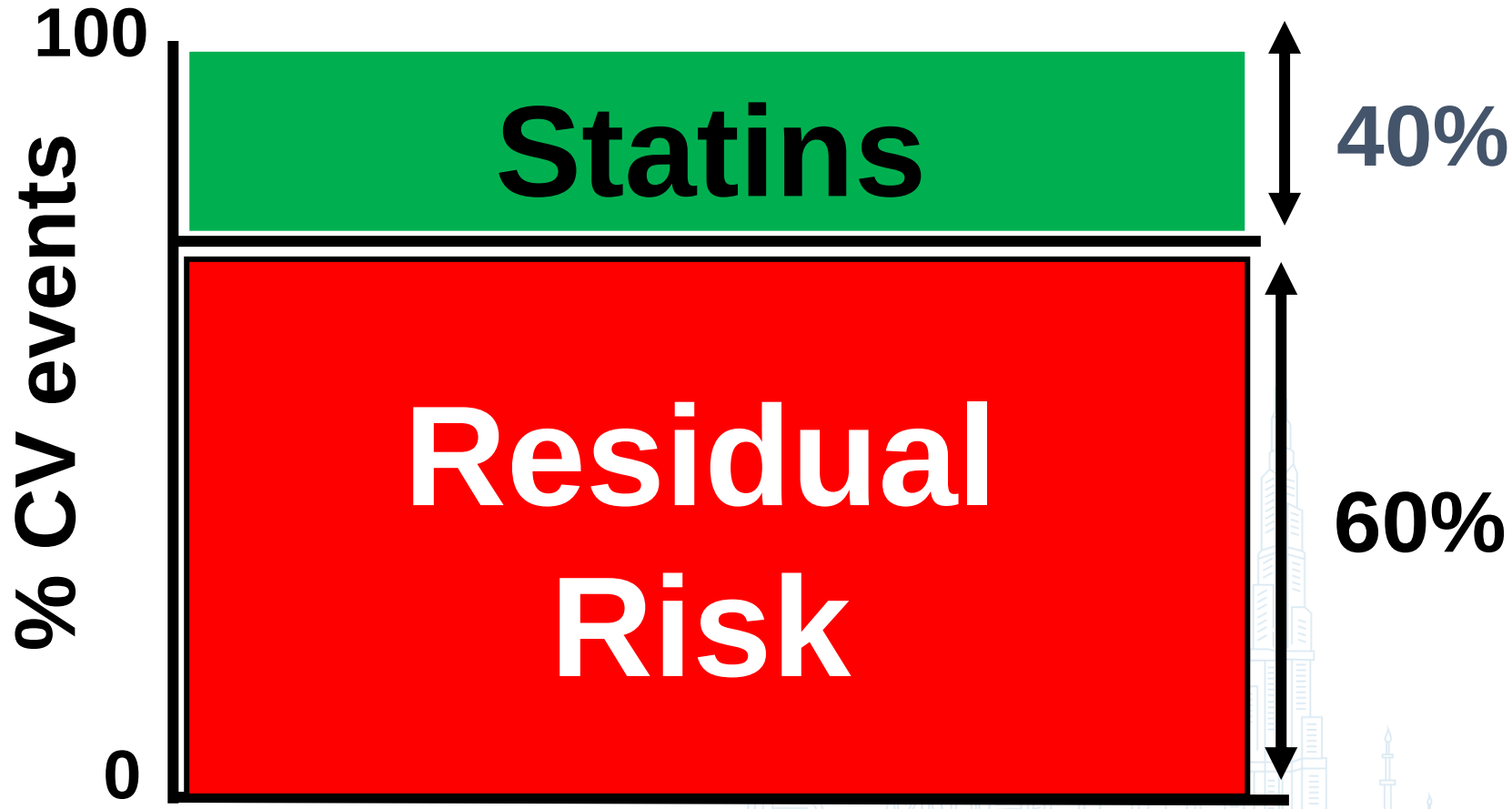
Increasing the statin dose can help but may not be enough[1]

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.

