Main author:
M. Mohsen Ibrahim, MD
Professor of Cardiology, Cairo University
President of Egyptian Hypertension Society

Writing group members (alphabetically):

M. Mohsen Ibrahim                      Cairo University
Gamela Nasr                            Suez Canal University
Ghada Youssef                          Cairo University
Mahmoud Ali                            Cairo University
Mohamed Orabi                          Suez Canal University
Nasser Taha                            Menia University
Advisory board members (alphabetically):

Ahmed Fathy Elkorey  
Alexandria University

Aziz Madkour  
Al-Azhar University

Azza Farrag  
Cairo University

Bassem Zarif  
NHI

Fathy Maklady  
Suez Canal University

Hassan Khaled  
Cairo University

Hossam Kandil  
Cairo University

Inas Shaltout  
Cairo University

Karim Said  
Cairo University

Magdy Abdel Hamid  
Cairo University

Mahmoud Hassanien  
Alexandria University

May Hassaballah  
Cairo University

Mohamed Osama  
NHI

Omar Awwad  
Ain Shams University

Ragab Abd El-Salam  
Zagazig University

Sameh Bakhoum  
Cairo University

Sameh Emil  
Military Medical Academy

Soliman Gharib  
Cairo University

Waleed Ammar  
Cairo University
Introduction

Dyslipidemia and need for guidelines.

Dyslipidemia covers a wide spectrum of plasma lipid abnormalities, including increase in total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), triglycerides (TGs), reduction in high density lipoprotein cholesterol (HDL-C), and an atherogenic triad of increased TGs, reduction in HDL-C and increase in small dense LDL particles.

Dyslipidemia can be primary due to genetic mutations affecting lipoprotein synthesis and metabolism, or secondary to specific causes such as diabetes mellitus (DM), hypothyroidism, nephrotic syndrome, chronic renal failure (CRF), pregnancy, and drugs.

Dyslipidemia (mainly increase in LDL-C) is a major independent risk factor for atherosclerotic cardiovascular disease (ASCVD) namely coronary artery disease (CAD), peripheral, and cerebrovascular disease.

In Egypt, mortality secondary to CAD is rapidly rising. According to WHO statistics (1), the age standardized mortality rates from CAD are one of the highest worldwide. One possible explanation is the high prevalence rates of CAD risk factors. Hypertension, dyslipidemia, DM, and obesity are common among Egyptians (2). Furthermore, only a minority of CAD Egyptian patients receive statin therapy (3). Despite chronic statin treatment, two-thirds of patients in the DYSIS-Egypt study had elevated LDL-C levels (4). It seems that statins are under prescribed in Egypt and when prescribed, LDL-C levels remain elevated because of inadequate dosage, interrupted treatment, and failure of follow-up.

In recent years, a number of international and regional guidelines were developed. In 2017, the Egyptian hypertension society (EHS) developed its first dyslipidemia guidelines. Being aware of the recent
developments in the field and possible limitations of international guidelines regarding their application in Egyptian community, we took the initiative of updating our guidelines. We tried to avoid some of the limitations of the international guidelines which are lengthy – some exceeding 300 pages (NICE), not easy to review by the busy practitioner. Majority use risk scoring systems such as Framingham Risk Score, MESA Risk Calculator, Reynold’s Risk Score, and SCORE which have not been tested in the Egyptian community and are not familiar to most of the Egyptian physicians.

We need a simple approach for definition and assessment of ASCVD risk, a risk scoring system best suitable for Egyptian patients and selecting more realistic therapeutic targets of lipid lowering therapy.

While preparing the new Egyptian guidelines, the writing group considered making guidelines to be short, brief and to the point, focusing on common and practical aspects in lipid management, providing up to date information, easy to apply, suitable for the Egyptian environment, cost effective, and affordable by the Egyptian health system. When possible, trying to compromise between the ideal and optimal approach in management against the minimal affordable care in a country where the majority are not health insured. Since the primary focus in prevention of ASCVD must be on lowering LDL-C and keeping it low throughout life, the role of statins and lipid lowering agents were discussed in some details in the Egyptian guidelines.

These guidelines address both the practitioners and specialists. Therefore, some basic knowledge was provided in many chapters.

The first chapter in guidelines addresses lipoprotein metabolism and types of plasma lipoproteins abnormalities. This is an area being unfamiliar to many practitioners. The second chapter discusses assessment of cardiovascular (CV) risk. At present, total CV risk assessment is the basis for appropriate management in terms of CVD prevention and therapy. Total CV risk should guide decisions on the
initiation of pharmacologic therapy and the intensity of treatment. The remaining chapters focus on therapeutic aspects and management of dyslipidemia in different populations. The availability of generic statins makes therapy of dyslipidemia affordable for the majority of patients. Implementation of these guidelines might help improve care of our cardiac patients and diminish the toll of atherosclerotic CVD in our community.

M. Mohsen Ibrahim, MD
Table of contents

Chapter 1. Lipoprotein Metabolism
  • Lipoprotein structure and function
  • Lipoprotein transport
  • Major lipoprotein abnormalities

Chapter 2. Assessment of global cardiovascular risk
  • What is meant by CV risk?
  • What are the established risk factors for atherosclerotic cardiovascular disease?
  • When to ask for risk factor screening?
  • How to estimate CV risk?
  • Who does not need Global risk assessment?
  • What are the ASCVD Risk enhancers?

Chapter 3. When to initiate statins and how to monitor statin therapy?
  • Before starting statins
    o Clinical and laboratory evaluation
    o Treatment of comorbidities
    o Lifestyle interventions and dietary modification
  • Indications of statins treatment - when to prescribe statin?
  • Initiation and intensity of statin therapy
  • Follow-up of people started on statins-Monitoring of statin treatment.
  • Statins resistance and statins intolerance
  • Statins pleotropic effects
  • Problems of Statins in Egypt

Chapter 4. What is the role of other lipid lowering agents?

