

Dyslipidemia

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Dyslipidemia

-percholesterolemia, or dyslipidemia, plays a major role in atherosclerosis and plaque formation leading to coronary heart disease (CHD) as well as other forms of atherosclerotic cardiovascular disease (ASCVD), such as carotid and peripheral artery disease.

- Cholesterol is used in biosynthesis of bile acids and steroid hormones.

- Cholesterol, triglycerides, and phospholipids circulate in the blood as lipoproteins, The major lipoproteins are:

1- chylomicrons

2- very low-density lipoprotein (VLDL)

3- intermediate-density lipoprotein (IDL)

4- LDL

5- high-density lipoprotein (HDL)

- A measured total cholesterol is the total cholesterol molecules in all these major lipoproteins

- Each lipoprotein has various proteins called apolipoproteins (Apos) embedded on the surface that serve four main purposes

(a) required for assembly and secretion of lipoproteins

(b) serve as major structural components of lipoproteins

(c) act as ligands for binding to receptors on cell surfaces;

(d) can be cofactors for inhibition of enzymes involved in the breakdown of triglycerides from chylomicrons and VLDL

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- The estimated value of LDL cholesterol is found using the Friedewald equation (after fasting for 9–12 hours):

LDL cholesterol (mg/dL) = total cholesterol – (HDL cholesterol + triglycerides/5), when lipids are expressed in units of mg/dL

or

LDL cholesterol (mmol/L) = total cholesterol – (HDL cholesterol + triglycerides/2.2), when lipids are expressed in units of mmol/L

- Where triglycerides/5 or triglycerides/2.2 estimate VLDL cholesterol in units of mg/dL or mmol/L, respectively

- Non-HDL including VLDL, IDL, and LDL

It is calculated as: Non-HDL cholesterol = total cholesterol – HDL cholesterol

Non-HDL cholesterol can be determined in a nonfasting state. More recently, some laboratories have transitioned to using the Martin-Hopkins equation to estimate LDL cholesterol instead of the Friedewald equation.6 The Martin-Hopkins equation is calculated as:

LDL cholesterol = total cholesterol – HDL cholesterol – triglyceride/adjustable factor

The Martin-Hopkins equation has demonstrated improved estimation of LDL cholesterol compared to the Friedewald equation.

Mechanism:

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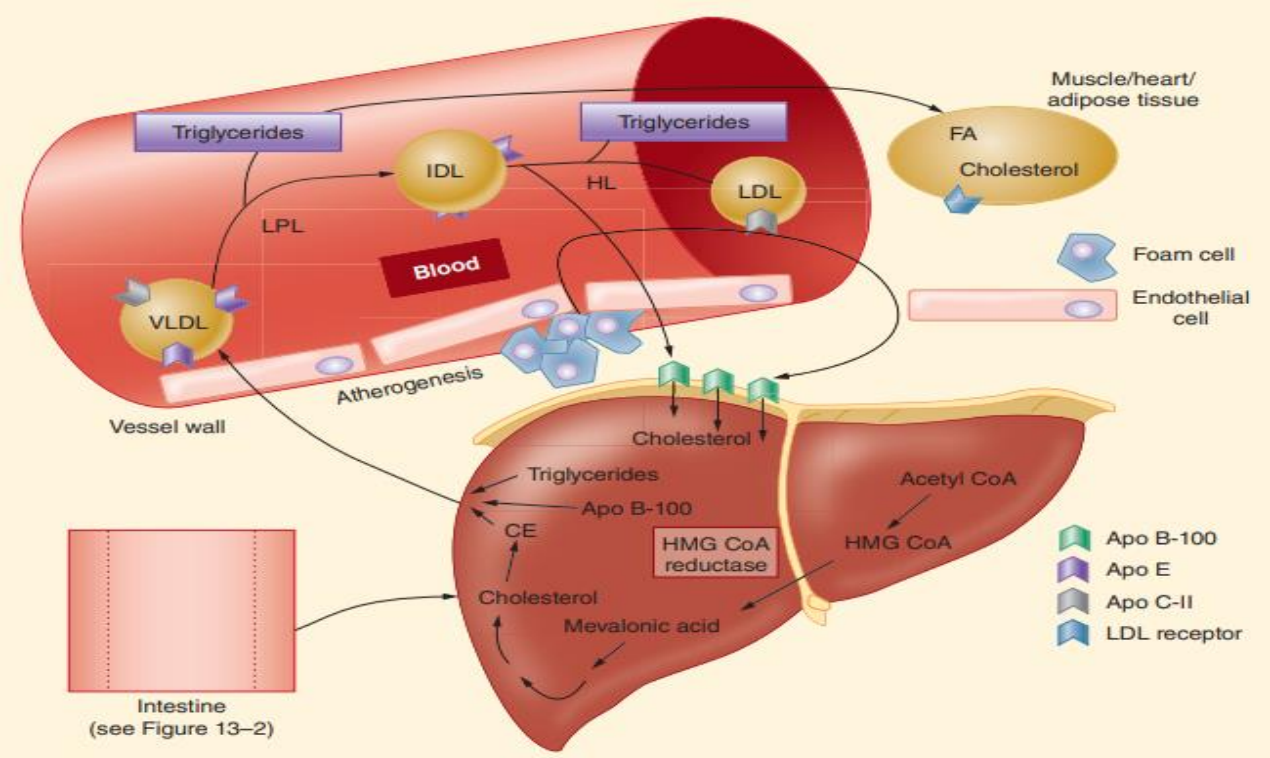