Treatment of CVD: Residual Risk



Case 1

Mr. Hassan; 40 years-old overweight, Smoker, **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: **???**

Guidelines on dyslipidemia

NATIONAL LIPID ASSOCIATION

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS
AACE
The Voice of Clinical Endocrinology

ESC
European Society of Cardiology

INTERNATIONAL ATHEROSCLEROSIS SOCIETY

Canadian Cardiovascular Society
Leadership. Knowledge. Community.

Guidelines with Targets

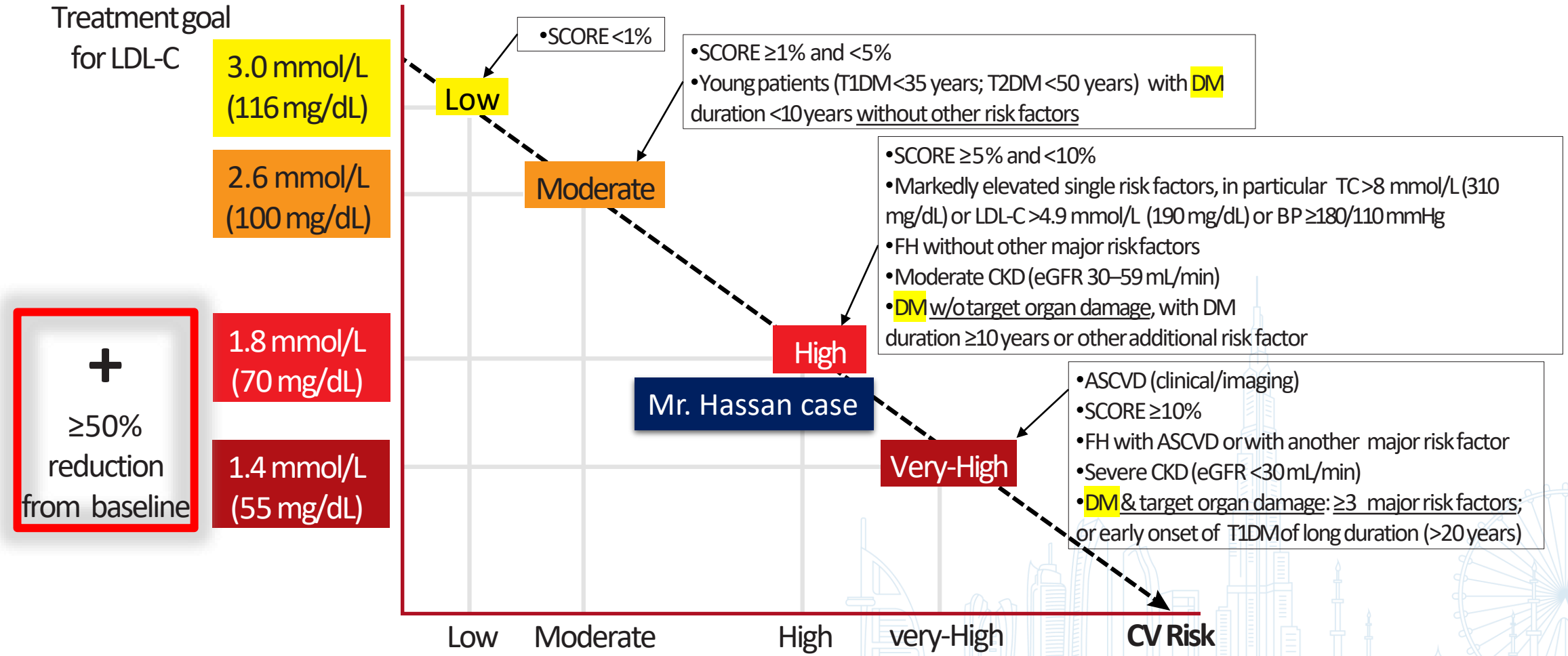
	Risk Group	AACE 2020	NLA	ESC/EAS 2019	CCS 2018	IAS
Secondary Prevention	**Extreme**	**LDL-C < 55 mg/dl NON-HDL-C < 80 mg/dl**				