Chapter 5. Management of dyslipidemia in specific groups
Chapter 6. When and how to treat hypertriglyceridemia?

Chapter 7. Non-pharmacological treatment
Chapter 1

Lipoprotein Metabolism

Lipoprotein structure and function

In blood plasma, lipids – cholesterol and triglycerides are bound to various proteins (apoproteins) to form lipoproteins (LPs). LPs vary in size, density, and lipid content, but all share the same structure, an inner water insoluble core made of cholesterol esters and triglycerides, and an outer water and lipid soluble layer of phospholipids, free cholesterol and apoproteins (Figure 1).

Apoproteins serve as ligands for tissue receptors, binding LPs to cellular receptors. LPs can be separated on ultracentrifuge to different particles, HDL and LDL are the smallest and heaviest, whereas chylomicrons and very low-density LPs (VLDL) are the largest and the lightest. Chylomicrons and VLDL (defined as triglycerides rich LPs) are rich in TGs whereas LDL and HDL are rich in cholesterol.

TGs are the body major source of energy. Fatty acids (FAs) are released from TGs through hormone sensitive lipase. FAs are utilized directly as fuel by muscles (skeletal, cardiac), or after following partial oxidation to ketone bodies in the liver by brain and other tissues.

LDL receptor (LDLR) is the preferential pathway through which LDLs are cleared from the circulation. LDLR (surface protein on liver cells) make a receptor mediated endocytosis of LDL particles, genetic mutation of this protein produces homozygous and heterozygous hypercholesterolemia.
Chapter 1. Lipoprotein Metabolism

Figure 1. (A) lipoprotein structure Source: JR Guyton. Basics of lipids and lipoprotein metabolism. Lipid clinic training program. (B) Lipoprotein Size and Density. Source: J Genest, P Libby: Braunwald Heart Disease 2012.

Lipoprotein transport

There are three pathways carrying LPs in plasma: exogenous, endogenous, and reversed cholesterol transport.

Exogenous pathway: responsible for directly carrying lipids from the intestine to the liver. Fat in diet after undergoing digestion in the small intestine is absorbed and packaged in jejunal enterocytes with apoB 48 forming chylomicrons which are secreted into the intestinal lymphatics to the thoracic duct and carried to the systemic circulation. Vascular endothelial cells in blood capillaries in muscle and adipose tissue have a lipoprotein lipase on their surface which hydrolyses TGs in chylomicrons resulting in release of fatty acids and formation of chylomicron remnants. Chylomicron remnants are removed by the liver and metabolized in hepatocytes releasing free cholesterol, TGs and amino acids which share in the formation of VLDLs (Figure 2).
Figure 2. The exogenous and endogenous lipoprotein metabolic pathways. LPL, lipoprotein lipase; FFA, free fatty acid; VLDL, very low-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; LDLR, low-density lipoprotein receptor; HL, hepatic lipase.


**Endogenous pathway:** responsible for carrying lipids as VLDLs from the liver to the periphery. In hepatocytes, cholesterol derived from chylomicron remnants in addition to cholesterol synthesized inside liver cells and cholesterol derived from LDL taken through LDL and scavenger receptors is assembled through microsomal transfer protein (MTP) with TGs, phospholipids, and apoB 100 and secreted as VLDL. VLDL carry lipids from liver to peripheral cells. VLDL formed in hepatocytes are secreted into the circulation where their TGs are hydrolyzed by lipoprotein lipase on capillary endothelium into intermediate density lipoproteins (IDL) and fatty acids. IDL is either
removed by the liver or undergoes further hydrolysis into low density lipoproteins (LDL) by hepatic lipase.

LDL carries cholesterol to peripheral tissues, and is taken by peripheral, and hepatic cells through LDL receptors present on cell membrane. The expression of LDL receptors on cell membrane is governed by cell requirements of cholesterol. Hepatic LDL receptors clear 70% of LDL from blood plasma. Excess free cholesterol in hepatocytes is oxidized to bile acids and excreted through the bile into the intestine (Figure 2).

**Reversed cholesterol transport:** cholesterol in excess of peripheral cells requirement is exported outside the cells to the extracellular space. Free cholesterol is taken by the newly formed discoid HDL particles formed from apoprotein A and phospholipids which are synthesized in the liver and intestine. In HDL particles, the enzyme LCAT (lecithin cholesterol acyl transferase) esterified free cholesterol into cholesterol ester (CE) with formation of mature HDL. CEs formed in HDL are exchanged for TGs present in TG rich lipoproteins namely VLDL, chylomicrons and IDL through LDL receptors after exchanging LDL cholesterol with TG.

**Low-density lipoproteins (LDL).**

Products of VLDL and IDL metabolism and they are the most cholesterol rich of all lipoproteins. About 40-60% of all LDLS are cleared by the liver.

**Very low-density lipoproteins (VLDL).**

They are synthesized in the liver, and transport TGs, and cholesterol to the peripheral tissues. VLDL increases with increases in hepatic free fatty acids (FFA) such as occur with high fat diet, and when excess adipose tissue releases FFAs directly into the circulation.
Major lipoprotein abnormalities.

1. Increased LDL-C.

LDL is the predominant cholesterol carrying lipoprotein (70%) in plasma. It is derived from catabolism of VLDL. It leaves the circulation mainly via LDL receptors on the surface of liver cells. Sum of LDL-C + VLDL-C = non-HDL-C which equals the total number of atherogenic particles in plasma. Non-HDL-C is more strongly related to the risk of atherosclerosis than LDL-C.