A variety of genetic mutations can occur during lipoprotein synthesis and metabolism that cause lipid disorders.

- Disorders that increase serum cholesterol are generally those that affect the number or affinity of LDL receptors and

- These patients commonly present with corneal arcus of the eye, xanthomas of extensor tendons of the hand and Achilles tendon, premature CHD (male < 45 years old and female < 55 years old).

- Elevations in triglycerides are generally associated with overproduction of triglyceride-rich VLDL, mutations in Apo E, or lack of LPL or Apo CII, which cause hyperchylomicronemia.

Table 13–1

Selected Characteristics of Primary Dyslipidemias

Disorder	Estimated Frequency	Metabolic Defect	Main Lipid Parameter
Autosomal dominant hypercholesterolemia			
Familial hypercholesterolemia	1/250,000–1/1 million	LDL-receptor negative	LDL-C > 500 mg/dL (12.93 mmol/L)
homozygous			
heterozygous	1/250–1/500	Reduction in LDL receptors	LDL-C 250–500 mg/dL (6.47–12.93 mmol/L)
Familial defective Apo B-100	1/1000	Single-nucleotide mutation	LDL-C 250–500 mg/dL (6.47–12.93 mmol/L)
PCSK9 gain-of-function mutations	Rare	Single-nucleotide mutation	LDL-C 250–500 mg/dL (6.47–12.93 mmol/L)
Polygenic hypercholesterolemia	Common	Metabolic and environmental	LDL-C 160–250 mg/dL (4.14–6.47 mmol/L)
Familial combined dyslipidemia	1/200–300	Overproduction of VLDL and/or LDL	LDL-C 250–350 mg/dL (6.47–9.05 mmol/L) TG 200–800 mg/dL (2.26–9.04 mmol/L)
Familial hyperapobetalipoproteinemia	5%	Increase Apo B production	Apo B > 125 mg/dL (1.25 g/L)
Familial dysbetalipoproteinemia (type III)	0.5%	Apo E2/2 phenotype	LDL-C 300–600 mg/dL (7.76–15.52 mmol/L)
Familial hypertriglyceridemia			
Type I	1/500,000–1/1 million	LPL-Apo CII system	TG > 1000 mg/dL (11.3 mmol/L)
Type IV	1/300	Unknown	TG 200–500 mg/dL (2.26–5.65 mmol/L)
Type V	1/205,000	Metabolic and environmental	TG > 1000 mg/dL (11.3 mmol/L)
Hypoalphalipoproteinemia	3%–5%	Defect in HDL catabolism	HDL-C < 35 mg/dL (0.91 mmol/L)

