Management of Dyslipidemia

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Gaps in lipid management

Treatment of dyslipidemia should not be considered as an isolated process, but rather within the context of integrated prevention of cardiovascular disease in each patient

Global Burden of Cardiovascular disease

Nº 1 — Cause of death worldwide

17.9 Million — People die each year from CVD

31 % — % of death due to CVD worldwide

85 % — % of death due to heart attack and stroke

https://www.who.int/en/newsroom/factsheets/detail/cardiovascular-diseases-(cvds)

CVD: cardiovascular Disease, No :Number

Cardiovascular Disease and Dyslipidemia in the Gulf

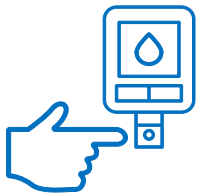
In the Gulf CVD is the most common cause of deaths accounting for up to **45% of all mortalities**[1]

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.

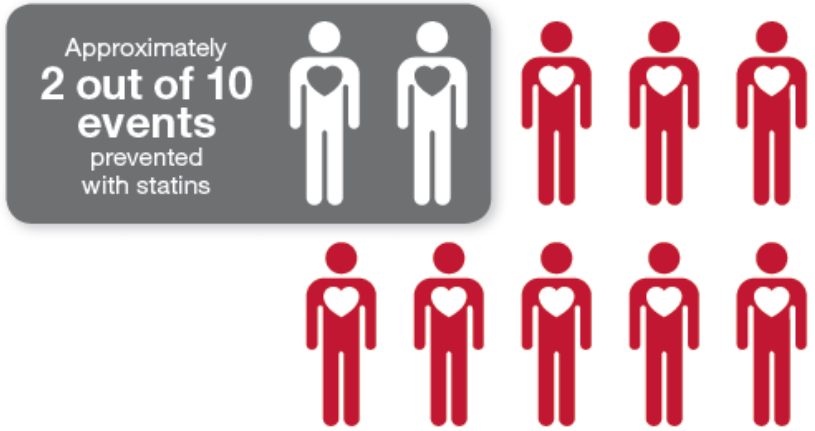
*CAD: Coronary Artery Disease

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)

CTT Meta-analysis: Effect of statins on major vascular events*

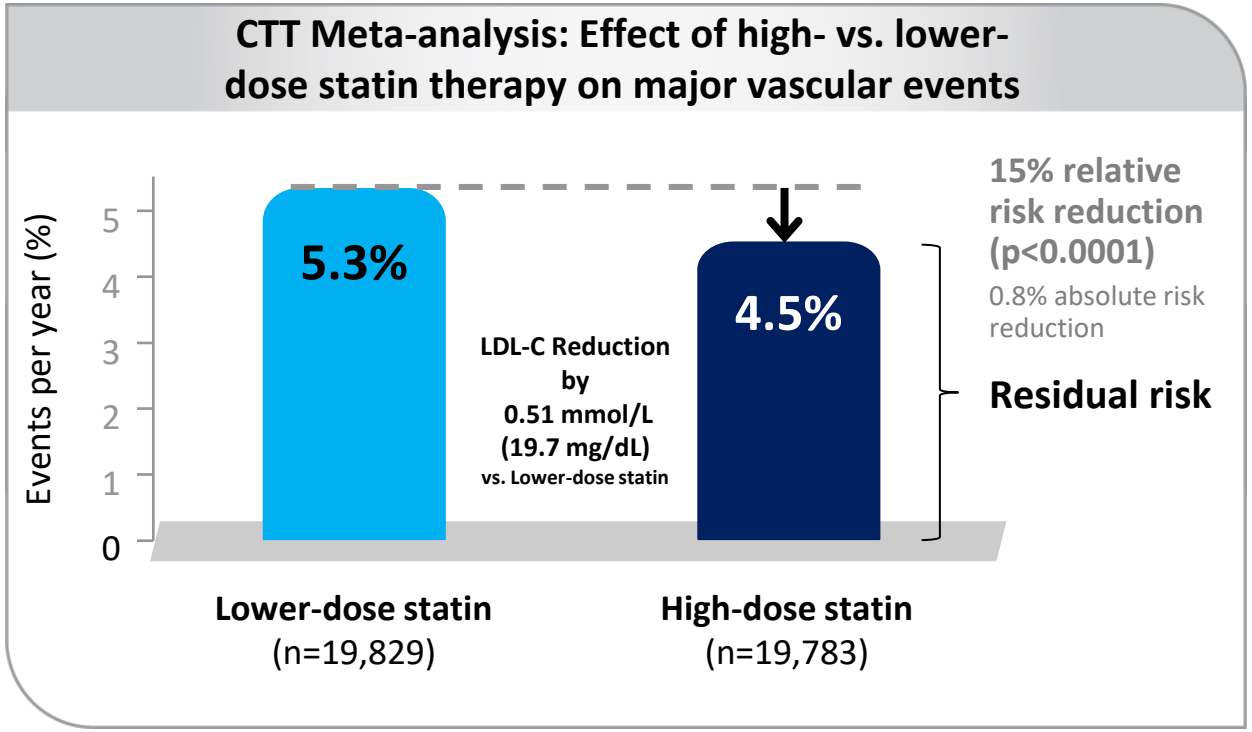


Remaining residual risk may be due to other modifiable and unmodifiable risk factors, including other lipid parameters, blood pressure, glycemic control, weight and genetic predisposition

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.

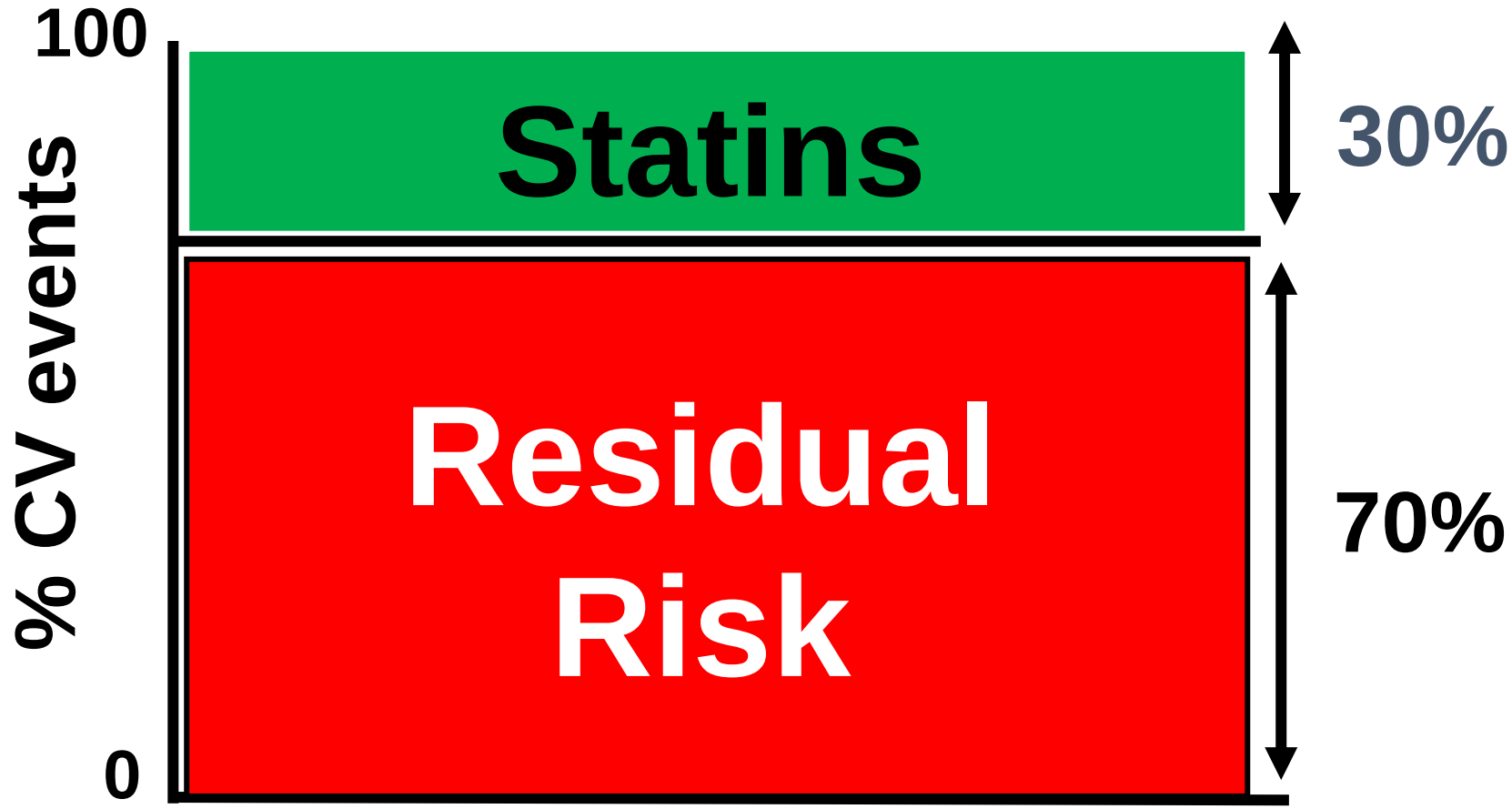
Increasing the statin dose can help but may not be enough[1]

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



Macrovascular residual risk in patients with type 2 diabetes

Study	Prevention type	Treatment	Diabetic population	Coronary risk reduction			Events not avoided (%)
				Overall population	Diabetic population (p)		
AFCAPS/TexCAPS[1]	I	Lovastatin	155	-37%	-43%	(NS)	56
Post CABG[2]	II	Lovastatin	116	-13%[a]	-47%	(NS)	53
CARE[3]	II	Pravastatin	586	-23%	-25%	(p=0.05)	75
LIPID[4]	II	Pravastatin	782	-24%	-19%	(NS)	81
PROSPER[5]	I/II	Pravastatin	623	-15%	+27%	(NS)	NA
ALLHAT-LLT[6]	I/II	Pravastatin	3,638	-12%	-11%	(NS)	89
4S[7]	II	Simvastatin	202	-32%	-55%	(p=0.002)	57
HPS[8]	II	Simvastatin	3,051	-24%	-18%	(p<0.0001)	82
HPS[8]	I	Simvastatin	2,912	-24%	-33%	(p<0.0003)	66
ASCOT-LLA[9]	I	Atorvastatin	2,352	-36%	-16%	(NS)	84
CARDS[10]	I	Atorvastatin	2,838	-37%	-37%	(p=0.001)	63
4D[11]	I/II	Atorvastatin	1,255	-18%	-18%	(p=0.03)	82
Meta-analysis[12]	I/II	Any	18,686	-21%	-23%	(p=0.001)	77

1. Heart Protection Study Collaborative Group. Lancet 2002;360:7-22. 2. Scandinavian Simvastatin Survival Study Group. Lancet 1994;344:1383-9. 3. Sever PS et al. Lancet 2003;361:1149-58. 4. Colhoun HM et al. Lancet 2004;364:685-96. 5. LaRosa JC et al. N Engl J Med. 2005;352:1425-35. 6. Shepherd J et al. Diabetes Care 2006;29:1220-6. 7. Wanner C et al. N Engl J Med. 2005;353:238-48. 8. Knopp RH et al. Diabetes Care 2006;29:1478-1485. 9. ALLHAT Collaborative Research Group. JAMA 2002;288:2998-3007. 10. Cholesterol Treatment Trialists' Collaboration. Lancet 2008;371:117-25.