2. Decreased HDL-C.

Levels below 40 mg/dl in men and 50 mg/dl in women confers increased risk of CAD, while levels exceeding 60 mg/dl in men and 66 mg/dl in women lessen the risk of CAD. Ratio of total plasma cholesterol/HDL-C is a better predictor of risk than cholesterol alone. Ratio of 5 or less is desirable.

3. Hypertriglyceridemia.

Increased TGs >200 mg/dl is abnormal and is associated with increased risk of ASCVD. Causes of hypertriglyceridemia include genetic predisposition, diabetes mellitus, hypothyroidism, metabolic syndrome, nephrotic syndrome, and obesity.

4. Combined dyslipidemia.

Combined dyslipidemia is typically characterized by elevations in LDL-C and triglyceride levels, often accompanied by decreased HDL-C level and increased levels of small, dense LDL. This common disorder results from overproduction of hepatically synthesized apolipoprotein B in very low-density lipoproteins.
Chapter 2

Assessment of global cardiovascular risk

1- What is meant by CV risk?

This is the risk of sudden cardiac death or developing acute coronary syndrome (ACS), or stroke mostly calculated for in the next 10 years or calculated as lifetime risk (especially for those who are low risk).

2- What are the established risk factors for atherosclerotic cardiovascular disease (ASCVD)?

Risk factors for ASCVD include the following:

- Age: Males >55 years and Females >65 years.
- Diabetes mellitus (fasting blood glucose level ≥126 mg/dL, post prandial ≥200 mg/dL on 2 different occasions, and HbA1c ≥6.5%).
- Arterial hypertension (>140/90 mmHg on 3 separate readings in 3 separate occasions or patients currently on treatment).
- Total S-Cholesterol >240 mg/dL, low HDL-C (<40 mg/dL in men and <50 mg/dL in women) or high LDL-C >160 mg/dL (however, hypercholesterolemia and its related treatment decisions is correlated to the degree of baseline CVD risk of any individual, as will be shown later in this text).
- Cigarette smoking.
- Obesity (BMI ≥30 kg/m²).
- Chronic kidney disease (CKD) (GFR <60 ml/min/1.73m²).
- Family history of premature ASCVD in a first degree relative (parents, siblings, or offspring) before the age of 45 years in males and 55 years in females.
3- When to ask for risk factor screening?

ASCVD Risk factors screening should be considered in the following populations:

- All healthy men >40 years of age, and healthy women >50 years of age or post-menopausal.
- All persons who have at least one of the followings:
  - Evidence of atherosclerosis in any vascular bed.
  - Diabetes mellitus.
  - Abdominal aortic aneurysm.
  - Family history of premature ASCVD, e.g., CAD before the age of 45 years in first degree relatives.
  - Arterial hypertension.
  - Central (abdominal) obesity (waist circumference >94 cm in men and >92 cm in women) or increased body mass index (BMI ≥30 kg/m²).
  - CKD (GFR <60 ml/min/ 1.73m²).
  - Xanthomas, xanthelasmas, premature arcus cornealis, genetic dyslipidemia.
  - Offspring of patients with severe dyslipidemia.

4- How to estimate ASCVD risk?

Based on the number of risk factors (RFs) that the person has and presence of established ASCVD; 4 risk categories can be identified:

- Low risk: one or no RFs.
- Intermediate risk: 2-3 RFs.
- High risk:
  - >3 RFs.
  - Markedly elevated single risk factor, in particular TC >310, LDL-C >190 mg/dL, or BP >180/110 mmHg.
  - Patients with Familial hypercholesterolemia without other major risk factors.
Patients with DM without target organ damage, or another additional risk factor.

- Moderate CKD (eGFR 30-59 mL/min/1.73 m²).

**Very high risk:**
- Established ASCVD (clinical, or by imaging).
- DM with target organ damage or at least 3 risk factors or type 1 DM for more than 20 years.
- Severe CKD (eGFR <30 ml/min/1.73m²).
- Familial hypercholesterolemia with ASCVD, or other major risk factors.

**5- Who does not need global risk assessment?**

**Global risk assessment** is not recommended in the following populations as generally they are already at very high or high total CV risk and need active management of all risk factors without regard to risk category:

- Documented ASCVD.
- Long standing diabetes mellitus (more than 10 years in type 2 DM and longer than 20 years in type 1 DM), or complicated diabetes.
- Familial hypercholesterolemia.
- Chronic kidney disease.
- Coronary artery calcium score (specialized computed tomography (CT) technique that measure Calcium containing plaques in the coronary arteries (CAC score) >100 Agatston units.
- Markedly elevated single risk factor: TC >310 mg/dL, LDL-C >190 mg/dL, BP >180/110 mmHg.

**6- What are the ASCVD Risk enhancers?**

- Apart from the traditional major CV risk factors, there are other risk factors that could be relevant for assessing total CVD risk.
Chapter 2. Assessment of global cardiovascular risk

- Very-high-risk or very-low-risk situations do not need additional search for other risk factors for risk assessment. Risk enhancers are group of factors that may reveal the potential underlying hidden risk in apparently low-intermediate risk individuals by traditional risk calculation.
- The following risk enhancers are likely to have reclassification potential i.e., identifying high vs low risk include:

1. Psychosocial stress (social isolation, or lack of social support).
2. CT coronary calcium score (CAC)*. Coronary artery calcium score has been shown to be the most effective tool to stratify risk and improve risk estimation with the best reclassification ability as follows:
   - Score Zero: low risk; no statin therapy unless diabetic, smoker or family history.
   - Score 1-99: favors statin specially in age >55y.
   - Score ≥100: statins are indicated.
3. Atherosclerotic plaques determined by carotid artery scanning.
4. Ankle-brachial index (ABI) <0.9.
5. Physical inactivity / Sedentary life.
7. Left ventricular hypertrophy.
8. Obstructive sleep apnea.
9. Metabolic factors (such as increased ApoB, lipoprotein(a), triglycerides, or C-reactive protein, and the presence of albuminuria).
10. Conditions specific to women as risk-enhancing factors:
    - Premature menopause (before age of 40).