Table 13–2

Secondary Conditions and Drugs That May Cause Dyslipidemia

	↑ LDL Cholesterol	↑ Triglycerides	↓ HDL Cholesterol
Other Conditions			
Anorexia nervosa	√		
Chronic kidney disease	√	√	
Diabetes mellitus		√	√
Hemodialysis patients		√	
Hypothyroidism	√	√	
Nephrotic syndrome	√	√	√
Obesity		√	√
Obstructive liver disease/biliary cirrhosis	√		
Renal disease		√	
Drugs			
Anabolic steroids	√		√
Atypical antipsychotics		√	√
β-Blockers		√	√
Corticosteroids	√	√	
Cyclosporine	√		
Estrogen		√	
Isotretinoin		√	√
Progestins	√		√
Protease inhibitors		√	√
Thiazide diuretics	√	√	

Table 13–3

Essential Components of Therapeutic Lifestyle Changes

Component	Recommendation
Dietary cholesterol	< 200 mg/day (5.17 mmol/L)
Saturated fats	Total fat range should be 25%–35% of calories consumed for most cases < 7% of total calories and reduce intake of trans fatty acids
Therapeutic options for LDL-lowering plant stanols/sterols	2 g/day
Increased viscous (soluble) fiber	10–25 g/day
Total calories	Adjust caloric intake to maintain desirable body weight and prevent weight gain
Physical activity	≥ 150 min/week of moderate intensity physical activity or ≥ 75 min/week of vigorous-intensity physical activity

Additionally, consumption of plant stanols/sterols and dietary fiber should be encouraged as they may reduce LDL cholesterol by 20% to 25%

-first marketed statin called lovastatin

-

The 2018 AHA/ACC guidelines identify four groups of adult patients targeted for statin treatment for both primary and secondary prevention

- Established clinical ASCVD (secondary prevention).

• Primary prevention with elevation of LDL cholesterol levels 190 mg/dL (4.91 mmol/L) or higher. عادة بحسبو المخاطر وبحددو هل محتاج نعطيه ستاتين او لا ولكن لما بكون مرتفع اعلى من 190 رح نعطيه ستاتين عالي لانه كتير مرتفع

• Primary prevention with diabetes mellitus (DM), age 40 to 75 years regardless of LDL cholesterol levels.

• Primary prevention without DM, age 40 to 75 years, with an estimated 10-year risk of 7.5% or greater, and LDL cholesterol levels 70 to 189 mg/dL (1.81–4.89 mmol/L).

هلا في فحص بعملوه بقيسو مدى احتمالية ومخاطر يصير عند المريض جلطة قلبية او دماغية او غيرها خلال (ال10 سنين يلي جاي)وهالفحص بنعمل للمرضى يلي عمرهم من 40-75 متل مو موجود بالصورة هون (70-189)=LDL وقيمة ال