Case 1

Mr. Hassan; 40 years-old **overweight**, **diabetic (type 2) for 10 years**

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

Guidelines with Targets

Risk Group	AACE 2020	NLA	ESC/EAS 2019	CCS 2018	IAS
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
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)**		

Secondary Prevention

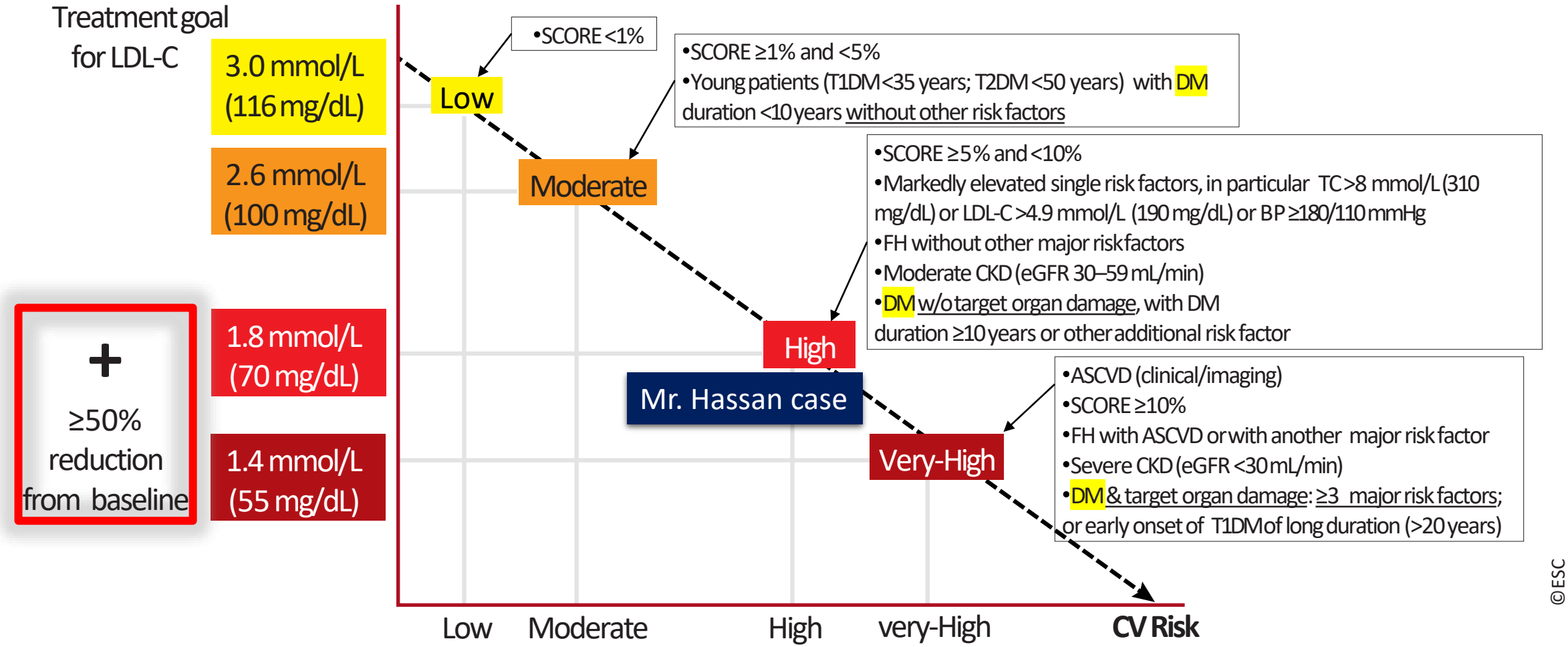
Primary Prevention

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



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Mr. Hassan; 40 years-old **overweight**, **diabetic (type 2) since 10 years**

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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 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
- HDL: 33 mg/dl
- Triglycerides: 280 mg/dl
- Non HDL: 125 mg/dl

Suggeted Management: **???**

Risk Category ESC/EAS 2019

NEW

Risk category: CVD PREVENTION	LDL-c	Non-HDL-c	Apo B
Very High Mr. ADAM case • 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
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Low • SCORE <1%	<115 mg/dl	<145 mg/dL	<90 mg/dL

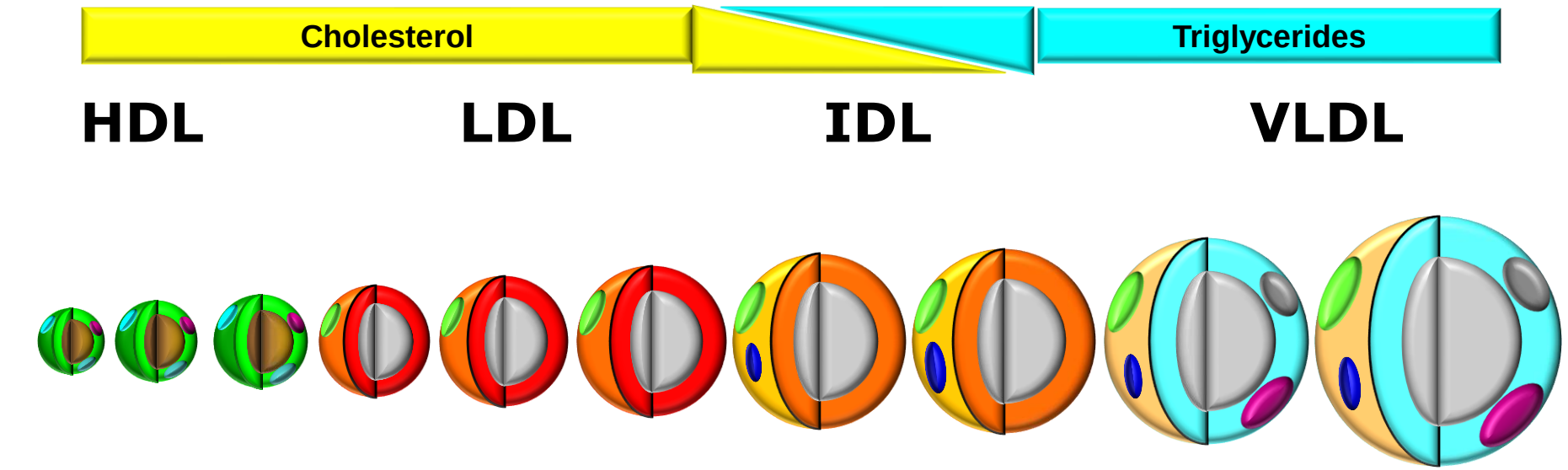
Recommendations for lipid analyses for cardiovascular disease risk estimation (1)

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

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-HDL Cholesterol



Anti Atherogenic Lipoproteins

Atherogenic Lipoproteins

Non HDL-C: Total Cholesterol minus HDL-C

Very easy to calculate, No extra cost!

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

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

Suggested Management: ???

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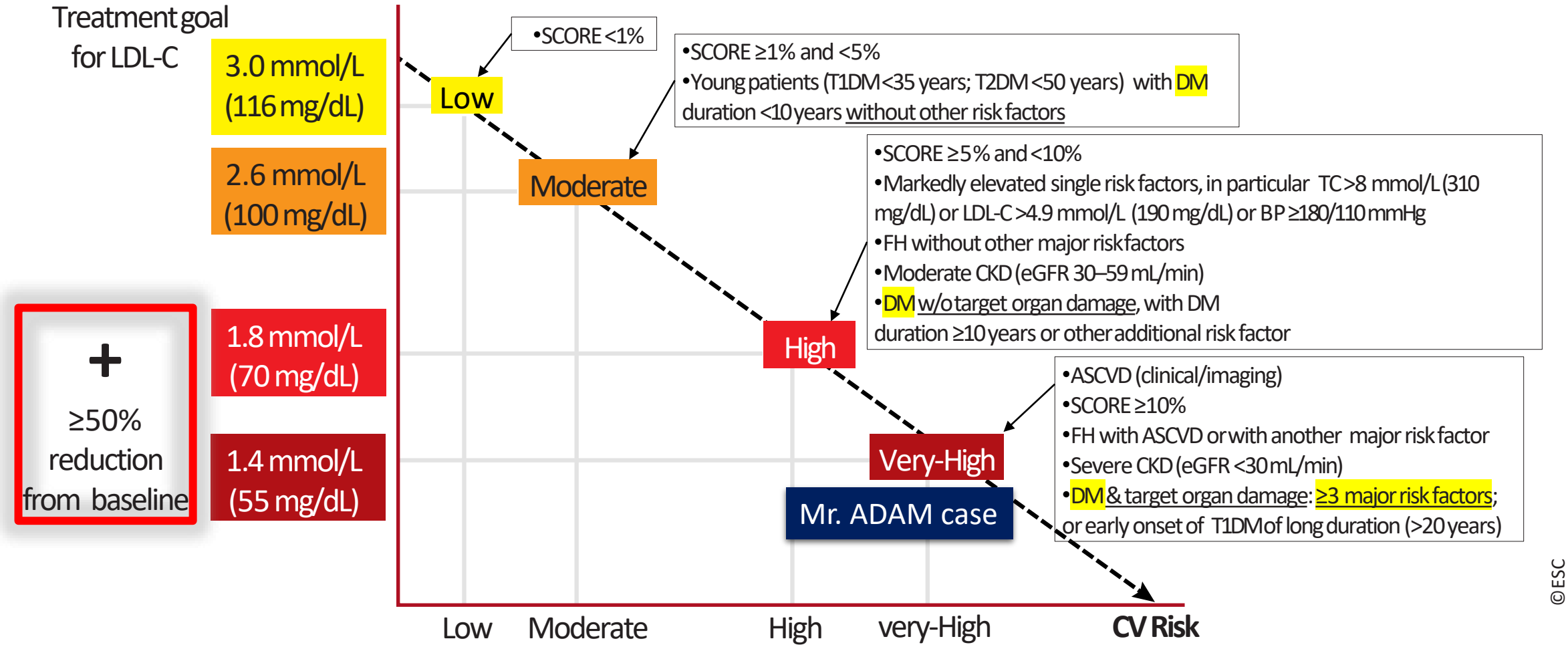

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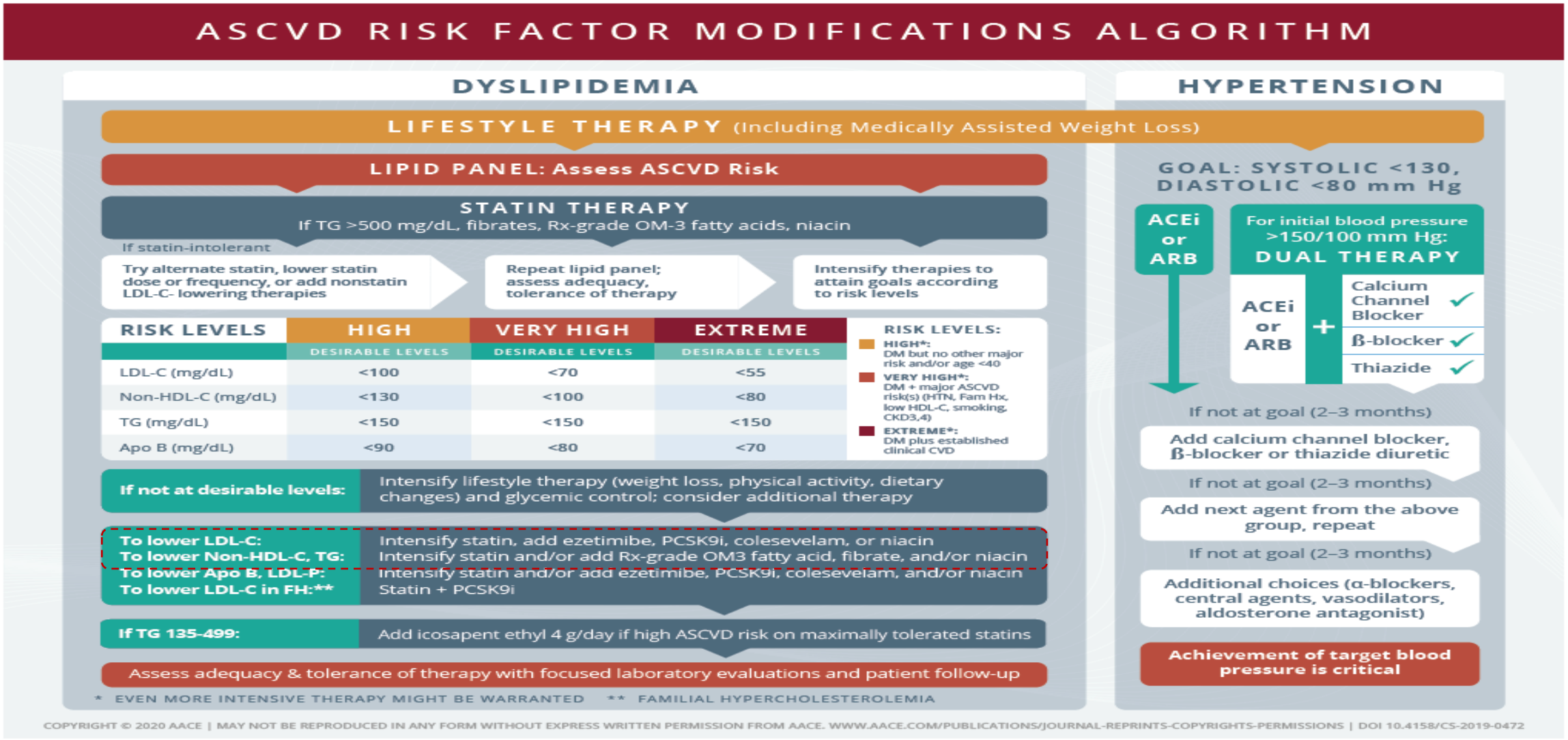
Suggested Management?