*Because of cost and availability, it is rarely ordered in Egyptian practice.
Chapter 2. Assessment of global cardiovascular risk

- Pregnancy-associated disorders (such as hypertension, preeclampsia, gestational diabetes mellitus, small for gestational age infant and premature delivery).
- Oral contraceptive pills.
Chapter 3

When to initiate statins and how to monitor statin therapy?

Statin therapy is one of the greatest therapeutic advances in modern medicine.

Decision to initiate statin therapy should not be taken lightly, since once started statin, intake will continue indefinitely.

Statins lower the risk of heart attack, stroke, and death in high-risk patients. Statins are mostly well tolerated; however, side effects are present in less than 10% of patients.

They decease hepatic cholesterol synthesis by inhibiting 3-hydroxy-3 methyl-glutaryl-coenzyme A (HMG, COA) reductase, which is a rate limiting step in cholesterol synthesis. This leads to up-regulated production of the cell surface LDL receptors, resulting in an increased rate of removal of LDL particles from plasma.

This chapter aims to answer two questions. First, when to initiate statins treatment and second, how to monitor and follow up patients on statin therapy.

I. Before starting statins.

A. Clinical and laboratory evaluation:
   • Aims:
     1. Assess type and severity of lipid abnormality.
     2. Diagnose and manage possible common secondary causes of dyslipidemia such as abdominal obesity, diabetes mellitus, hypothyroidism, nephrotic syndrome, hepatic disease, autoimmune disease, drug intake, or metabolic syndrome.
### Definition of metabolic syndrome

<table>
<thead>
<tr>
<th></th>
<th>Criteria</th>
</tr>
</thead>
</table>
| Abdominal obesity   | >102 cm in men  
                      | >88 cm in women                               |
| Triglycerides       | ≥150 mg/dL                                    |
| HDL-Cholesterol     | <40 mg/dL in men  
                      | <50 mg/dL in women                            |
| Fasting blood glucose| ≥110 mg/dL                                    |
| Blood pressure      | ≥130/85 mmHg                                   |

3. Identify other drugs that may interact with statins leading to statins toxicity, or to resistance to statin treatment.
4. Diagnose familial hypercholesterolemia (heterozygous).
   - **Clinical evaluation:**
     - Family and personal history of ASCVD, diabetes mellitus, kidney diseases, psychic disorders.
   - **Diet and lifestyle:** sedentary – stressful – cigarette smoking.
   - **History of medications intake and drug sensitivity:**
     - Statins  
     - Steroids  
     - Estrogens  
     - Progesterone  
     - Antipsychotics  
     - Antineoplastic-Diuretics- Amiodarone  
     - Calcium channel blockers  
     - Other drugs as immunosuppressant medications (cyclosporine), some antibacterial, and antifungal therapy (clarithromycin and itraconazole).
   - **History of muscle pains.**
   - **Physical examination:** BMI, abdominal obesity, corneal arcus, skin xanthomas, carotid, and peripheral artery disease.
   - **Laboratory evaluation - Blood testing:**
     - Blood sugar, HbA1c, urea, creatinine, TSH, and SGPT.
- Special tests in selected patients: ApoB concentration, hsCRP, and LP(a). Repeat blood testing for lipid profile after 2 weeks if the initial test is abnormal.

B. Treatment of co-morbidities.
The following conditions should be identified and corrected: smoking status, high BP, obesity, diabetes mellitus, impaired renal function, hypothyroidism, autoimmune disease, and depression.

C. Lifestyle interventions and dietary modification.
In absence of need for immediate statin therapy, a period of 3-6 months of lifestyle intervention is recommended aiming at body weight reduction if obese, low saturated fat and low cholesterol diet (daily cholesterol intake should be <300 g) and physical exercise (at least 150 minutes/week of moderate exercise such as brisk walking).

II. Indications of statins treatment - when to prescribe statins?

1. Primary prevention: (in individuals without clinical ASCVD).
Statins are given for primary prevention if lifestyle modification fails to lower LDL-C to the recommended levels.
In asymptomatic patients with high LDL-C, the decision to initiate statins for primary prevention is based upon the level of LDL-C and the patient's global atherosclerotic CV risk profile.

The following are indications of statins for primary prevention:
   a. Elevated LDL-C >190 mg/dL in two estimations in absence of ASCVD risk factors.
   b. Elevated LDL-C >160 mg/dL in patients with 2-3 ASCVD risk factors.
c. Elevated LDL-C >130 mg/dL in patients with CKD, >3 ASCVD-RFs. or diabetes mellitus.
d. LDL-C marginally high (130-159 mg/dL) in intermediate risk individuals (2-3 risk factors). Consider the level of risk factor namely age (>65 years), severity of hypertension, smoking, CKD, family history, and low HDL-C.

2. **Secondary prevention:** (in patients with established ASCVD). Statins are given to all patients. The intensity of statin treatment depends upon the level of risk, the possibility of sudden cardiac death, need for urgent hospitalization or development of acute myocardial infarction or stroke. In less urgent situations, assessment of the global ASCVD risk profile, and predicting the possibility of developing a major CV event (ACS, MI, stroke) or death in the next 10 years will determine the intensity of statin therapy.