	Very high	LDL-C < 70 mg/dl NON-HDL-C < 100 mg/dl	LDL-C < 70 mg/dl NON-HDL-C < 100 mg/dl	**LDL-C < 55 mg/dl (< 1.4 mmol/l) NON-HDL < 80 mg/dl (< 2.2 mmol/l)**	LDL-C < 2.0 mmol/l). Non-HDL < 2.6 mmol/l	LDL-C < 70 mg/dl NON-HDL-C < 100 mg/dl
	High	LDL-C < 100 mg/dl NON-HDL-C < 130 mg/dl	LDL-C < 100 mg/dl NON-HDL-C < 130 mg/dl	**LDL-C < 70 mg/dl (< 1.8 mmol/l) NON-HDL < 100 mg/dl (<2.6 mmol/l)**	LDL-C < 2.0 mmol/l). Non-HDL < 2.6 mmol/l	LDL-C < 100 mg/dl NON-HDL-C < 130 mg/dl
Primary Prevention	**Moderate**	LDL-C< 100 mg/dl NON-HDL-C < 130 mg/dl	LDL-C < 100 mg/dl NON-HDL-C < 130 mg/dl	**LDL-C < 100 mg/dl (< 2.6 mmol/l) NON-HDL < 130 mg/dl (< 3.4 mmol/l)**	LDL-C < 2.0 mmol/l). Non-HDL < 2.6 mmol/l	LDL-C < 100 mg/dl NON-HDL-C < 130 mg/dl
	Low	LDL-C< 130 mg/dl NON-HDL-C < 160 mg/dl	LDL-C < 100 mg/dl NON-HDL-C < 130 mg/dl	**LDL-C < 116 mg/dl (< 3 mmol/l)**		