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

AACE 2020- Dyslipidemia Algorithm



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

Non HDL Cholesterol 2020 AACE Guidelines[1]

IV. ASCVD Risk Categories and Treatment Goals

Risk category	Risk factors[a] and 10-year risk	Treatment goals (mg/dL)			
		LDL-C	Non-HDL-C	Apo B	TG
Extreme risk	• Progressive ASCVD including unstable angina • Established clinical ASCVD plus diabetes or CKD ≥3 or HeFH • History of premature ASCVD (<55 years, male; <65 years, female)	<55	<80	<70	<150
Very high risk	• Established clinical ASCVD or recent hospitalization for ACS, carotid, or peripheral vascular disease, or 10-year risk >20% • Diabetes with ≥1 risk factor(s) • CKD ≥3 with albuminuria • HeFH	<70	<100	<80	<150
High risk	• ≥2 risk factors and 10-year risk 10-20% • Diabetes or CKD ≥3 with no other risk factors	<100	<130	<90	<150
Moderate risk	• <2 risk factors and 10-year risk <10%	<100	<130	<90	<150
Low risk	• No risk factors	<130	<160	NR	<150

[a]Major risk factors: advancing age, elevated non-HDL-C, elevated LDL-C, low HDL-C, diabetes, hypertension, CKD, cigarette smoking, family history of ASCVD.

Abbreviations: ACS = acute coronary syndrome; apo B = apolipoprotein B; ASCVD = atherosclerotic cardiovascular disease; CKD = chronic kidney disease; HDL-C = high-density lipoprotein cholesterol; HeFH = heterozygous familial hypercholesterolemia; LDL-C = low-density lipoprotein cholesterol; NR = not recommended; TG = triglyceride.

The Non-HDL-C (total cholesterol – HDL-C) should be calculated to assist risk stratification in individuals with moderately elevated **TG (200 to 500 mg/dL), Diabetes, and/or established ASCVD (Grade B, Bel 2)[2]**

1- AACE/ACE MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OF CARDIOVASCULAR DISEASE ALGORITHMDOI 10.4158/CS-2020-0490

2- Jellinger et al. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY GUIDELINES FOR MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OF CARDIOVASCULAR DISEASE, NDOCRINE PRACTICE Vol 23 (Suppl 2) April 2017

Recommendations for drug treatments of patients with hypertriglyceridemia (ESC 2019 Guidelines)

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

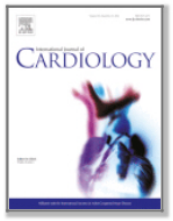
The n-3 (or omega-3) fatty acids [eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)] can be used at pharmacological doses to lower TGs. n-3 fatty acids (2—4 g/day) affect serum lipids and lipoproteins, in particular VLDL concentrations. The underlying mecha-

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

ELSEVIER

International Journal of Cardiology

Volume 225, 15 December 2016, Pages 268-283



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]

4.2. Primary treatment target: non-HDL-C levels

A number of authors and international guidelines report non-HDL-C levels (Box 3) to be more predictive of ASCVD risk than are LDL-C levels [4], [21], [22], [72]. Several international guidelines have recommended non-HDL-C as a co-primary treatment target [4], [21], [22]. Reductions in non-HDL-C levels by a range of lipid-lowering drug classes are associated with decreased ASCVD events, with an approximately 1:1 relationship between non–HDL-C decrease (%) and coronary heart disease reduction [73]. 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 [4]. Non-HDL-C levels may be of particular clinical relevance in Middle Eastern populations. We therefore recommend non-HDL-C as a primary treatment target, alongside LDL-C. Treatment goals should be non-HDL-C levels

Nasreen A. Sayed et al. Consensus clinical recommendations for the management of plasma lipid disorders in the middle East, int J. of Cardio, 15 Dec 2015

Consensus Clinical Recommendations for the management of Plasma lipid disorders in the Middle East

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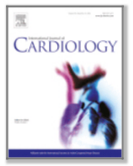

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Classifications of cholesterol and triglyceride levels [22].

Lipid levels (mmol/L)	Lipid levels (mg/dL)	Classification
Non–HDL-C		
3.4	<130	Desirable
3.4–4.1	130–159	Above desirable
4.1–4.9	160–189	Borderline high
4.9–5.7	190–219	High
>5.7	≥220	Very high
LDL-C		
<2.6	<100	Desirable
2.6–3.3	100–129	Above desirable
3.3–4.1	130–159	Borderline high
4.1–4.9	160–189	High
>4.9	≥190	Very high
HDL-C		
<1.0	<40 (males)	Low
<1.3	<50 (females)	Low
TG		
<1.7	<150	Normal
1.7–2.2	150–199	Borderline high
2.2–5.6	200–499	High
>5.6	≥500	Very high

should be aimed for, we recommend reducing elevated plasma TG levels as a secondary treatment goal. We recommend that a TG level > 200 mg/dL (2.3 mmol/L) warrants treatment.

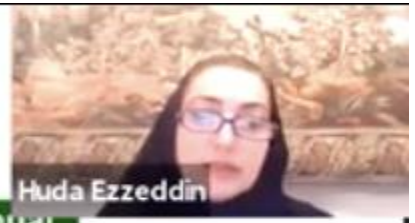
Nasreen A. Sayed et al. Consensus clinical recommendations for the management of plasma lipid disorders in the middle East, int J. of Cardio, 15 Dec 2015

ESC 2019 Recommendations

Fenofibrate + Statins combination

In primary prevention patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356]	IIb	B
In high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356]	IIb	C

Combination of statins with gemfibrozil enhances the risk of myopathy, and its association with statins must be avoided. There is no or very little increased risk for myopathy when combining statins with other fibrates, such as fenofibrate, bezafibrate, or ciprofibrate.[259,260]



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)	√		√

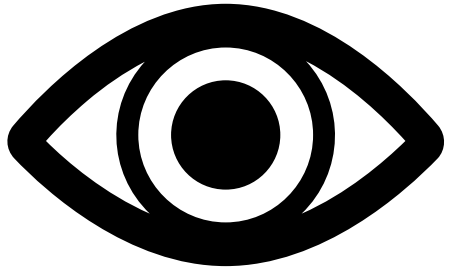
*Less stringent targets between 7.5% and 8.0% (58 to 64 mmol/mol) can be recommended for elderly, patients with short life expectancy, recurrent hypoglycaemia, and hypoglycaemia unawareness[5,6].
†The recommended frequency of HbA1c testing is 2-4 times per year[7].
‡The recommended frequency of lipids 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.

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

Consistent clinical evidence indicates that Fenofibrate is protective against the progression of Diabetic Retinopathy associated with T2DM[1]

Fenofibrate raised apolipoprotein A-I (apo A-I) levels
which is an independent protective factor in the development of DR[2,3]

Fenofibric acid (the active metabolite) prevents the apoptosis
of human retinal endothelial cells[4]



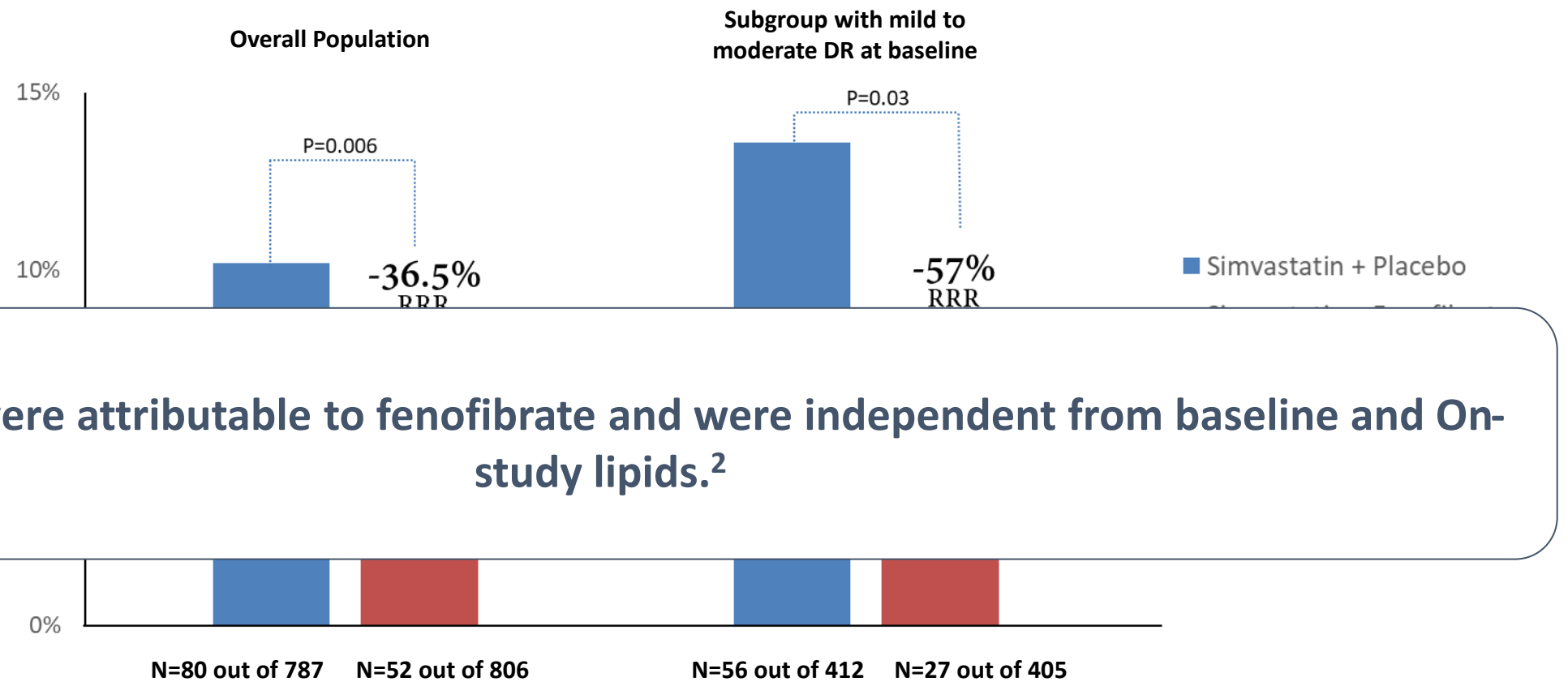
Fenofibric acid carries antioxidant and anti-inflammatory activity
which may lessen the adverse effects of oxidative and inflammatory stress implicated in the development of DR[4]

1. Noonan JE, Jenkins JA, Ma J-X et al. An update on the Molecular Actions of Fenofibrate and Its Clinical Effects on Diabetic Retinopathy and Other Microvascular End Points in Patients With Diabetes. Diabetes, 2013; 62: 3968-3975.
2. Sharma N, Ooi J-L, Ong J, Newman D. The use of fenofibrate in the management of patients with diabetic retinopathy: an evidence-based review. Australian Family Physician, 2015; 44 (6): 367-370.
3. Sasongko MB, Wong TY, Nguyen TT. et al, Serum Apolipoprotein AI and B Are Stronger Biomarkers of Diabetic Retinopathy Than Traditional Lipids. Diabetes Care, 2011; 34: 474-479.
4. Wong TY, Simo R, Mitchell P. Fenofibrate – A Potential Systemic Treatment for Diabetic Retinopathy? Am J Ophthalmol 2012; 154: 6–12.

Fenofibrate significantly reduced the progression of Diabetic Retinopathy (DR)

Progression of DR with Fenofibrate compared to placebo [1,2]

Results for all groups after 4 years



These results were attributable to fenofibrate and were independent from baseline and On-study lipids.[2]

Randomized study, including 10,251 participants with type 2 diabetes who were at high risk for cardiovascular disease to receive either intensive or standard treatment for glycemia and also for dyslipidemia (160 mg daily of fenofibrate + simvastatin) or for systolic blood pressure control (target <120 or <140 mmHg). A subgroup pf 2,856 patients was evaluated for the effects of these interventions at 4 years. Primary outcome was the composite endpoint of either the progression of DR by 3 or more steps on the Early Treatment Diabetic Retinopathy Study (ETDRS) Severity Scale or the development of proliferative DR necessitating laser photocoagulation or vitrectomy.