### III. Initiation and intensity of statin therapy.

- **Definition of intensity of statin treatment:**
  - High intensity: aiming at lowering LDL-C by ≥50%, or reach an LDL-C <70 mg/dL.
  - Moderate intensity: lowering LDL-C by 30-49%.
  - Low intensity: lowering LDL-C by less than 30%.

- **Indications of immediate (once diagnosed) high intensity statins:**
  - In patients with ACS (acute MI, unstable angina), recent or acute stroke, statins are given in the maximal tolerated dose without delay. Lifestyle intervention should proceed in parallel.
Chapter 3. When to initiate statins and how to monitor statin therapy?

- Complicated type 2 DM, or diabetics more than 20 years duration should also have high intensity statins.
- In all other conditions, statins are started at lower to moderate dose while LDL-C is monitored at 3-6 months.
- Dose of statin is increased gradually to reach the target LDL-C level.
- Total CV risk will guide decision on the intensity of statin treatment.

- **Moderate intensity statin** therapy is indicated in adults with DM (uncomplicated, less than 10 years duration) and in patients with LDL-C >190 mg/dL in absence of ASCV risk factors or LDL-C >160 mg/dL in presence of risk factors or LDL-C >130 mg/dL in presence of stable chronic ASCVD.

- **Classification of statins:**

  1. High intensity: aiming at least 50% reduction in LDL-C.

    Examples:
    - Atorvastatin 40-80mg daily.
    - Rosuvastatin 20-40 mg daily.

  2. Moderated intensity: aiming at 30-49% reduction in LDL-C.

    Examples:
    - Atorvastatin 10-20mg daily.
    - Pitavastatin 1-4 mg daily.
    - Rosuvastatin 5-10 mg daily.

  3. Low intensity statin therapy:

    - Simvastatin 20-40 mg daily.
    - Pravastatin 40-80 mg daily.
Expected low-density lipoprotein cholesterol reductions for combination therapies. LDL-C = low-density lipoprotein cholesterol; PCSK9 = proprotein convertase subtilisin/kexin type 9. Adapted from Mach et al.

- For low and moderate risk patients, if LDL-C level fails to reach the goal after 6 months of lifestyle interventions, then a low/moderate intensity statin therapy is initiated.
- Statins are started at low dose if there is significant renal impairment, in the elderly, the potential of drug interaction, and/or history of statins intolerance. Then the dose is titrated upwards to achieve LDL-C treatment goals.
- In patients with CKD (eGFR <30 ml/min/m²), the recommended statins are atorvastatin, pitavastatin, and fluvastatin which are excreted through hepatic metabolism.
Chapter 3. When to initiate statins and how to monitor tatin therapy?

- Target LDL-C

<table>
<thead>
<tr>
<th>Risk profile</th>
<th>Definition of risk profile</th>
<th>Target LDL level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk patients</td>
<td>No or one RF</td>
<td>140-150 mg/dL</td>
</tr>
<tr>
<td>Intermediate risk patients</td>
<td>2-3 RFs</td>
<td>110-120 mg/dL</td>
</tr>
<tr>
<td>High risk patients</td>
<td>- &gt;3 RFs or</td>
<td>&lt;90 mg/dL</td>
</tr>
<tr>
<td></td>
<td>- DM or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- CKD or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Chronic stable ASCVD</td>
<td></td>
</tr>
<tr>
<td>Very high-risk patients</td>
<td>- ACS or</td>
<td>&lt;70 mg/dL*</td>
</tr>
<tr>
<td></td>
<td>- Stroke or</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Acute atherosclerotic vascular event</td>
<td></td>
</tr>
<tr>
<td></td>
<td>despite statin treatment</td>
<td></td>
</tr>
</tbody>
</table>

* Achievement of LDL levels to less than 55 mg/dl may be recommended if economically feasible.

IV. Follow-up of people started on statins - monitoring of statin treatment.

- Blood lipid profile should be done 6-8 weeks after initiation of statin therapy, and then every 12 months after reaching the target LDL-C.
- Lifestyle measures: healthy, low saturated fat, low cholesterol diet, regular physical exercise, discontinuation of smoking, and weight reduction if obese, should be stressed in parallel with statin therapy.
- In high-risk patients, if LDL-C did not reach the target level after 3 month of intensive statin treatment, additional lipid lowering agent is prescribed.
- In patients who cannot take statins because of side effects, muscle or liver toxicity, dose of statin is reduced or given on alternative days.
- Statins are discontinued if symptoms persist in patients with persistent elevation of muscle and/or liver enzymes.
- In presence of muscle symptoms (myalgia), pain, tenderness, stiffness, rigidity, spasms, serum CK should be estimated. If CK is elevated >10 times the upper limit of normal, statins are discontinued. If CK elevation is 3-10 times upper limit of normal, testing should be repeated within 2 weeks, if still elevated, dose of statin is reduced to one half, and the test is repeated after 8-12 weeks. If CK did not change, continue statin at half dose. If exceeds 10 times the upper limit of normal, discontinue statin and replace it with another lipid lowering drug.
- In presence of signs and symptoms of liver toxicity (e.g., nausea, vomiting, jaundice, fatigue, weakness, upper abdominal pain, tender liver), estimate blood level of liver enzymes (transaminases; SGOT), if elevated more than three times the upper limit of normal, discontinue statins. If elevated less than 3 times, repeat the test, and continue statin at half the dose.

**Statin resistance and statin intolerance.**

- **Definition of statin resistance.**

  Refractory elevation of LDL-C despite aggressive statin therapy.

- **Causes:**

  1. Lack of patient's compliance. Patient is not taking statins at the recommended dose, or interrupting treatment because of side effects, intolerance, and cost of chronic treatment. This leads to pseudo-resistance.
  2. Drug interaction: intake of medication that might interfere with statins action or can cause dyslipidemia such as antipsychotics, corticosteroids, immune suppressive drugs, and amiodarone treatment.
3. Unhealthy lifestyle, ignoring dietary recommendations. Diet can have a substantial effect on lipid levels.