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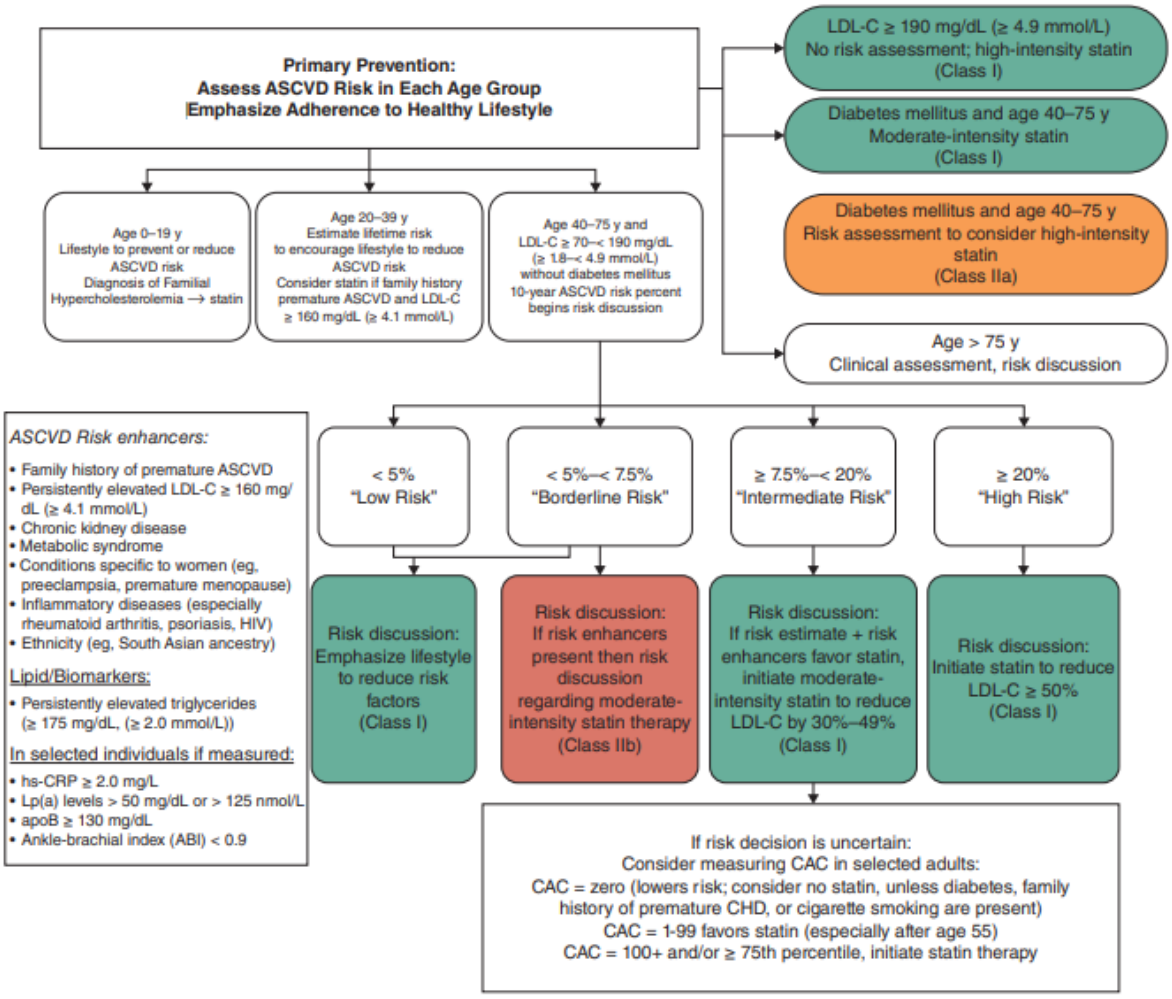

- Individuals without clinical ASCVD should be screened for major ASCVD risk factors, and quantitative risk scoring should be obtained for adults 20 years or older

- If ASCVD risk score reaches the high-risk threshold (> 20%), assign patient to high-risk category. If risk-enhancing factors are present, consider assigning to the high-risk category

If initiation of statin therapy is uncertain based on quantitative risk assessment, additional ASCVD risk enhancers can be considered such as:

• LDL cholesterol 160 mg/dL (4.14 mmol/L) or higher.

• Persistently elevated triglycerides 175 mg/dL (2 mmol/L) or higher (three or more readings)

. • Family history of premature ASCVD, chronic kidney disease, inflammatory disease, ethnicity (eg, South Asian ancestry).

• Apo B 130 mg/dL (1.3 g/L) or higher.

• Lipoprotein (a), or Lp(a), 50 mg/dL (0.5 g/L) or higher.

• High-sensitivity C-reactive protein (hs-CRP) of 2 mg/L or higher.

• Coronary artery calcium (CAC) score of 100 or higher.

• Ankle-brachial index (ABI) less than 0.9.

• Elevated lifetime ASCVD risk.

-In adults 40 to 75 years of age without diabetes mellitus and with LDL cholesterol between 70 and 189 mg/dL (1.81 and 4.89 mmol/L) who fall into the intermediate-risk category (score of ≥ 7.5%–19.9%) the AHA/ACC guidelines recommend checking a CAC score to help with the decision about starting a statin or not.