1. ACCORD Study Group; ACCORD Eye Study Group. Effects of Medical Therapies on Retinopathy Progression in Type 2 Diabetes. N Engl J Med. 2010; 363(3): 233-44.
2. ACCORD Eye Study Group. Effects of Medical Therapies on Retinopathy Progression in Type 2 Diabetes. The ACCORD Eye Study, Lipid Intervention. Clinical Study Report 1000289863. 15 May 2013

11. Microvascular Complications and Foot Care: *Standards of Medical Care in Diabetes—2020*

Diabetes Care 2020;43(Suppl. 1):S135–S151 | https://doi.org/10.2337/dc20-s011

Adjunctive Therapy

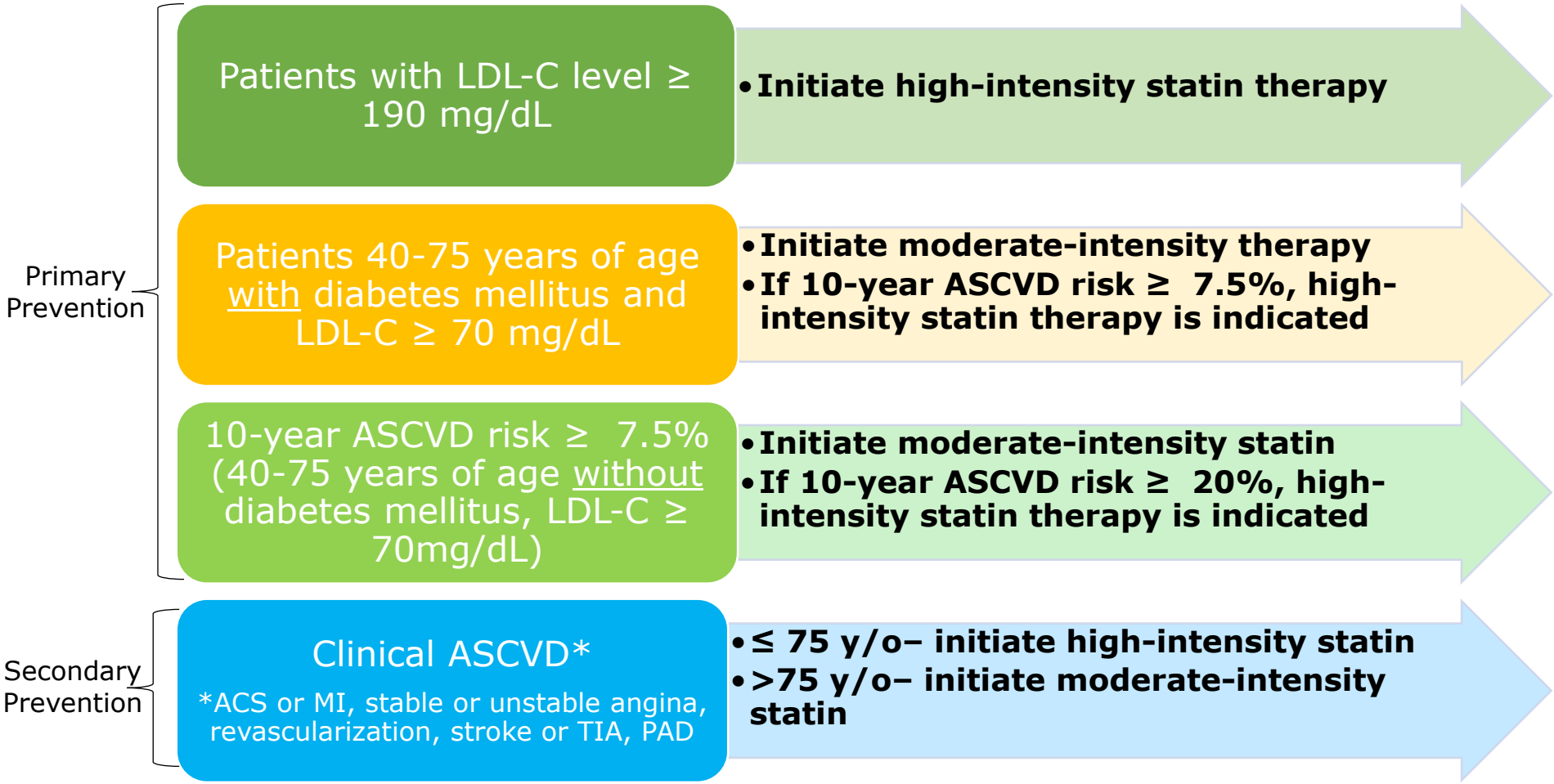
Lowering blood pressure has been shown to decrease retinopathy progression, although tight targets (systolic blood pressure <120 mmHg) do not impart additional benefit (106). ACE inhibitors and ARBs are both effective treatments in diabetic retinopathy (126). In patients with dyslipidemia, retinopathy progression may be slowed by the addition of fenofibrate, particularly with very mild nonproliferative diabetic retinopathy at baseline (104,127).

Diabetes Care 2020;43(Suppl. 1):S135–S151 | https://doi.org/10.2337/dc20-s011

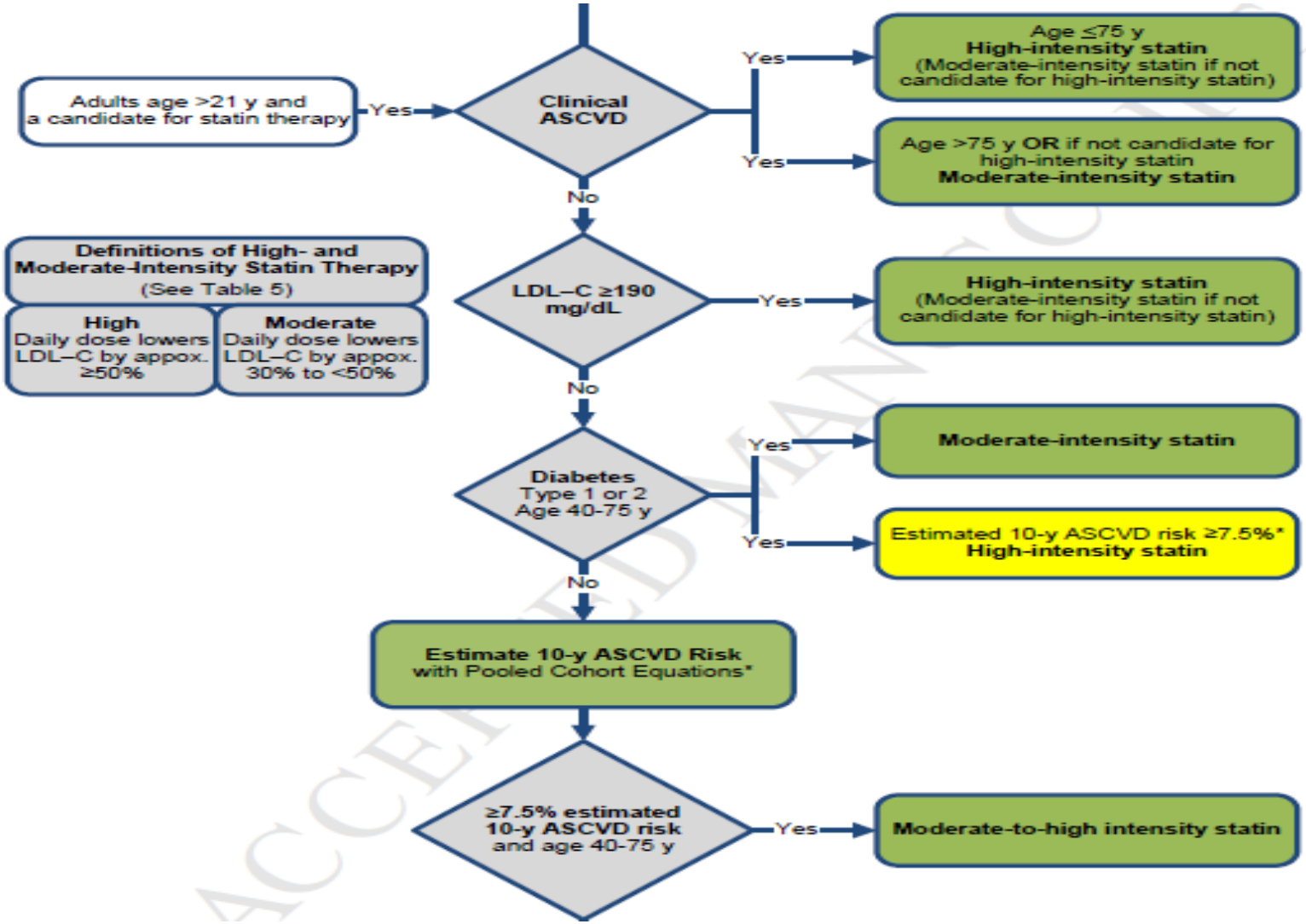
2018 AHA/ACC Guideline Recommendations[5]

The Management of Blood Cholesterol

Statin Benefit Groups[5]

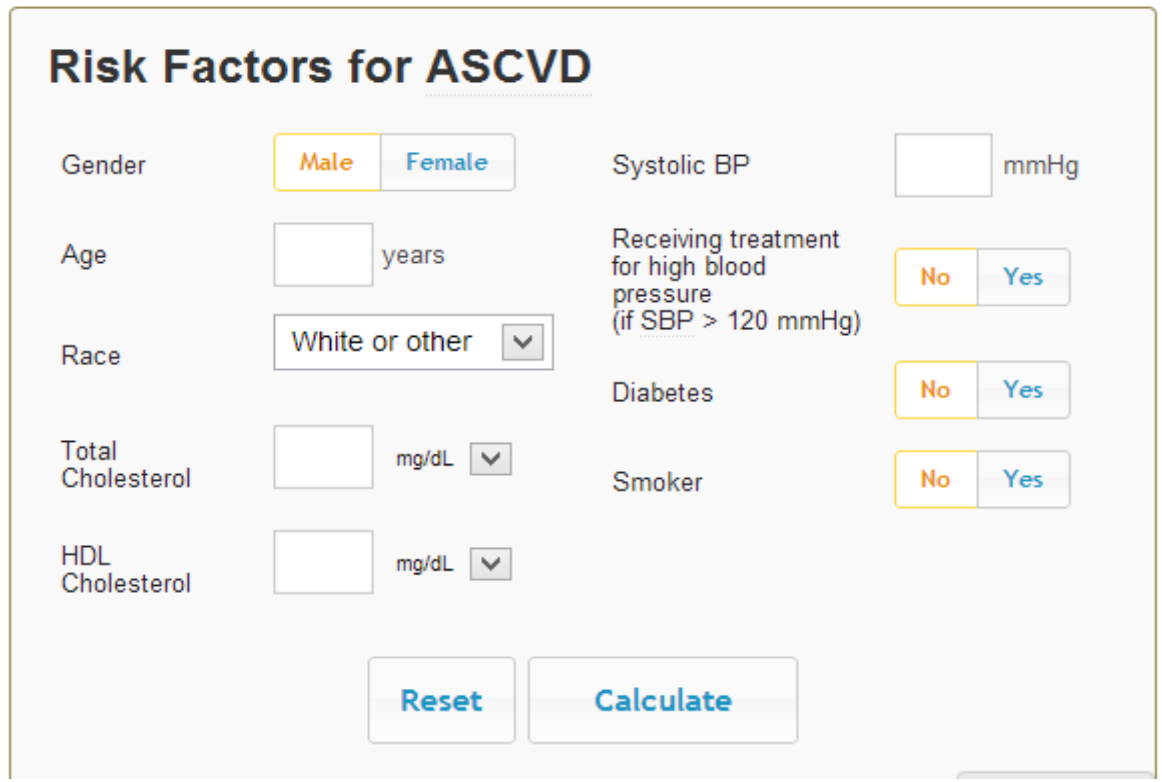


A treatment diagram has been created with 4 major patient groups and statin intensity groups