4. Genetic and other factors: the resistance to statins can be related to differences in drug absorption, drug transport, intrahepatic drug metabolism, and drug excretion mechanisms. Not only genetic but environmental factors can influence the LDL-C response to statins. Patients with hypertension, smokers and inflammation have a smaller statin-induced LDL-C reduction. In inflammatory states, higher concentrations of statins may be required.

5. The resistance to statins has been associated with polymorphism in a number of genes, but there is no evidence to advocate pharmacokinetic testing before initiating therapy with statins. Testing for LP(a) elevation is recommended in patients with statin resistance and positive family history or ASCVD and normal lipid profile.

**Management of statins resistance.**

1. Exclude pseudo resistance and ensure that the patient is compliant to statins treatment and dietary recommendations.

2. Discontinue medications that might interfere with statins actions.

3. Increase statin dose.

4. Estimate LP(a) in presence of family history.

5. Replace the statin with another statin or add other lipid lowering agent. Add ezetimibe, if fail, add PCSK9 inhibitor.
## Reasons for non-adherence to treatment (WHO).

<table>
<thead>
<tr>
<th>Category</th>
<th>Reasons</th>
</tr>
</thead>
</table>
| A. Patients       | - Perceived lack of effect  
                    | - Poor health literacy  
                    | - Physical impairment (vision, cognition)  
                    | - Mental health conditions (depression, anxiety)  
                    | - Social isolation  
                    | - Cognitive impairment (dementia) |
| B. Medical condition | - Complexity of medical treatment  
                    | - Impact of comorbidities (e.g., depression)  
                    | - Polypharmacy due to multiple comorbidities |
| C. Therapy        | - Polypharmacy  
                    | - Side effects |
| D. Socio economic | - Out of pocket cost  
                    | - Difficult access to pharmacy  
                    | - Lack of social support  
                    | - Homelessness |
| E. Health system  | - Poor communication  
                    | - Not automatic refills  
                    | - No patient’s assistance programs |

## Statin intolerance.

The most common presentation of statins intolerance is muscle symptoms (myalgia) which can occur in up to 15% of treated patients. In most instances, the symptoms are mild, and completely reversible shortly after the statin is stopped.

### Factors associated with increased risk of statin intolerance:

A. Patients related factors:
   1. Advanced age (>80 y).
   2. Female sex.
3. Pre-existing neuromuscular conditions.
4. Known history of myopathy or family history of myopathy syndrome.
5. Pre-existing liver and/or kidney disease.
6. Untreated hypothyroidism.
7. Genetic factors: polymorphisms regulating liver cytochrome enzyme pathways.

B. Exogenous and potentially modified factors:
   1. High-dose statin therapy.
   2. Excessive exercise.
   3. Drug interactions: gemfibrozil, antipsychotics, amiodarone, verapamil, cyclosporine, macrolide antibiotics, and azole antifungal drugs.
   4. Excessive grapefruit juice intake.

**Residual risk.**

Residual risk is the risk of death, MI, and stroke, which persists despite ongoing dyslipidemia treatment and achievement of therapeutic targets for LDL-C. Residual risk is linked to a number of risk factors including factors related to other patterns of dyslipidemia rather than LDL, like [Lp (a), TG] or other non-dyslipidemia risk factors like arterial hypertension, hyperglycemia, inflammatory disease, and inappropriate lifestyle. Risk remains even in individuals who follow intensive statin therapy and have achieved LDL-C concentration to the target level.

Some patients could benefit from a decrease in residual risk through an earlier introduction of statin treatment, more intensive therapy, and combination therapy. Correction of other ASCVD risk factors, and psychological stress is important.

Recently it has been demonstrated that non-HDL cholesterol and ApoB are better predictors of future risk of myocardial infarction, and death than LDL-C in statin treated patients.
Estimation of non-HDL cholesterol and ApoB is recommended if affordable, and laboratory facilities are available. It might replace LDL-C estimation in management of dyslipidemia.

**Treatment of statins intolerance**

1. Make sure that there is no reversible cause such as drug interactions, and hypothyroidism: maximize lifestyle interventions.
2. With mild symptoms, reduce the dose of statin.
3. With intolerable symptoms, stop the statin. When symptoms resolve, attempt rechallenge (give statin again) with low dose of same or different statin drug.
4. Give statin intermittently, 2-3 times/week or every other day.
5. Use an alternative statin plus ezetimibe, or bile acid sequestrants.

**V. Non-lipid (pleotropic) effects of statins.**

1. **Anti-inflammatory effects**
   - Decrease proinflammatory cytokine production.
   - Decrease CRP production.
   - Reduce plaque inflammation independent of the effects on serum cholesterol.

2. **Antithrombotic effects**
   - Inhibit tissue factor expression and activity.
   - Increase fibrinolytic activity (decrease PAI-1).
   - Decrease platelet activity and aggregation.

3. **Effects on endothelial function**
   - Inhibit superoxide generation.
   - Inhibit endothelin synthesis.
   - Increase expression and activity of NO synthesis.

4. **Effects on smooth muscle cells (SMC) proliferation and migration**
   - Inhibition of proliferation and migration of vascular SMCs.
Clinical relevance of pleotropic effects of statins

- Benefits of statins in patients with low LDL-C concentration suggests actions other than lipid lowering effects only.
- CAD risk reduction occurred much earlier (30 days) than expected based on lipid lowering effects only.
- Atherosclerotic plaque stabilization reduces plaque inflammation independent of the effects on serum cholesterol.