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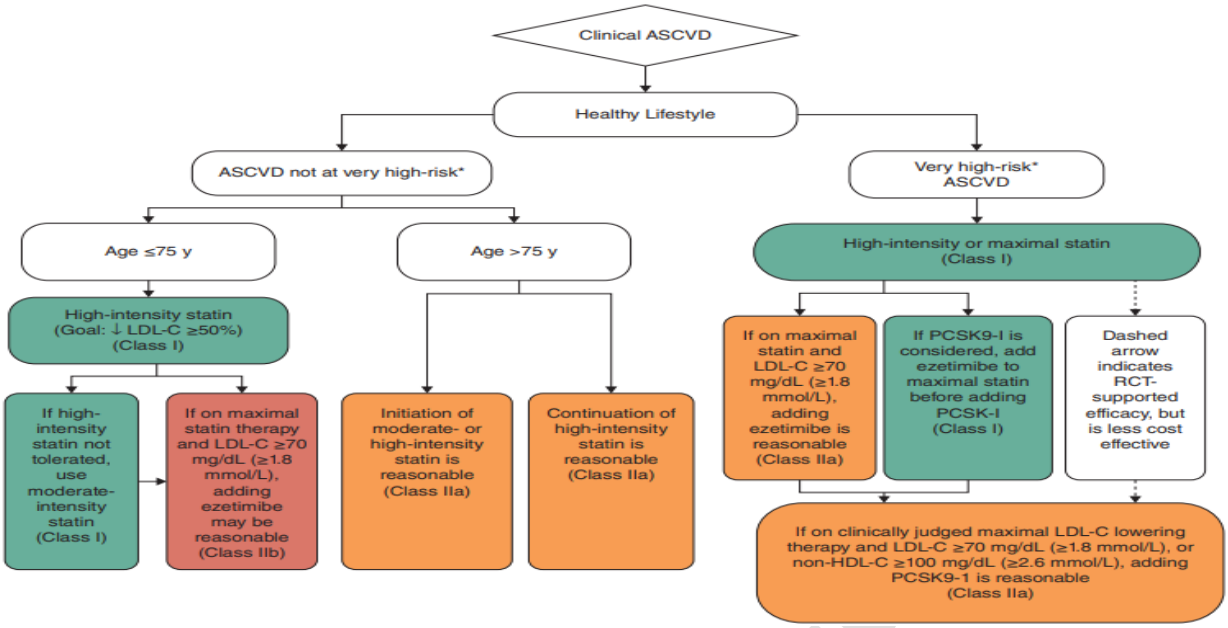

بهي الصورة رح نميز كل عمر شو نوع الستاتين يلي بقدر اعطيه لانه عادة الكبار بالعمر فوق ال75 ما بتحملو الهاي ستاتين(وبيعتمد حسب حالة الشخص) ونتعلم كيف نمشي بالخطوات فاول العلاج الستاتينات وبعدها بشوف لو لسا ما وصل الجول شو نعطي وهكذا..

هلا بشكل عام رح نمشي عالجايد لاين لنحدد هل المريض بده ستاتين او لا ولما اقرر انه صار لازم اعطيه هون رح انتبه لانواعهم بهالجدول المهم احفظوه جدول 13-5

-A follow-up LDL cholesterol 4 to 12 weeks after initiating therapy is used to assess response

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Table 13–5

High, Moderate, and Low-Intensity Statin Therapy as Indicated by the American Heart Association/American College of Cardiology (AHA/ACC) Guidelines[4]

	High Intensity	Moderate Intensity	Low Intensity
LDL-C Lowering[a]	≥ 50%	30%–49%	< 30%
Statins	**Atorvastatin (40[b])–80 mg** **Rosuvastatin 20 (40) mg**	**Atorvastatin 10 (20) mg** **Rosuvastatin (5) 10 mg** **Simvastatin 20–40 mg** **Pravastatin 40 (80) mg** **Lovastatin 40 (80) mg** Fluvastatin XL 80 mg **Fluvastatin 40 mg twice daily** Pitavastatin 1–4 mg	Simvastatin 10 mg **Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