Pooled Cohort Risk Assessment Equations

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

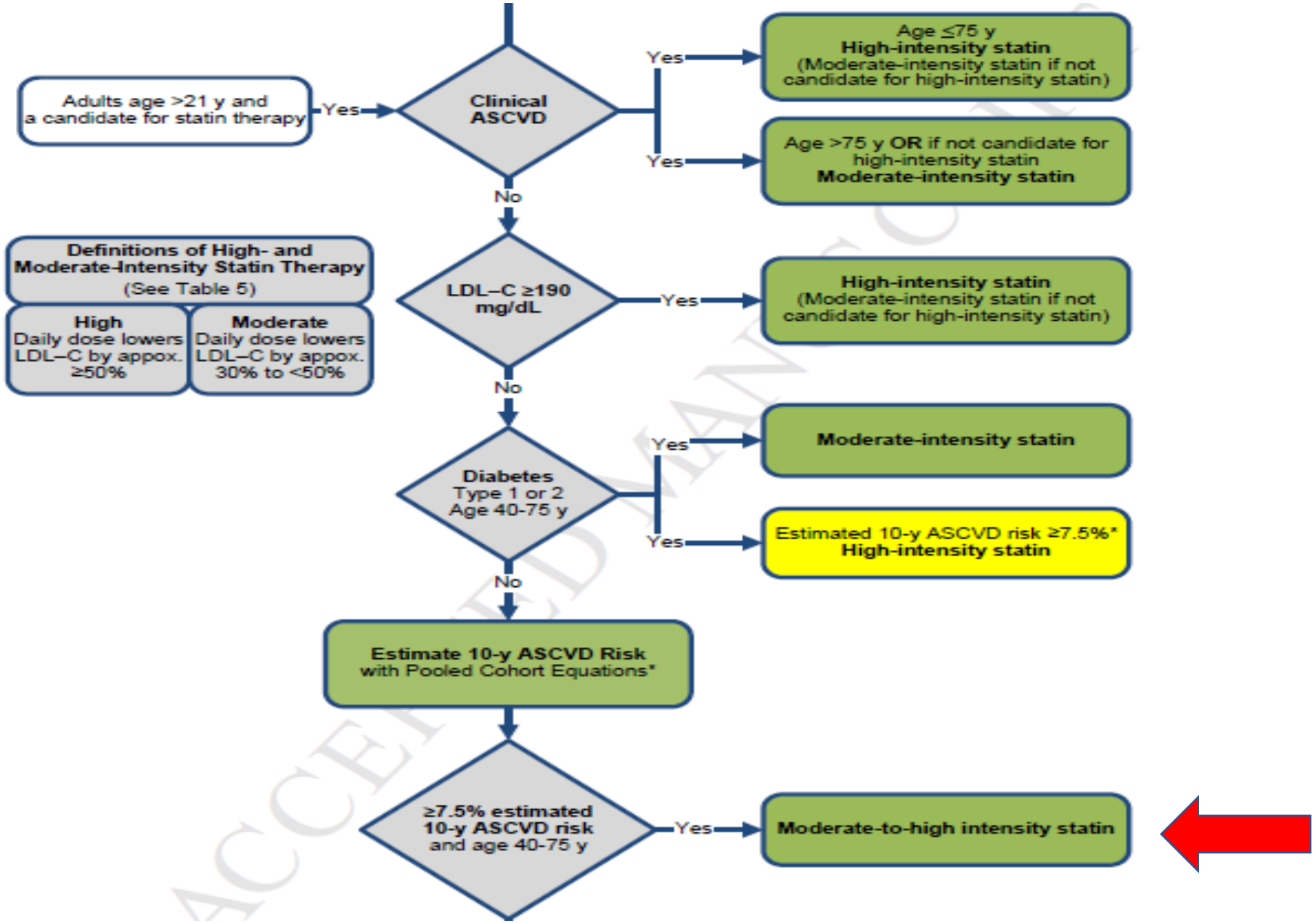


http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx

Case 1

62-year-old male

- Total cholesterol: 140
- Low HDL: 35
- SBP: 130 mmHg
- Not taking anti-hypertensive medications
- Non-diabetic
- Non-smoker
- Calculated 10 yr. risk of ASCVD : 9.1%


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

- Moderate to high intensity statin

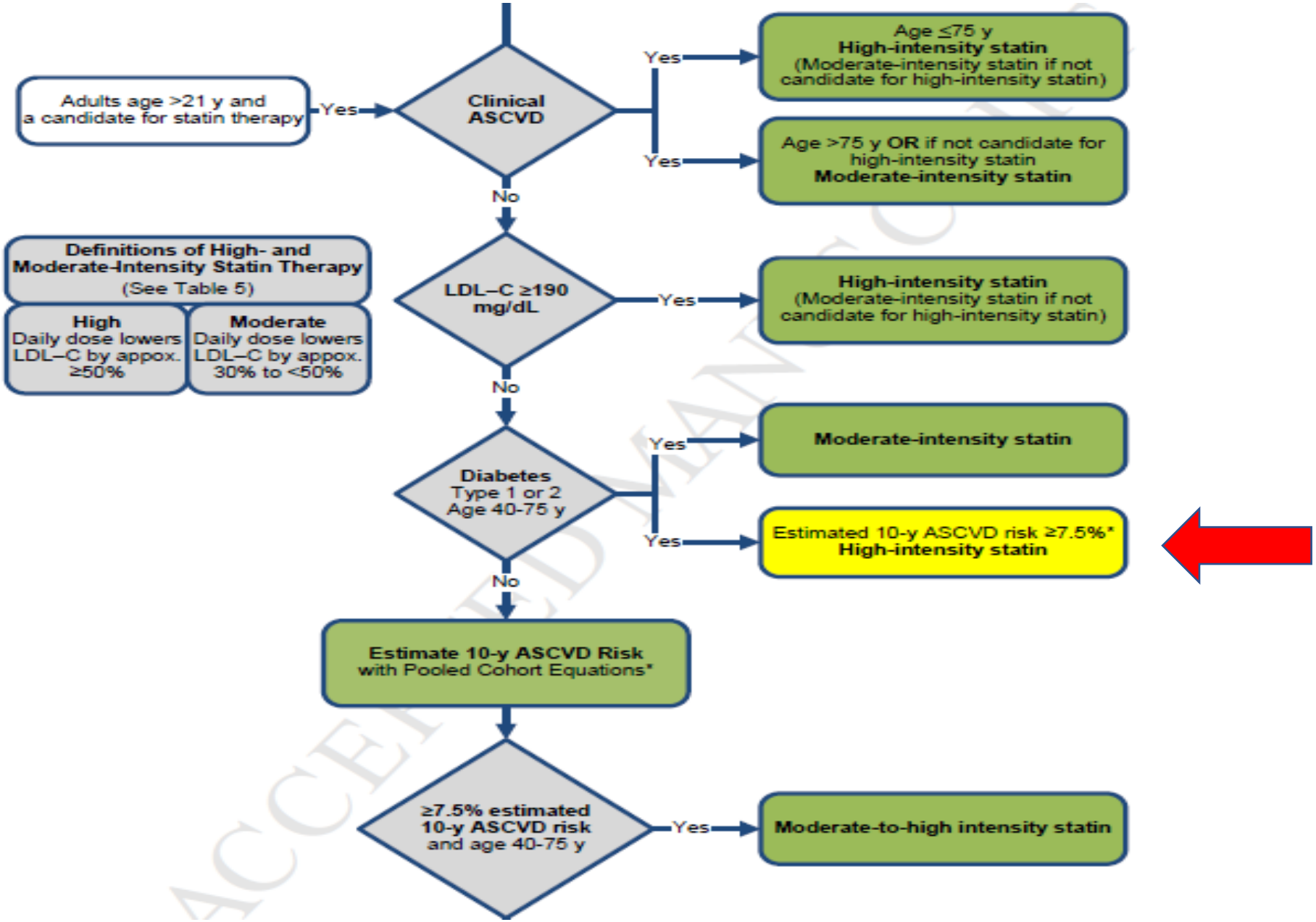
Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

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*

Case 2

50-year-old white female

- Total cholesterol 180
- HDL: 50
- SBP: 130
- taking anti-hTN meds
- +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)
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Age >75 y OR if not candidate for high-intensity statin
Moderate-intensity statin
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(See Table 5)
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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)*

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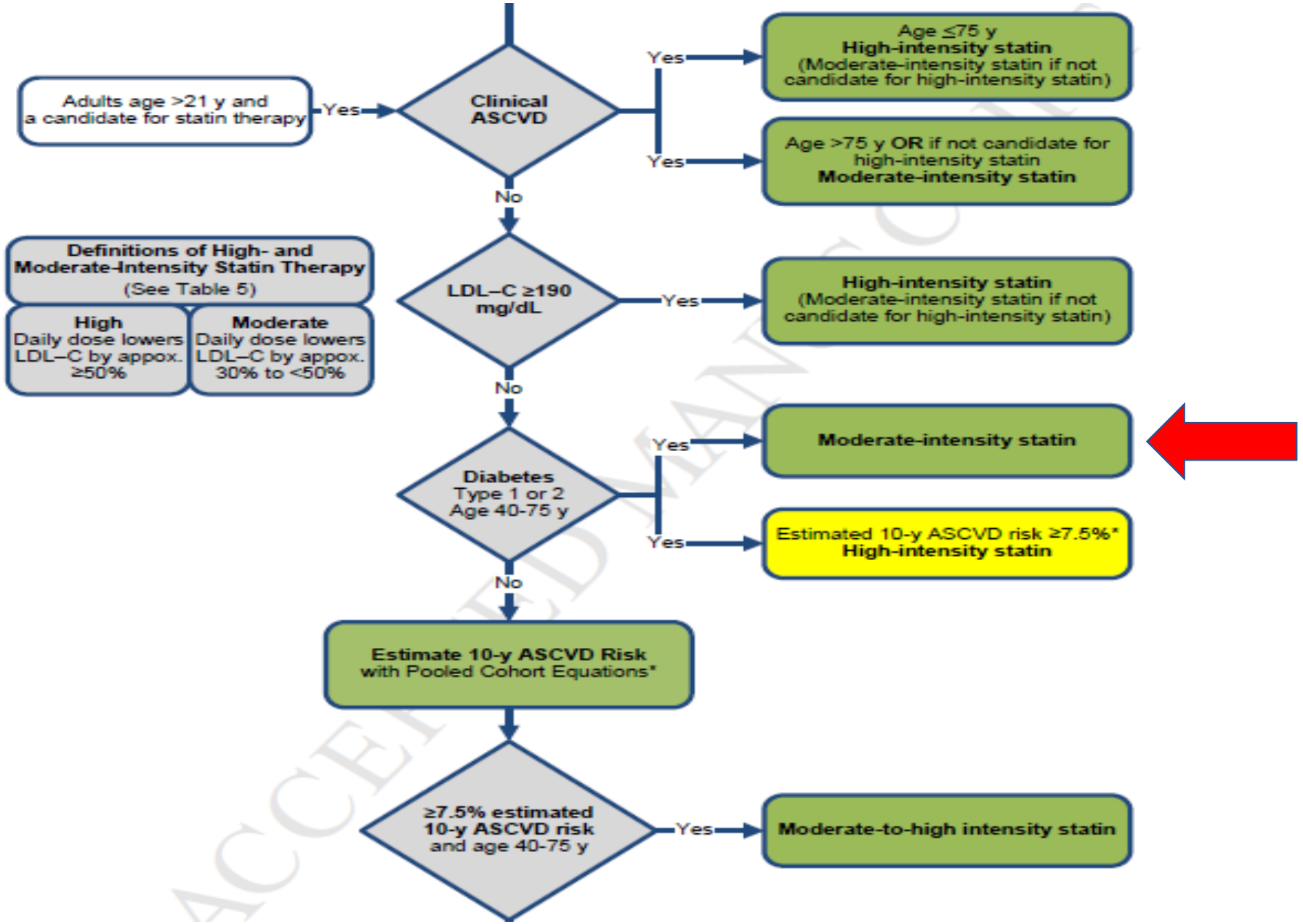
Case 3

48 yr. female

- Total cholesterol 180
- HDL: 55
- SBP: 130
- Not taking anti-hTN meds
- +diabetic
- Non-smoker
- Calculated 10 yr. risk ASCVD : 1.8%


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)
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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