Anti-ischemic actions

- Anti-anginal properties equivalent to the standard pharmacologic therapy. Reduce the duration of transient myocardial ischemia and improve exercise time with significant reduction in the frequency of angina episodes.
- Myocardial perfusion imaging (dipyridamole stress testing) showed smaller perfusion defect after a short period of statin treatment. Changes in myocardial perfusion did not correlate with improvement in cholesterol profile.

Mechanism of anti-ischemic actions of statins

- Early anti-ischemic effects: possibly secondary to improvement in endothelial function and coronary flow through increasing nitric oxide and decreasing endothelin-1.
- Late improvement may be secondary to regression of atherosclerosis and reduction in size of atherosclerotic plaque. High dose statin (rosuvastatin 40 mg/day) for 2 months resulted in atheroma volume shrink in IVUS. However, the predominant benefit of statins is through stabilization of lipid laden plaques rather than regression of atherosclerosis.

VI. Problems of Statins in Egypt.

1. Limited data. Only a single study; Dyslipidemia International Study (DYSIS), is an Egyptian cohort (2013), showed that the
goal LDL-C levels were not achieved by 67.2% of Egyptians, rising to 72% in both high and very high-risk patients. Despite chronic statin treatment, two-third of patients in the DYSIS-Egypt study had elevated LDL-C.

2. Unawareness of medical community with global CV risk assessment & indications of statins (therapeutic inertia).

3. Fear of statins side effects.

4. Lack of monitoring of lipid profile.

5. Statins given in inadequate dosage.


7. Discontinuation of statins after LDL-C lowering.

Chapter 4

What is the role of other lipid lowering agents?

Ezetimibe (cholesterol absorption inhibitor in the intestinal tract)

- It lowers LDL-C by 15-25% (65%-75% when combined with maximal statin dose).
- No dosage adjustment is necessary in patients with mild hepatic impairment or mild-to-severe renal insufficiency.
- The addition of ezetimibe to statin therapy does not appear to increase the incidence of elevated CK levels beyond what is noted with statin treatment alone.
- Generic combination of statin and ezetimibe rendered the cost-effectiveness of such combination favorable.
- It is a safe drug.
- Should be tried before PCSK9 inhibitors.
- Dose 10 mg/day.
- Indications for Ezetimibe.
  - patients who cannot achieve goal on maximum tolerated dose of statins.
  - patients who are intolerant to statins.

PCSK9 inhibitors (Alirocumab, Evolocumab)

- Monoclonal antibodies that inhibit PCSK9 which is a protein that regulates recycling of LDL-C receptors.
- Reduce LDL-C by 60% - 75% when combined with statins and 85% when combined with statins and Ezetimibe.
- Given every 2-4 weeks by subcutaneous injection after failure of maximal dose statin and ezetimibe to achieve LDL-C target in very high-risk patients.
• No known adverse effects of very low LDL-C concentrations [e.g., <1 mmol/L (40 mg/dL)].

Adding PCSK9 in:

- High risk patients who cannot achieve goal on maximum tolerated dose of statins plus Ezetimibe e.g., patients with recent ACS if goal not achieved in 4-6 weeks.
- Patients who are intolerant or those with significant dyslipidemia with persistently elevated LDL-C level despite maximally tolerated statin treatment plus Ezetimibe.
- Cost is a major limitation of its use at present.
- They may be cost effective in:
  o Patients with clinical CVD not achieving LDL-C targets.
  o Familial dyslipidemia with CVD or significant risk factors.
  o Patients with very high levels of LDL-C.
- Dose: Alirocumab: initial dose is 75 mg subcutaneously (SC) every 2 weeks up to maximal dose of 150 mg SC every 2 weeks. Evolocumab:140mg subcutaneously every 2 weeks or 420 mg subcutaneously once a month.

**Bile acid sequestrants**

• They inhibit bile acid absorption from intestine.
• They reduce LDL-C by 15-25% but increase plasma TGs.
• Examples: cholestyramine, colesvelam. Colesevelam has a glucose lowering effect.
• Should be administered 4 hours before or 1 hour after meals.
• Can interact with many drugs including statins.
• Colesevelam is well tolerated can be given with statins and other drugs.
• Safe to be used in pregnant women and children.
Chapter 4. What is the role of other lipid lowering agents?

- Dose: Daily dose of 24 g of cholestyramine, 20 g of colestipol, or 4.5 g of colesvelam.

**Fibrates**

- Used primarily for TGs lowering and occasionally for increasing HDL-C.
- Routine use of these drugs in CVD prevention is not recommended.
- Reduce serum TG level and increase HDL-C through activation of peroxisome proliferator activated receptor–α (PPAR-α) and lipoprotein lipase (LPL).
- Examples: Fenofibrate, Bezaﬁbrate, and Gemﬁbrozil.
- Fibrates are the most potent TGs lowering agents with reductions of 45-55%.
- In T2DM they reduced non-fatal MI by 21% but not mortality.
- Routine monitoring of the liver enzymes is recommended.
- Not suitable for patients with gall bladder disease, pregnancy, lactation, liver disease and severe kidney diseases.
- May be used in primary prevention in high-risk patients with statin if triglyceride level is >200 mg/dl.
- Fenofibrate dose is 0.1 g three times per day.

**Niacin (Nicotinic acid).**

- Reduces TGs by 20-30% in a dose-dependent fashion.
- Reduces TGs by reducing lipolysis and depress TGs synthesis in the liver.
- Inhibits hormone sensitive lipase in adipose tissue, thus decreasing the supply of free fatty acids necessary for TG synthesis.
- Niacin raises HDL levels significantly while decreases VLDL and LDL levels.
Chapter 4. What is the role of other lipid lowering agents?