Risk Category ESC/EAS 2019

NEW

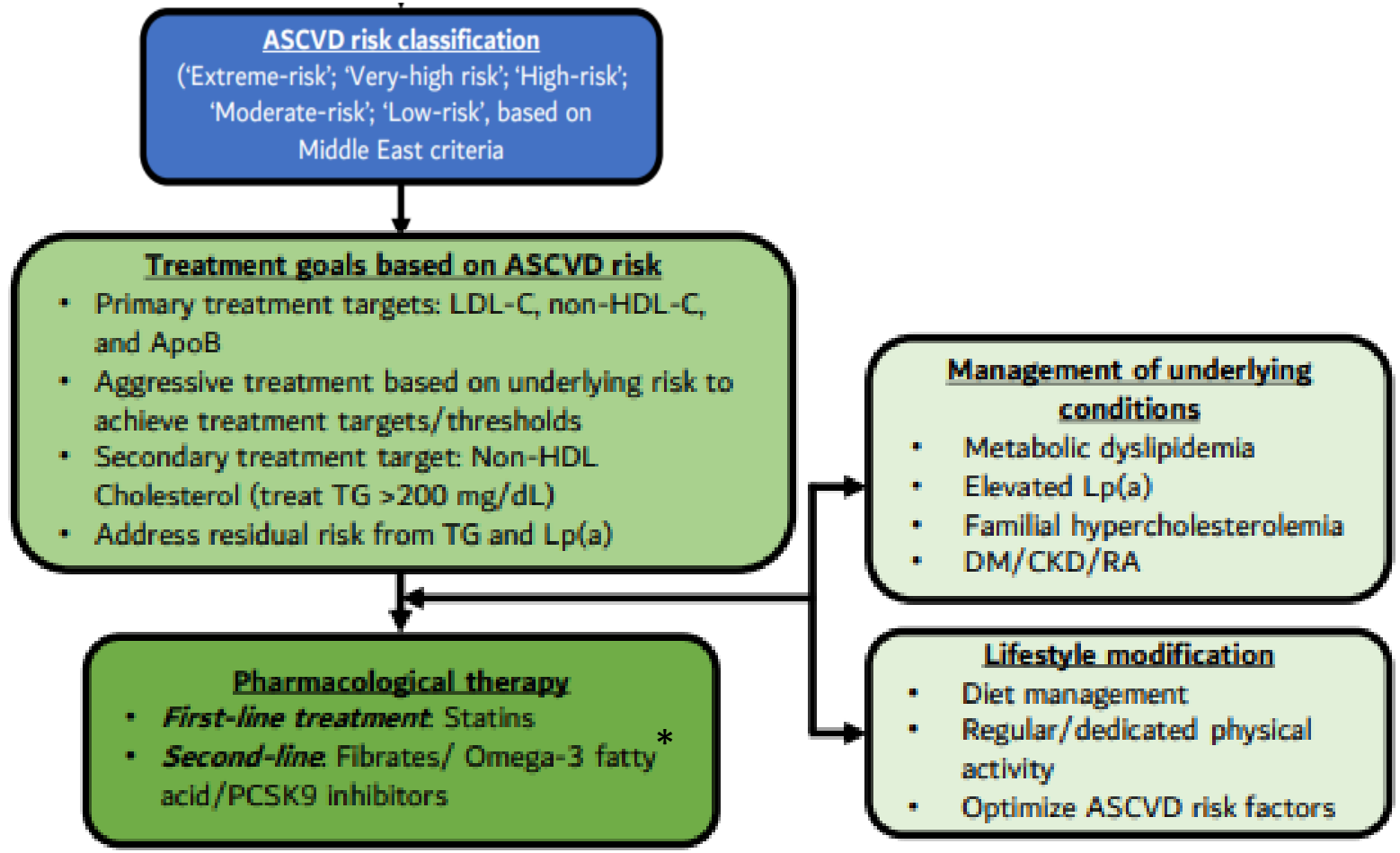
Risk category: CVD PREVENTION	LDL-c	Non-HDL-c	Apo B
Very High • ASCVD (clinical/imaging) • SCORE ≥10% • FH with ASCVD or with another major risk factor • Severe CKD (eGFR <30 mL/min) • DM & target organ damage: ≥3 major risk factors; or early onset of T1DM of long duration (>20 years)	<55mg/dL	<85mg/dL	<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



Assessment and management of patients with suspected dyslipidemia

Primary treatment targets:
LDL-C , **Non-HDL-C** , Apo-B



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His Blood glucose level is controlled using OAD therapy

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- Non HDL: 192 mg/dl (GOAL LEVEL <100 mg/dL)

Suggested Management: ???

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- Non HDL: 192 mg/dl (GOAL LEVEL <100 mg/dL)

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

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

- Increase Atorvastatin dose to 20mg daily, 1 tablet at night.and titrate up to the maximum tolerable dose of statin . **OR** Add Ezetimibe once daily..

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: ???

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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 • 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