- Moderate 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
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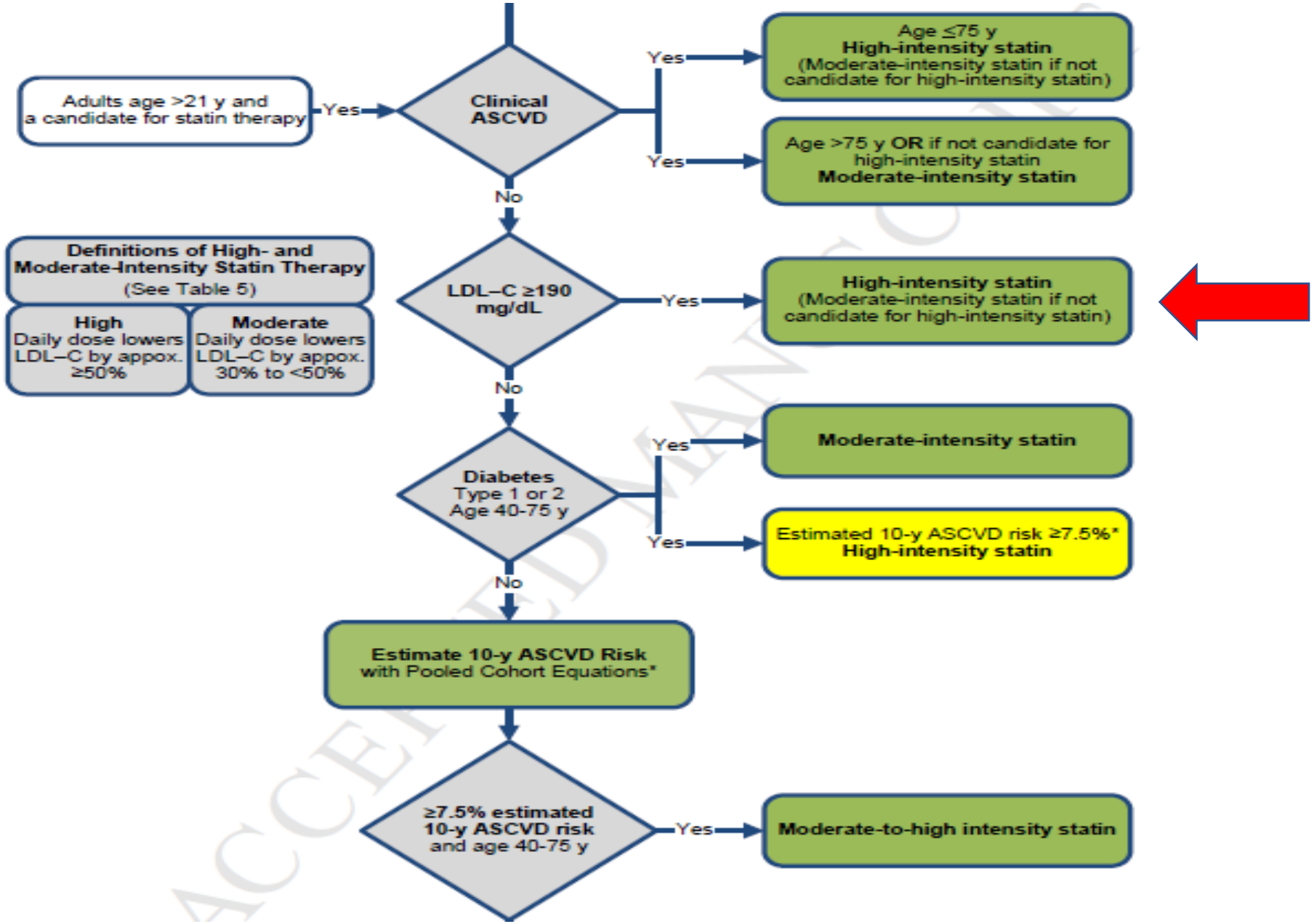
Case 4

22 yr.male

- LDL: 195
- SBP: 120
- Not taking anti-hTN meds
- Non-diabetic
- Non-smoker


Adults age >21 y and a candidate for statin therapy
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Clinical ASCVD
Yes
Age ≤75 y
High-intensity statin
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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)*

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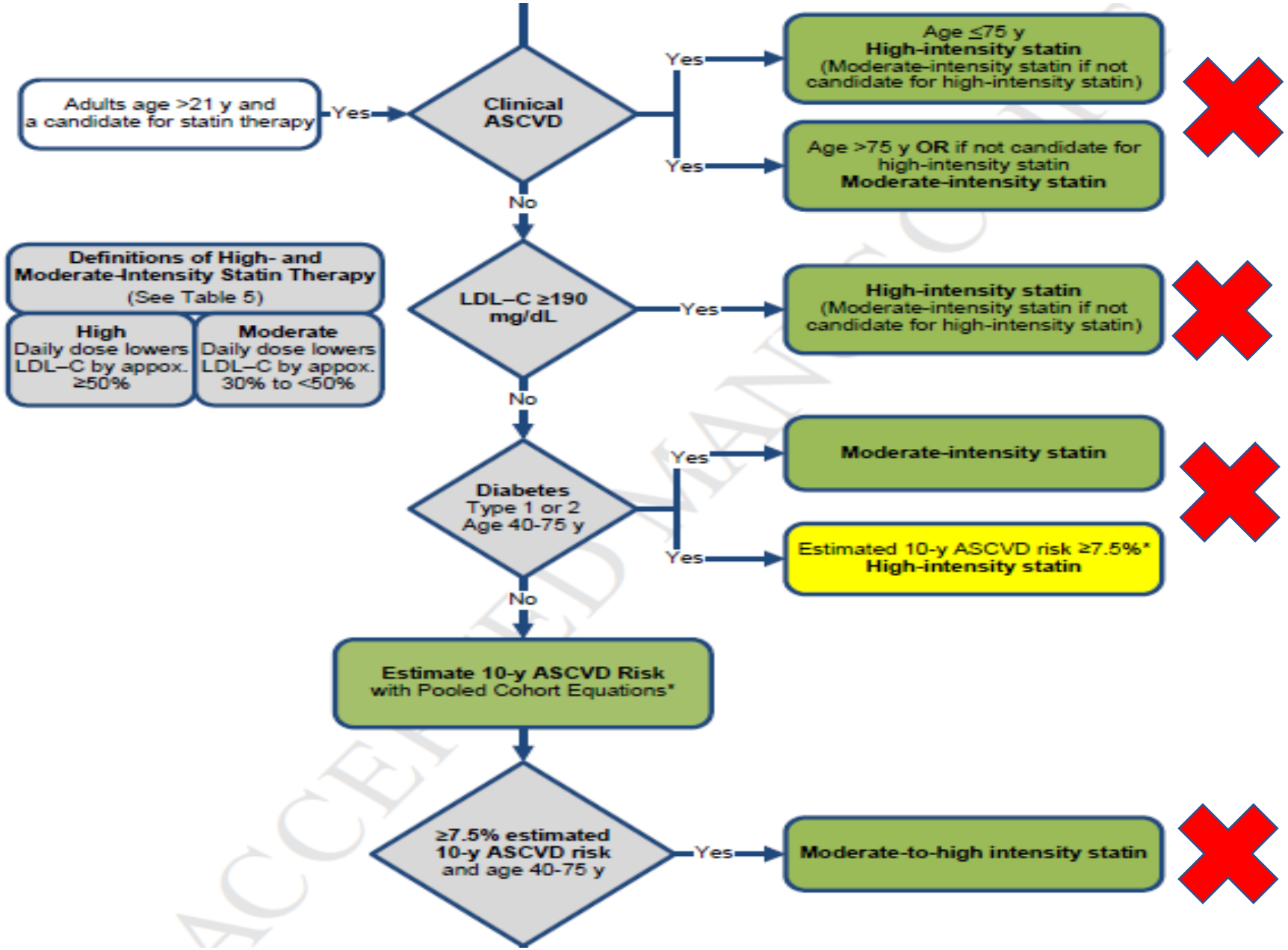
Case 5

66 yr. female

- High Total cholesterol: 230
- HDL: 55
- SBP: 150
- taking anti-hTN meds
- Non-diabetic
- Non-smoker
- Calculated 10 yr risk of ASCVD : 2.0 %


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)
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Moderate-intensity statin
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Type 1 or 2
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Moderate-intensity statin
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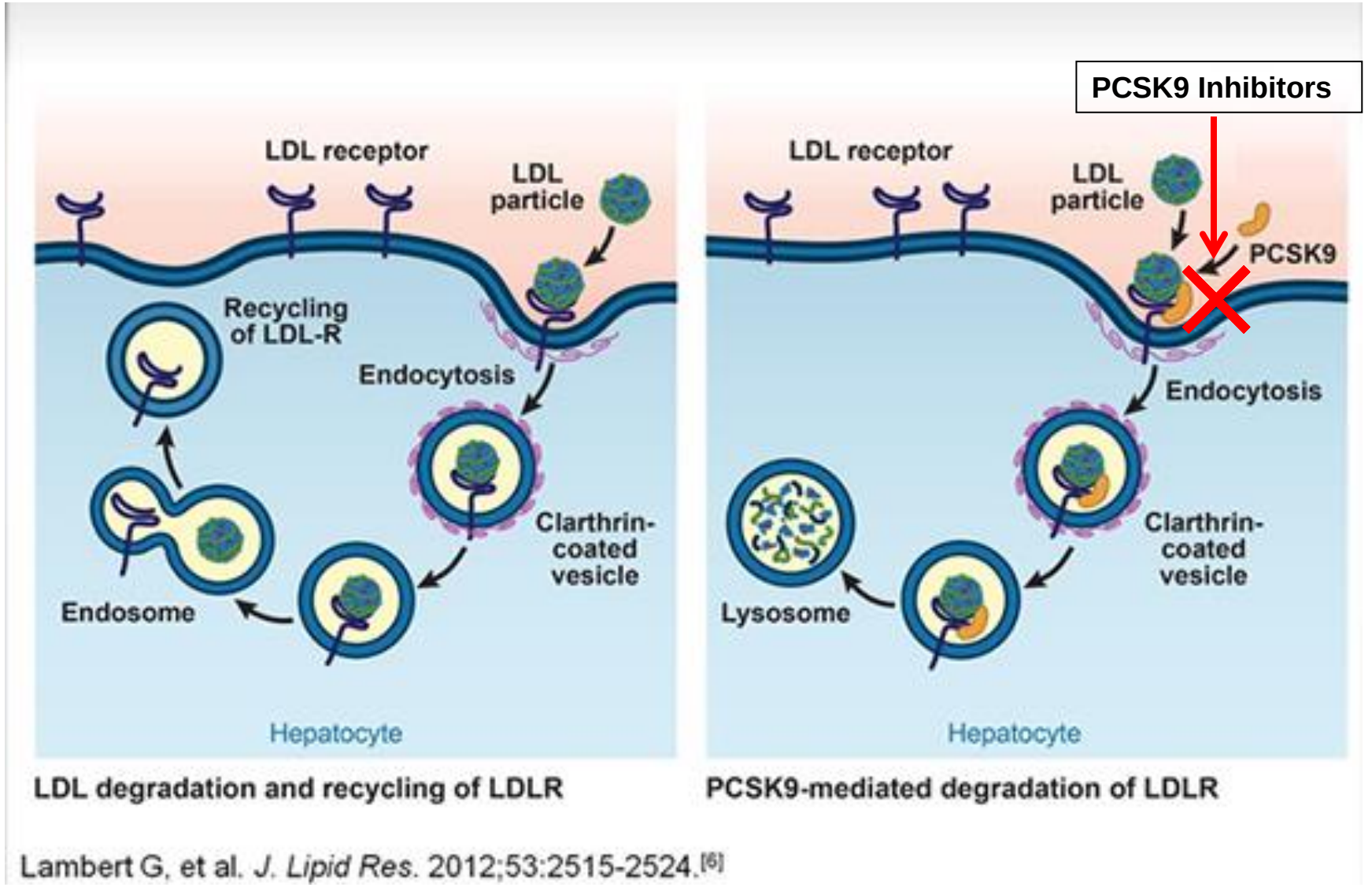
Estimated 10-y ASCVD risk ≥7.5%*
High-intensity statin
No
Estimate 10-y ASCVD Risk
with Pooled Cohort Equations*
≥7.5% estimated 10-y ASCVD risk
and age 40-75 y
Yes
Moderate-to-high intensity statin

- Statin therapy NOT recommended

Products Available

PCSK9 Inhibitors[2]

Mechanism of Action



Lambert G, et al. *J. Lipid Res.* 2012;53:2515-2524.[6]

PCSK9 Inhibitors

- Human monoclonal antibodies
  - Praluent® (alirocumab)
  - Repatha® (evolocumab)

- Available as brand name only

	Labeled Indications	Dosing	Cost (per mL)
Praluent® (alirocumab)	Hyperlipidemia, primary Secondary prevention of cardiovascular events	SubQ: 75mg once every 2 weeks or 300mg once every 4 weeks May increase to a maximum dose of 150mg every 2 weeks	Auto-injector 75mg/mL: $672 150mg/mL: $672
Repatha® (elirocumab)	Hyperlipidemia, primary Homozygous familial hypercholesterolemia Prevention of cardiovascular events in patients with established CV disease	SubQ: 140mg once every 2 weeks or 420mg once a month	Auto-injector 140mg/mL: $270 Cartridge system 420mg/3.5mL: $167.14 ($584.99 total)

- Minimal adverse effects
  - >10% → local injection site reactions
- Nasopharyngitis reported in >10% of patients taking evolocumab