-The NLA emphasized that non-HDL cholesterol is a better primary target for modification than LDL cholesterol and is now considered a co-target with LDL cholesterol

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Table 13–6

National Lipid Association Classifications of Cholesterol and Triglyceride Levels in mg/dL (mmol/L)[7]

Lipids	
Non-HDL Cholesterol[a]	
< 130 (3.36)	Desirable
130–159 (3.36–4.12)	Above desirable
160–189 (4.13–4.90)	Borderline high
190–219 (4.91–5.68)	High
≥ 220 (5.69)	Very high
LDL Cholesterol	
< 100 (2.59)	Desirable
100–129 (2.59–3.35)	Above desirable
130–159 (3.36–4.12)	Borderline high
160–189 (4.13–4.90)	High
≥ 190 (4.91)	Very high
HDL Cholesterol	
< 40 (1.03) (men)	Low
< 50 (1.29) (women)	Low
Triglycerides	
< 150 (1.70)	Normal
150–199 (1.70–2.25)	Borderline high
200–499 (2.26–5.64)	High
≥ 500 (5.65)	Very high[b]

من الجدول السابق الجول الهم ؟ احفظوهم 😊

The goal of treatment is :

-LDL<100 but if the pt high risk (the goal is <70).

-HDL>40 (men) / HDL>50(women)

-TG<150

-cholestrol<200 (هي مني)

In 2020, AACE/ACE updated their guidelines with continued emphasis on lifestyle recommendations.They provide five different risk categories ranging from low risk to extreme risk 4-13موجودين بجدول

Their treatment goals for extreme risk patients go as low as

- an LDL cholesterol less than 55 mg/dL (1.42 mmol/L)

-non-HDL cholesterol less than 80 mg/dL (2.07 mmol/L).

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Recommendations for Treatment

▶ Step 1: Screening and Classification of Initial Lipoprotein Lipid Levels

-The NLA and AACE/ACE recommend that all adults older than 20 years are screened at least every 5 years to obtain a lipid profile

- Children between 2 and 20 years old should be screened for high cholesterol if their parents have premature CHD or if one of their parents has total cholesterol greater than 240 mg/dL (6.21 mmol/L).

▶ Step 2: Rule Out Secondary Causes of Dyslipidemia

▶ Step 3: Identify Patients with Very High-Risk Conditions

Individuals with established clinical ASCVD من الصورة يلي فوق or DM with greater or equal to two ASCVD risk factors من الجدول يلي تحت or evidence of atherosclerosis-mediated end-organ damage are considered very high risk patient:

- non-HDL cholesterol : < 100 mg/dL (2.59 mmol/L)

-LDL cholesterol: < 70 mg/dL (1.81 mmol/L)

*for extreme-risk patients:

non-HDL cholesterol : < 80 mg/dL (2.07 mmol/L)

-LDL cholesterol :< 55 mg/dL (1.42 mmol/L)

- so that recommend statin therapy as initial pharmacotherapy when non-HDL cholesterol or LDL cholesterol is equal to or above these targets/ thresholds.

- For patients with DM, consideration can be given to use at least moderate-to-high-intensity statin therapy, irrespective of baseline cholesterol levels.

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The 2018 AHA/ACC guidelines recommend nonstatin therapy (ezetimibe or proprotein convertase subtilisin/kexin 9 [PCSK9] inhibitors) in addition to maximum tolerated statin therapy in patients who are very high risk and continue to have an LDL cholesterol above the 70 mg/dL (1.81 mmol/L) threshold .

هلا بالجدول هاد كل جايد لاين كانت تكتب قيم معينة فنحن رح نركز على 2020 ونعرف الجول الهم هلا وانتو بتقرؤا بالكيس رح تطلعو عالكيس من عمر وشو عنده امراض سكري لحاله ولا سكري مع امراض قلبية او ريسك انه يصير عنده امراض بالقلب متل جدول الريسك فاكتور (برضو احفظوه) ورح ناخد كل المعلومات يلي بتحددلي هالمريض شو اسخدمله ستاتين او لا ولو ستاتين اعطي (لو او هاي ستاتين) وهكذا..