Mr. ADAM case

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

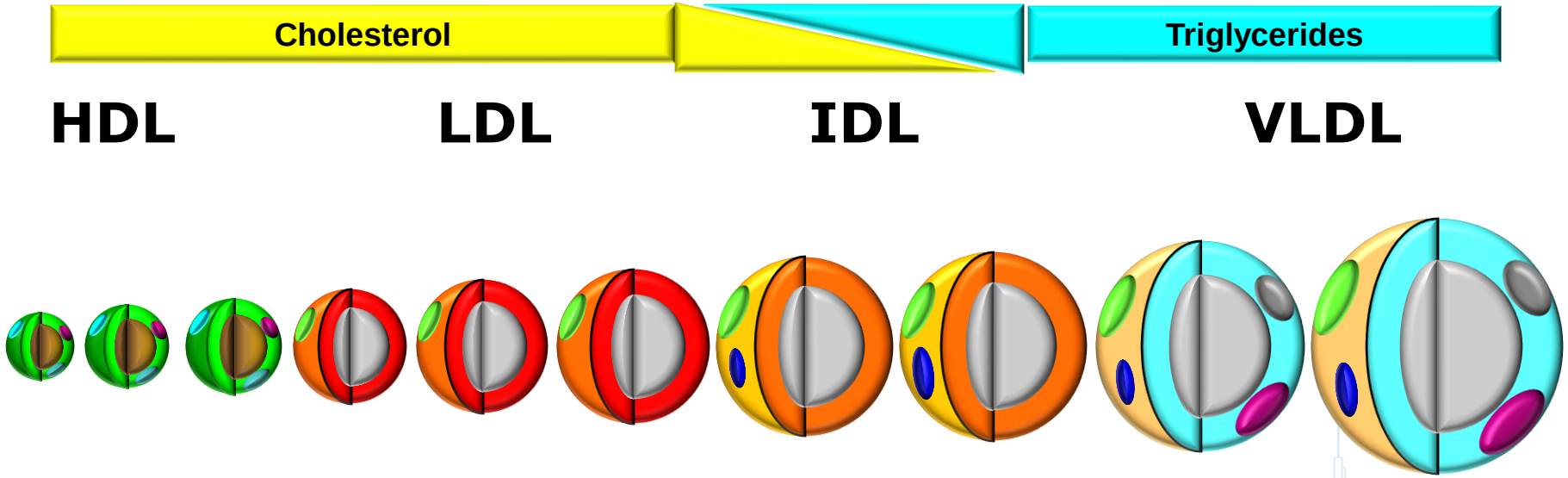
©ESC

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

©ESC

Non-HDL Cholesterol



Anti Atherogenic Lipoproteins

Atherogenic Lipoproteins

Non HDL-C: Total Cholesterol minus HDL-C

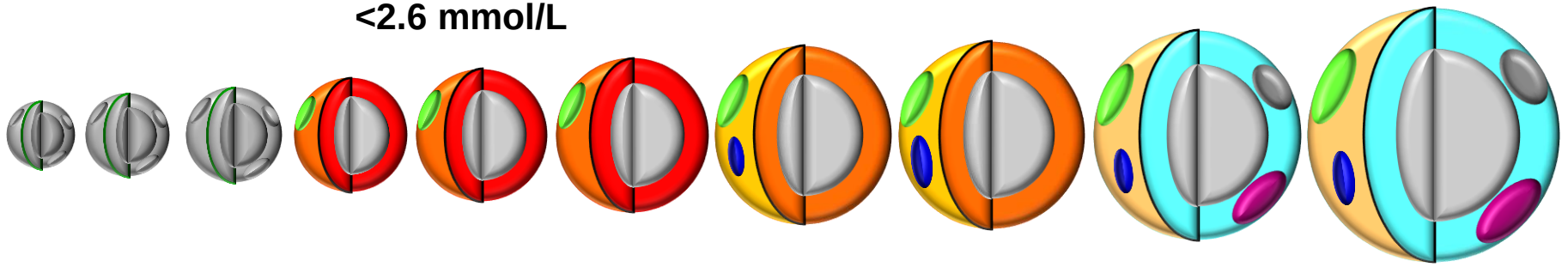
Very easy to calculate, No extra cost!