Storage

- Refrigerate (2°C to 8°C) and protect from light
- If rer must be used within 30 days

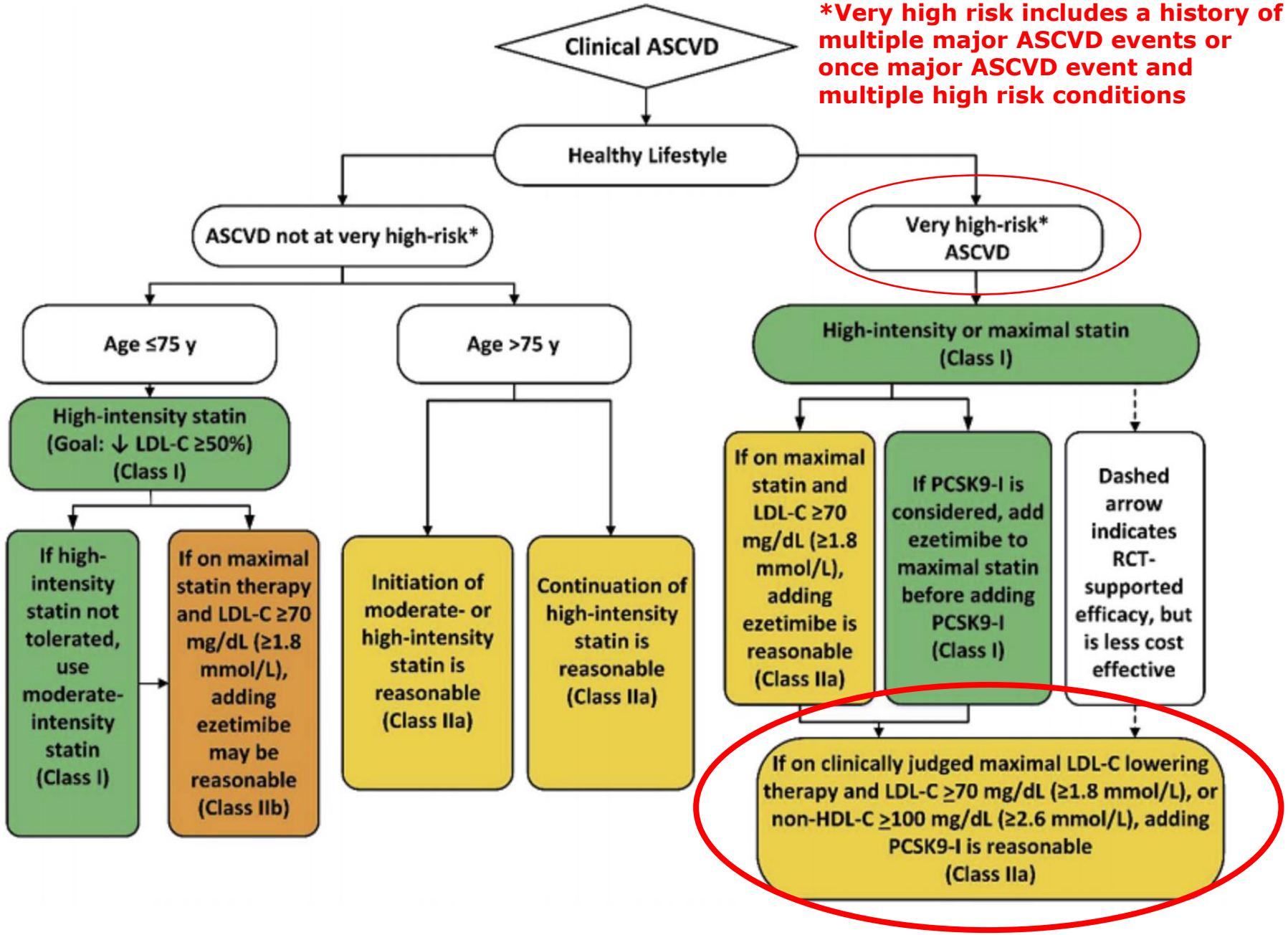
Primary Prevention[5]

- Patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL) **and** on maximally tolerated statin plus ezetimibe
  - **Addition of PCSK9 inhibitor may be considered if:**
    - LDL-C level on statin plus ezetimibe remains ≥ 100 mg/dL and the patient has multiple factors that increase subsequent risk of ASCVD events

Primary Prevention[5]

- Patients with severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL) **and** on maximally tolerated statin plus ezetimibe
  - **Addition of PCSK9 inhibitor may be considered if:**
    - LDL-C level on statin plus ezetimibe remains ≥ 100 mg/dL and the patient has multiple factors that increase subsequent risk of ASCVD events

FIGURE 1 Secondary Prevention in Patients With Clinical ASCVD



***Very high risk includes a history of multiple major ASCVD events or once major ASCVD event and multiple high risk conditions**

Summary of National Guidance for Lipid Management for Primary and Secondary Prevention of CVD

ACCELERATED ACCESS COLLABORATIVE

NHS

INITIAL CONSIDERATIONS:

- Measure non-fasting ***full lipid profile*** (total cholesterol, HDL-C, non-HDL-C, triglycerides) and HbA1c as part of an initial baseline assessment.
- Consider secondary causes of hyperlipidaemia and manage as needed.
- Ensure appropriate baseline and follow up tests as detailed on page 2. Measure BMI.
- Identify and exclude people with contraindications/drug interactions
- If non-fasting triglyceride above 4.5mmol/L see page 2.

PRIMARY PREVENTION

Consider statin therapy for adults who do not have established CVD but fall into the categories below. Use QRISK risk assessment tool where appropriate (see page 2, *'Primary Prevention Risk Assessment'*)

- Age ≤84 & QRISK ≥10% over next 10 years
- Type 2 diabetes & QRISK ≥10% over next 10 years
- Type 1 diabetes, if they have one or more of the following:
  - Over 40 years
  - Had diabetes for >10 years
  - Have established nephropathy
  - Have other CVD risk factors
- CKD eGFR < 60 mL/min/1.73m² and/or albuminuria
- Age ≥85 years if appropriate consider comorbidities, frailty & life expectancy

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

Consider additional risk factors, if present, together with QRISK score (treated for HIV, severe mental illness, taking medicines that cause dyslipidaemia, systemic inflammatory disorder (e.g. SLE), impaired fasting glycaemia, recent change in risk factors)

PRIMARY PREVENTION

If lifestyle modification is ineffective or inappropriate offer statin treatment.

Atorvastatin 20mg daily

- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months;
  - discuss treatment adherence, timing of dose, diet and lifestyle
  - If at higher risk (based on comorbidities, risk score or clinical judgement – see page 2 *'Additional Risk Factors'*) consider increasing the dose every 2-3 months up to a maximum dose of atorvastatin 80mg daily.
  - For how to increase in people with CKD see *'Special Patient Populations'* (page 2).
- If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 *'Extent of lipid lowering with available therapies'*)
- If maximum tolerated dose of statin does not achieve non-HDL-C reduction > 40% of baseline value after 3 months consider adding Ezetimibe 10mg daily (NICE TA385)
- If statin treatment is contraindicated or not tolerated;
  - See AAC Statin Intolerance Algorithm for advice regarding adverse effects (click here)
  - Ezetimibe 10mg monotherapy may be considered. Assess response after 3 months.
  - Ezetimibe 10mg/bempedoic acid 180 mg combination may be considered when ezetimibe alone does not control non-HDL-C/LDL-C well enough (NICE TA694).

If non-HDL-C reduction remains < 40% of baseline despite maximal tolerated lipid lowering therapy (including people with intolerances and contraindications) consider referral to specialist lipid management clinic according to local arrangements

SEVERE HYPERLIPIDAEMIA

If TC>7.5mmol/L and/or LDL-C >4.9mmol/L and/or non-HDL-C >5.9mmol/L, a personal and/or family history of confirmed CHD (<60 years) and with no secondary causes: suspect familial hypercholesterolaemia (possible heterozygous FH)

Do not use QRISK risk assessment tool

DIAGNOSIS AND REFERRAL

Take fasting blood for repeat lipid profile to measure LDL-C.

Use the **Simon Broome** or **Dutch Lipid Clinic Network** (DLCN) criteria to make a **clinical diagnosis of FH**.

Refer to Lipid Clinic for further assessment if **clinical diagnosis of FH** or if TC>9.0mmol/L and/or LDL-C >6.5mmol/L and/or non-HDL-C >7.5mmol/L or Fasting triglycerides > 10mmol/L (regardless of family history) (page 2)

TREATMENT TARGETS IN FH

If clinical diagnosis of FH and/or other risk factors present follow the recommended treatment management pathway for primary or secondary prevention as for non-FH, ***BUT***

Aim to achieve at least a 50% reduction of LDL-C (or non-fasting non-HDL-C) from baseline.

Consider specialist referral for further treatment and/or consideration of PCSK9i therapy IF

- they are assessed to be at very high risk of a coronary event**
- OR therapy is not tolerated
- OR LDL-C remains >5mmol/L (primary prevention)
- OR LDL-C remains >3.5mmol/L (secondary prevention)

despite maximal tolerated statin and ezetimibe therapy.

**defined as any of the following:

- Established coronary heart disease
- Two or more other CVD risk factors

SECONDARY PREVENTION

Offer statin therapy to adults with CVD, this includes angina, previous MI, revascularisation,stroke or TIA or symptomatic peripheral arterial disease. Do not delay statin treatment if a person has acute coronary syndrome. Take a lipid sample on admission (within 24 hours)

Identify and address all modifiable risk factors - smoking, diet, obesity, alcohol intake, physical activity, blood pressure and HbA1c.

SECONDARY PREVENTION

Do not delay statin treatment in secondary prevention while managing modifiable risk factors.

Prescibe a high intensity statin:

Atorvastatin 80mg daily

Use a lower dose of atorvastatin if there is a potential drug interaction, high risk of or experiencing adverse effects, or patient preference.

Offer atorvastatin 20mg if CKD (people with GFR< 60 mL/min/1.73m²).

- Measure full lipid profile again after 3 months (non-fasting).
- High intensity statin treatment should achieve reduction of non-HDL-C > 40% from baseline. If not achieved after 3 months
  - discuss treatment adherence, timing of dose, diet and lifestyle measures
  - If started on less than atorvastatin 80mg and the person is judged to be at higher risk (based on comorbidities, risk score or clinical judgement - see page 2 *'Additional Risk Factors'*), consider increasing to 80mg atorvastatin. For how to increase in people with CKD see *'Special Patient Populations'* (page 2).
- If non-HDL-C baseline value is not available*, consider target non-HDL-C < 2.5mmol/L (approximately equivalent to LDL-C < 1.8mmol/L) as recommended by Joint British Societies (JBS3).
  **this scenario is not covered by NICE CG181*
- If patients on a high-intensity statin have side effects, offer a lower dose or an alternative statin (see page 2 *'Extent of lipid lowering with available therapies'*)

If maximum tolerated dose of statin does not control non-HDL-C/LDL-C well enough after 3 months confirm statin adherence, then consider the following options based on shared decision making* with the patient

If recommended statin treatment is contraindicated or not tolerated - follow AAC Statin Intolerance Algorithm for advice regarding adverse effects (click here).

If statin intolerance is confirmed, consider:

- **Ezetimibe 10mg** monotherapy. Assess response after 3 months (TA385)
- **Ezetimibe 10mg/bempedoic acid 180 mg** combination when ezetimibe alone does not control non-HDL-C sufficiently. (NICE TA694)

If non HDL-C remains > 2.5mmol/L despite other lipid lowering therapies consider Injectable therapies - arrange a fasting blood test and assess eligibility criteria (TA393/394, TA733)

Ezetimibe 10mg daily (NICE TA385). Reassess after three months. If non-HDL-C remains > 2.5mmol/L; consider **injectable therapies** arrange a fasting blood test and assess eligibility

* See overleaf for information to support shared decision making

** Inclisiran and PCSK9i should not be prescribed concurrently

Injectable therapies**

If non-HDL-C > 2.5mmol/L; Arrange fasting blood test to measure LDL-C to assess eligibility:

- **Inclisiran** - if fasting LDL-C ≥ 2.6mmol/L despite maximum tolerated lipid lowering therapy (TA733)

OR

- **PCSK9i** - see overleaf for LDL-C thresholds. (TA393/4)

If eligibility criteria are not met, consider **ezetimibe 10mg daily** (if not previously considered)

MANAGEMENT

This guidance applies to new patients and may also be taken into consideration for those already on statins at their annual review. If 40% reduction of non-HDL-C not achieved, offer high intensity statins. Discuss with people who are stable on a low- or medium-intensity statin the likely benefits and potential risk of side effects if changed to a high-intensity statin when they have a medication review and agree with the person whether a change is needed.