Table 13–4

US Guidelines for Management of Dyslipidemias

Source	Fasting Lipid Panel Measurement for Risk Assessment	Recommended Lipoprotein Target of Therapy	Treatment Goals and Thresholds
2013 American College of Cardiology/American Heart Association: Blood Cholesterol Guideline for ASCVD Prevention[3]	Yes Used to evaluate for more severe forms and secondary dyslipidemias and to assess anticipated therapeutic response and adherence to statin therapy	No recommendation	No recommendation
National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia (2014)[7]	Fasting or nonfasting	Non-HDL-C and LDL-C Apo B (secondary target)	LDL-C: < 70 mg/dL (1.81 mmol/L) for very high-risk patients < 100 mg/dL (2.59 mmol/L) for high-risk, moderate-risk, and low-risk patients Non-HDL-C: < 100 mg/dL (2.59 mmol/L) for very high-risk patients < 130 mg/dL (3.36 mmol/L) for high-risk, moderate-risk, and low-risk patients Apo B: < 80 mg/dL (0.80 g/L) for very high-risk patients < 90 mg/dL (0.90 g/L) for high-risk, moderate-risk, and low-risk patients
American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for	Yes	Non-HDL-C and LDL-C and Apo B	LDL-C: < 55 mg/dL (1.42 mmol/L) for extreme-risk patients < 70 mg/dL (1.81 mmol/L) for very high-risk patients < 100 mg/dL (2.59 mmol/L) for high-risk and moderate-risk patients < 130 mg/dL (3.36 mmol/L) for low-risk patients

			< 90 mg/dL (0.90 g/L) for high-risk, moderate-risk, and low-risk patients
American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease (2020)[8]	Yes	Non-HDL-C and LDL-C and Apo B	LDL-C: < 55 mg/dL (1.42 mmol/L) for extreme-risk patients < 70 mg/dL (1.81 mmol/L) for very high-risk patients < 100 mg/dL (2.59 mmol/L) for high-risk and moderate-risk patients < 130 mg/dL (3.36 mmol/L) for low-risk patients Non-HDL-C: < 80 mg/dL (2.07 mmol/L) for extreme-risk patients < 100 mg/dL (2.59 mmol/L) for very high-risk patients < 130 mg/dL (3.36 mmol/L) for high-risk and moderate-risk patients < 160 mg/dL (4.14 mmol/L) for low-risk patients Apo B: < 70 mg/dL (0.70 g/L) for extreme-risk patients < 80 mg/dL (0.80 g/L) for very high-risk patients < 90 mg/dL (0.90 g/L) for high-risk and moderate-risk patients TG: <150 mg/dL (1.70 mmol/L) for all risk categories
2018 AHA/ACC/ AACVPR/AAPA/ABC/ ACPM/ADA/AGS/ APhA/ASPC/NLA/ PCNA Guideline on the Management of Blood Cholesterol[4]	Fasting or nonfasting	LDL-C and non-HDL-C	LDL-C and non-HDL-C: ≥ 50% reduction in LDL-C in patients with clinical ASCVD, consider adding nonstatin if LDL-C > 70 mg/dL (1.81 mmol/L) and non-HDL-C >100 mg/dL (2.59 mmol/L) if very high risk ≥ 50% reduction in LDL-C in patients with LDL-C ≥ 190 mg/dL (4.91 mmol/L), consider adding nonstatin if LDL > 100 mg/dL (2.59 mmol/L) ≥ 50% reduction in LDL-C in patients with diabetes and ASCVD risk factors ≥ 30% reduction in LDL-C in intermediate-risk patients with diabetes and ASCVD risk factors ≥ 30% reduction in LDL-C in intermediate-risk patients (ASCVD risk score ≥ 7.5% to < 20%)