Click to edit Master title style

AT TARGET
<100 mg/dl
<2.6 mmol/L

=

Triglycerides



HDL LDL IDL VLDL

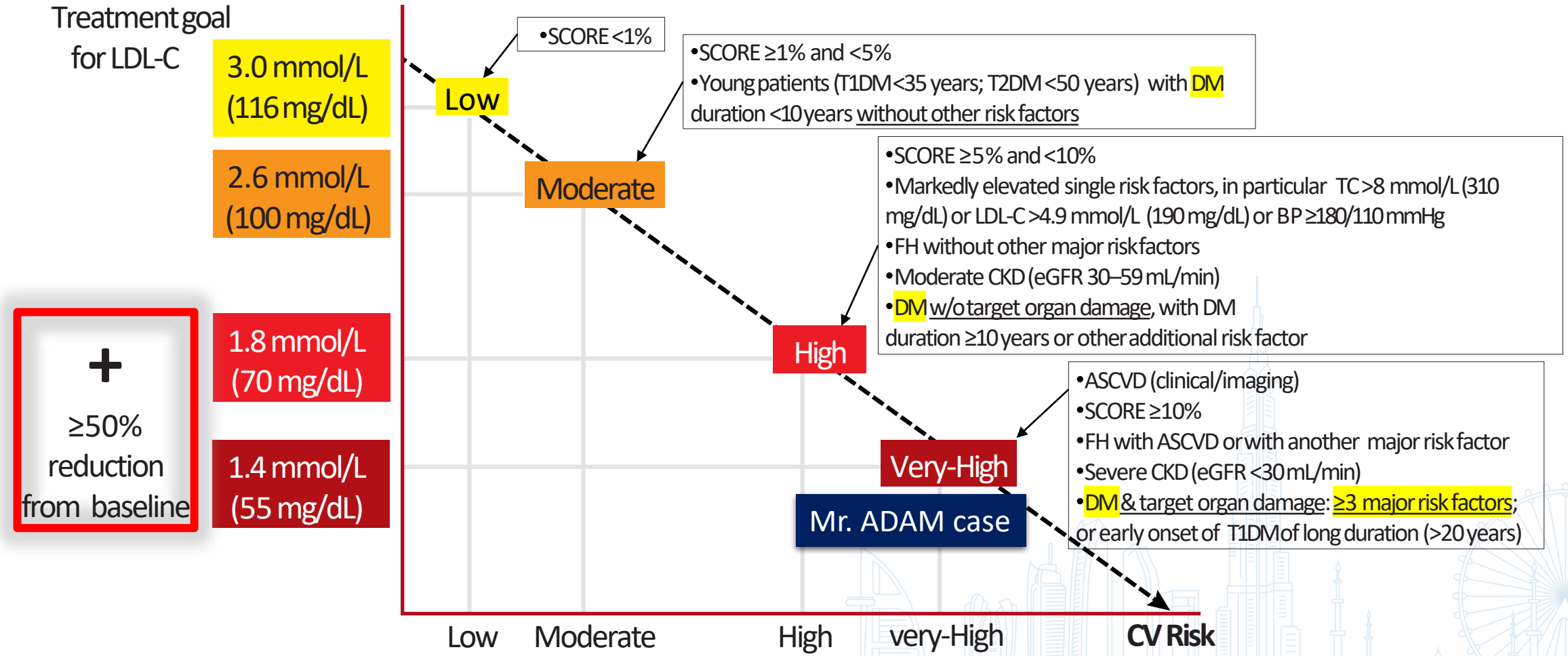
Anti Atherogenic Lipoproteins

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

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



Case 2

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

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

eGFR is 45 ml/min

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?

- Food Supplement Omega 3 OR
- Prescription Omega 3 Ethyl Ester (FDA approved)? OR
- Fenofibrate 145mg

Case 2

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

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- 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

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

Take Home Messages

- **In all individuals, emphasize a heart-healthy lifestyle across the life course**

- . In patients with clinical ASCVD, reduce low-density lipoprotein cholesterol (LDL-C) with high-intensity statin therapy or maximally tolerated statin therapy.
- In very high-risk ASCVD, use a LDL-C threshold of 55 mg/dL to consider addition of non statins to statin therapy.
- In patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL without calculating 10-year ASCVD risk
-

Take Home Messages

- In patients with clinical ASCVD who are judged to be very high risk and considered for PCSK9 inhibitor therapy, maximally tolerated LDL-C lowering therapy should include maximally tolerated statin therapy and ezetimibe
- Treat beyond LDL cholesterol
- Non-HDL cholesterol is the first target after LDL
- Pharmacological therapy: First Line treatment: statins Second line: Fibrates or/and RX Omega-3 Fatty acids/PCSK9i
-

THANK YOU