Ezetimibe, alirocumab, evolocumab or inclisiran can be added when patients' LDL-C levels are not lowered enough with the maximally tolerated dose of statins. Bempedoic acid with ezetimibe is an option when statins are contraindicated or not tolerated, and when ezetimibe alone does not control LDL-C well enough. Do not offer a fibrate, nicotinic acid, bile acid binder or omega-3 fatty acids alone or in combination with statin, for the prevention of CVD (Check NICE CG181 for exceptions).

PRIMARY PREVENTION RISK ASSESSMENT

QRISK3 is the current version of the QRISK calculator. www.qrisk.org/three

- Do not use this risk assessment tool for people with established CVD or those who are at high risk of developing CVD because of FH or other inherited disorders of lipid metabolism.
- Do not use a risk assessment tool to assess CVD risk in people with type 1 diabetes, or eGFR less than 60 mL/min/1.73 m² and/or albuminuria.
- Consider people aged ≥ 85 at increased risk of CVD because of age alone particularly people who smoke or have raised BP.

Additional Risk Factors

Note, standard CVD risk scores including QRISK may underestimate risk in people who have additional risk because of underlying medical conditions or treatments. These groups include the following groups of people;

- severe obesity (BMI>40kg/m²) increases CVD risk
- treated for HIV
- serious mental health problems
- taking medicines that can cause dyslipidaemia such as antipsychotic medication, corticosteroids or immunosuppressant drugs
- autoimmune disorders such as SLE, and other systemic inflammatory disorders
- non-diabetic hyperglycaemia
- significant hypertriglyceridaemia (fasting triglycerides 4.5-9.9mmol/L)
- recent risk factor changes e.g. quit smoking, BP or lipid treatment

Consider socio-economic status as an additional factor contributing to CVD risk.

If QRISK < 10% over the next 10 years - Give lifestyle advice and ensure regular review of CVD risk in line with guidance.

SPECIAL PATIENT POPULATIONS

Type 1 Diabetes

While NICE recommends offering statins to patients with Type 1 diabetes as detailed in the algorithm, it also states to consider statins in all adults with type 1 diabetes.

Chronic Kidney Disease

Offer atorvastatin 20mg for the primary or secondary prevention of CVD to people with CKD (eGFR less than 60 mL/min/1.73m² and/or albuminuria)

Increase the dose if a greater than 40% reduction in non-HDL-C is not achieved and eGFR is 30 mL/min/1.73m² or more.

Agree the use of higher doses with a renal specialist if eGFR is less than 30 mL/min/1.73m²

ABBREVIATIONS

ALT: alanine aminotransferase
AST: aspartate aminotransferase
CHD: coronary heart disease
CKD: chronic kidney disease
CVD: cardiovascular disease
FH: familial hypercholesterolaemia
LDL-C: low density lipoprotein cholesterol
non-HDL-C: non-high density lipoprotein cholesterol
PCSK9I: proprotein convertase subtilisin kexin 9 monoclonal antibody inhibitor
SLE: systemic lupus erythematosus
SPC: summary of product characteristics
TC: total cholesterol

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

- **Rosuvastatin** may be used as an alternative to atorvastatin if compatible with other drug therapy. Some people may need a lower starting dose (see BNF).
- Low/medium intensity statins should only be used if intolerance or drug interactions.
- **Ezetimibe** when combined with any statin is likely to give greater reduction in non-HDL-C or LDL-C than doubling the dose of the statin.
- **PCSK9i** (NICE TA393, TA394) alone or in combination with statins or ezetimibe produce an additional LDL-C reduction of approximately 50% (range 25-70%).
- **Bempedoic acid** when combined with ezetimibe (TA694) produces an additional LDL-C reduction of approximately 28% (range 22-33%) but no clinical outcome evidence is currently available.
- **Inclisiran** (TA733) alone or in combination with statins or ezetimibe produces an additional LDL-C reduction of approximately 50% (range 48-52%) but no clinical outcome evidence is currently available.

MONITORING

Baseline Measurements

In addition to full lipid profile, measure renal, thyroid and liver profiles (including albumin) and HbA1c to exclude secondary causes and co-morbidities.
Measure baseline liver transaminase (ALT or AST) before starting a statin.
Measure CK if unexplained muscle pain before starting a statin.
CK should not be measured routinely especially if a patient is asymptomatic.

	Primary Prevention		Secondary prevention	
	Lipid Profile	ALT or AST	Lipid Profile	ALT or AST
Baseline	✓	✓	✓	✓
3 months	✓	✓	✓	✓
6-9months	If <40% non-HDL-C reduction, up titration required. Repeat full lipid profile and ALT or AST within 3 months of each up-titration of statin dose or addition of ezetimibe as required			
12 months	✓	✓	✓	✓
Yearly	✓*		✓*	

Provide annual medication reviews for people taking statins to discuss effectiveness of therapy, medicines adherence, lifestyle modification and address CVD risk factors.
**Consider an annual non-fasting full lipid profile to inform the discussion around effectiveness of lipid lowering therapy and any medicines non-adherence.*

Monitoring

Repeat full lipid profile is non-fasting.
Measure liver transaminase within 3 months of starting treatment and then within 3 months of every additional up titration and then again at 12 months, but not again unless clinically indicated.

If ALT or AST are greater than 3 times the upper limit of normal then do not initiate a statin or discontinue statin therapy already prescribed and repeat the LFTs in a month.

If ALT or AST are elevated but are less than 3 times the upper limit of normal then:

- Continue the statin and repeat in a month.
- If they remain elevated but are less than 3 times the upper limit of normal then continue statin and repeat again in 6 months.

TITRATION THRESHOLD / TARGETS

	NICE titration threshold	JBS3
Primary prevention	Intensify lipid lowering therapy if non-HDL-C reduction from baseline is less than 40%	non-HDL-C <2.5mmol/L (LDL-C <1.8mmol/L)
Secondary Prevention		
FH	Optimise lipid lowering therapy to achieve at least 50% reduction in LDL-C (or non-HDL-C.)	

If baseline cholesterol is unknown in the setting of secondary prevention use the use Joint British Societies' JBS3 consensus recommendation.
Non-HDL-C = TC minus HDL-C
LDL-C = non-HDL-C minus (Fasting triglycerides*/2.2)
*valid only when fasting triglycerides are less than 4.5 mmol/L

SPECIALIST SERVICES

Scope of specialist service available locally may include; lipid clinic, PCSK9i clinic (offering initiation and subsequent follow up), FH genetic diagnosis and cascade testing, lipoprotein apheresis service. NICE eligibility criteria for PCSK9i and fasting LDL-C thresholds are summarised below.

NICE TA393 Alirocumab NICE TA394 Evolocumab	Without CVD	With CVD	
		High risk [1]	Very high risk [2]
Primary non-FH or mixed dyslipidaemia	Not recommended	LDL C > 4.0 mmol/L	LDL C > 3.5 mmol/L
Primary heterozygous-FH	LDL C > 5.0 mmol/L	LDL C > 3.5 mmol/L	

[1] History of any of the following: ACS; coronary or other arterial revascularisation procedures; CHD, ischaemic stroke; PAD. [2] Recurrent CV events or CV events in more than 1 vascular bed (that is, polyvascular disease).

Bempedoic acid/ezetimibe and inclisiran are available in primary care and do not require initiation by specialist services.' PCSK9i may be available for prescribing in primary care: see local initiation pathways.

TRIGLYCERIDES

Triglyceride concentration	Action
Greater than 20mmol/L	**Refer to lipid clinic for urgent specialist review** if not a result of excess alcohol or poor glycaemic control. At risk of acute pancreatitis.
10 - 20mmol/L	Repeat the TG measurement with a fasting test (after an interval of 5 days, but within 2 weeks) and review for potential secondary causes of hyperlipidaemia. Seek specialist advice if the TG concentration remains > 10mmol/litre. At risk of acute pancreatitis
4.5 - 9.9mmol/L	If non-fasting triglycerides are greater than 4.5mmol/L, repeat with a fasting TG measurement. Be aware that the CVD risk may be underestimated by risk assessment tools, optimise the management of other CVD risk factors present and seek specialist advice if non-HDL-C concentration is > 7.5 mmol/litre.

STATIN INTOLERANCE

Statin intolerance is defined as the presence of clinically significant adverse effects from statin therapy that are considered to represent an unacceptable risk to the patient or that may result in adherence to therapy being compromised.

For people who are intolerant of the recommended statin treatment see the NHSE AAC statin intolerance algorithm, available on the NHSE AAC page (Click here)

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ACCELERATED ACCESS COLLABORATIVE

NHS

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Approved by the National Institute for Health and Care Excellence (NICE), Dec 2021.

Lipid Management Pathway

December 2018
Review December 2020
Ref: NICE Lipids CG181;
ESC lipid guideline 2016

HSC Health and Social Care Board

Who needs lipid treatment?

- **1⁰ prevention up to 84 yrs or type 2 diabetes if ≥10% 10yr CV risk on QRISK2 or any patient ≥85 yrs** if appropriate
- **?familial dyslipidaemia** e.g. total chol >7.5mmol/l and FHx IHD or TG>10mmol/l – refer to lipid specialist. Do not use QISK2
- **Type 1 diabetes – Offer statin treatment for the primary prevention for aged >40 years, OR have had diabetes for >10 years, OR have established nephropathy, OR have other CVD risk factors**
- **2⁰ prevention**: all with established CV disease (CHD, cerebrovascular, peripheral vascular). Do not use QRISK2.

Acute Coronary Syndrome

Stable CV disease

If not already taking a statin commence **atorvastatin 80mg***
Start with a lower dose of atorvastatin if potential drug interactions, risk of adverse effects or patient preference

Recheck lipids & LFTs in 3mths

non-HDL-C>40% reduction or LDL-C<1.8mmol/l **

yes → **If HDL<1mmol/l (<1.3 in females)**
Reinforce lifestyle advice (especially exercise, obesity management and smoking cessation)

If high TG, recheck fasting TG.

If fasting TG>1.7mmol/l
- Reinforce lifestyle advice
- Reduce excess alcohol
- Optimise control if diabetic
- *If markedly elevated (>4.5mmol/l) discuss with lipid specialist*

→ Check
- Lipids annually (fasting if TG concern)

no

(If not already on, switch to) **atorvastatin 80mg*** od

Recheck lipids & LFTs in 3mths

- Discuss statin adherence and timing of dose
- Try 3 different statins before concluding statin intolerance†

non-HDL-C>40% reduction or LDL-C<1.8mmol/l **

yes → (same as above)

no

Not achieving target despite maximum tolerated statin dose:
if LDL-C between 1.8 to 3.5mmol/l consider adding **ezetimibe 10mg** od
if LDL-C >3.5-4.0mmol/l despite the above treatment, consider referral to a lipidologist or a cardiologist with lipid interest for consideration of PCSK9 inhibitors (NICE TA 393 / NICE TA 394)

1⁰ Prevention, Diabetes or CKD

If not already on a statin commence **atorvastatin 20mg**

Recheck LFTs & lipids in 3mths

If non-HDL reduction <40% from pre-statin baseline, check adherence, diet, lifestyle and consider increasing atorvastatin

Before starting treatment:

- **Check baseline bloods**: Lipids (immediate if acute event), LFTs, U&E, +/-CK if symptoms/risk of myopathy
- If AST/ALT>3x or CK>5x ULN, do not start statin but look for cause & consider specialist referral
- **Consider and manage 2⁰ causes** (TFTs, dipstick for proteinuria)
- **Tell the patient** their baseline cholesterol levels +/-targets
- **Give lifestyle advice** (especially regarding smoking, alcohol, obesity). In 1⁰ prevention, reassess QRISK2 after lifestyle change.

Notes:

Do NOT use simvastatin 80mg.

*If risk of myopathy including the elderly, or CrCl<30mL/min, consider a lower starting dose of statin.

*If CrCl<10mL/min, do not increase atorvastatin to 80mg before discussing with lipid specialist (NI Nephrology forum)

** Single lipid measurements can vary by ~10%. If borderline, consider repeating the measurement before changing treatment.

† If atorvastatin intolerance, try at least 2 further statins starting at lowest dose e.g. simvastatin 10-40mg, pravastatin 20-40mg, rosuvastatin 5-10mg or fluvastatin 20-40mg before concluding statin intolerance.


Questions??
Thank You!