Table 13–7

Risk Factors for Atherosclerotic Cardiovascular Disease (ASCVD) According to the National Lipid Association (NLA)[a,7]

Risk Factor	Definition
Age (years)	Male ≥ 45; female ≥ 55
Family history of premature CHD events[b]	Male first-degree relative at < 55 years Female first-degree relative at < 65 years
Hypertension[c]	SBP ≥ 140 mm Hg DBP ≥ 90 mm Hg
Low HDL cholesterol	< 40 mg/dL (1.03 mmol/L) in males < 50 mg/dL (1.29 mmol/L) in females
Cigarette smoking	Current

▶ Step 4: Identify Patients with High-Risk Conditions:

The 2018 AHA/ACC guidelines have set a LDL cholesterol goal of a 50% reduction in those with established clinical ASCVD and recommend the addition of nonstatin therapy with either ezetimibe or a PCSK9 inhibitor when this goal and/or LDL cholesterol target of less than 70 mg/dL (1.81 mmol/L) are not achieved.

- The NLA and AACE/ACE set non-HDL cholesterol and LDL cholesterol goals at less than 130 mg/dL (3.36 mmol/L) and less than 100 mg/dL (2.59 mmol/L) for high-risk primary prevention patients and at less than 100 mg/dL (2.59 mmol/L) and less than 70 mg/dL (1.81 mmol/L) for secondary prevention patients, respectively.

▶ Step 5: Identify Patients Without Established ASCVD and Need for Risk Assessment

- The NLA and AACE/ACE have established goals for nonHDL cholesterol and LDL cholesterol of less than 130 mg/ dL (3.36 mmol/L) and less than 100 mg/dL (2.59 mmol/L), respectively, in patients considered high risk (eg, two or more CV risk factors and a 10%–20% estimated risk of ASCVD in 10 years)

متى ببلش اعطي دوا ؟

when non-HDL cholesterol: equal to or above 190 mg/dL (4.91 mmol/L)

or LDL cholesterol :equal to or above 160 mg/dL (4.14 mmol/L)

▶ Step 6: Treatment of Elevated Triglycerides

Patients with severely elevated serum triglycerides **exceeding 500** mg/dL (5.65 mmol/L) are at increased risk of pancreatitis, especially when levels are extremely elevated above 1000 mg/dL (11.3 mmol/L),So that Reducing triglycerides in these individuals becomes the primary target for intervention

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واكيد ببداية العلاج منشجع النونفارماكولوجي من رياضة وتنزيل وزن ويقلل دهون كاربوهيدرات وكحول وغيرها وبحالة اخذ ادوية خلو ببالكم انه **الجول انزله لاقل من 150**

-Niacin, fibrates, and long-chain omega-3 fatty acids (OM3FA) are the most effective agents in patients with fasting triglyceride concentrations greater than 1000 mg/dL (11.3 mmol/L).

-For patients with triglycerides 500 to 999 mg/dL (5.65–11.29 mmol/L), a triglyceridelowering agent or a statin (if no history of pancreatitis) may be reasonable.

-Bile acid sequestrants should be avoided in patients with a triglyceride value of 300 mg/dL (3.39 mmol/L) or higher as they can increase triglycerides.

-Fibrate therapy needs to be used with caution in patients with renal dysfunction

-gemfibrozil should not be used in patients with stage 4 chronic kidney disease (CKD) or greater.

-For patients with high triglycerides between 200 and 499 mg/dL (2.26 and 5.64 mmol/L), statins will generally be <u>first line</u>

<u>-</u> (FDA)approved→ (icosapent ethyl) : as adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction (MI), stroke, coronary revascularization, and unstable angina requiring hospitalization in adult patients with triglyceride levels greater than or equal to 150 mg/dL (1.70 mmol/L) and established ASCVD or DM and two or more additional risk factors for CV disease (ie, male > 55 years of age or female > 65 years of age, tobacco smoker, hypertension, low HDL cholesterol, hs-CRP > 3 mg/L, renal dysfunction, retinopathy, albuminuria, ABI greater than 0.9)**.**

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