- The most common side effects of niacin are:
  1. Skin vasodilatation (flushing and itching).
  2. Reversible increase in plasma levels of liver transaminases (AST and ALT).
  3. Its combination with statins may lead to an increased risk of myopathy and rhabdomyolysis.
- Two large trials have shown no beneficial effect and an increased frequency of serious adverse effects with niacin therapy.

**New anti-dyslipidemic drugs**

These are new agents that proved effective in correcting dyslipidemia.

**Bempedoic acid**

- Is an oral pro-drug, activated in the liver to inhibit ATP-citrate lyase (ACL), which acts upstream of HMG-CoA reductase. This upregulates LDL-R, increasing LDL-C clearance. Dose is 180 mg PO once daily in combination with maximally tolerated statin therapy.

**Lomitapide**

- Lomitapide inhibits the microsomal triglycerides transport protein.

- It is an oral drug that is indicated in patients with homozygous familial hypercholesterolemia to reduce LDL-C, total cholesterol, and non-HDL-C as an adjunct to statins and low-fat diet.

- It should be started at a low dose PO once daily, and escalated gradually based on tolerability and response, while liver functions should be checked before starting the drug and during therapy. The maximal dose not to exceed 60 mg/day.

- Side effects include nausea, vomiting, diarrhea, and abdominal pain.
Chapter 4. What is the role of other lipid lowering agents?

**Mipomersen**

- Antisense oligonucleotide targeted at human apolipoprotein B-100, leading to reduction of synthesis of atherogenic lipids including LDL-C.

- It is given by subcutaneous injection in patients with homozygous familial hypercholesterolemia as an adjunct to lipid lowering drugs and diet.

- Side effects are reactions at the injection site, and steatosis.

**CETP inhibitors**

- Cholesterol ester transfer protein (CETP) inhibition increases concentration of HDL-C (by ≥100%), and decreases concentration of LDL-C.

- Examples: Anacetrapib, and Evacetrapib.

- The beneficial effect of these agents on the reduction of ASCVD events is not yet proven.

**Icosapent ethyl (IPE)**

- Synthetic derivative of the omega-3 fatty acid eicosapentaenoic.
- An omega-3 poly unsaturated fatty acid that reduces synthesis and enhances clearance of triglycerides.
- Very effective in lowering plasma triglycerides with additional beneficial effects on the atherosclerotic pathway through improvement in lipid oxidation, inflammation, plaque volume, membrane stabilization and dyslipidemia.
- Dose: 2 g twice /day.
- IPE plus statins were associated with slowed atherosclerotic plaque progression.
Chapter 4. What is the role of other lipid lowering agents?

**Inclisiran**

Small RNA molecule that blocks the transcription of PCSK9 reducing its level in hepatocytes resulting in an increased expression of LDL-C receptors in hepatocyte membrane. Dosing is twice a year.
Chapter 5

Management of dyslipidemia in special groups

A. Diabetes Mellitus

- Atherogenic dyslipidemia (elevated TG and LDL-C concentrations, low HDL-C concentration) occurs in patients with diabetes and metabolic syndrome.

- DM is an independent risk factor for ASCVD, whether it is type 1 or type 2 DM.

- Primary prevention of ASCVD is indicated for patients with DM older than 40 years, regardless of their risk assessment. People with IGT are at a significant risk of development of ASCVD.

- Statins are recommended for all patients with DM but there is not enough evidence on whether statin therapy is beneficial for primary prevention in diabetic patients 20-39 years of age.

- There is benefit of statins treatment irrespective of the pre-existing serum LDL-C level.

- LDL-C level should be reduced by $\geq 50\%$ from baseline values to absolute values $<90$ mg/dL using moderate-high intensity statin therapy. If the goal is not reached, ezetimibe (10 mg/day) may be added.

- There is a possible clinical benefit from TG lowering therapy as an add on to statin treatment in patients with atherogenic dyslipidemia.

- High intensity statin is indicated in patients with DM if they have risk modifiers (albuminuria, low eGFR, retinopathy, neuropathy).
B. Acute coronary syndromes.

- Patients younger than 75 years with ACS, should receive/continue high intensity statin therapy or maximally tolerated dose to achieve LDL-C goal.

- If LDL-C goal is not achieved despite maximally tolerated dose of statin, ezetimibe should be added, and if the goal is still not achieved after 4-6 weeks, PCSK9 inhibitor combination should be considered.

- Patients older than 75 years with ACS, should receive/continue high intensity statin therapy to achieve LDL-C goal, but only after consideration of the drug adverse effects, patients’ frailty, life span and possibility of drug-drug interactions.

- In patients who had recurrent attacks of ACS despite reaching an LDL goal (<70 mg/dL), statins should be upgraded to a higher intensity, and ezetimibe should be added.

C. Chronic kidney disease.

- Patients with CKD are at a high/very high risk of ASCVD.

- Patients with non-dialysis dependent CKD and elevated LDL-C level, should initiate/continue statin therapy. If LDL-C is not at goal, ezetimibe may be added to statins.

- It is not advisable to initiate statins in patients with dialysis-dependent CKD.

- Patients on dialysis who are already taking statins, should continue statin therapy.

- Medications excreted via hepatic metabolism (Atorvastatin, Fluvastatin, Pitavastatin, Ezetimibe) are preferred in renal failure and CKD.
- For patients with kidney transplantation who are in need for statin therapy, refer to a nephrology consultant.

**D. Elderly (>75 years).**

- The recommendations for initiation of anti-dyslipidemic therapy in patients with an ASCVD are the same for all age groups.
- The treatment goal for LDL cholesterol is the same for all age groups.
- Elderly patients (>75 years) should be managed cautiously because in addition to the limited evidence of drug benefits, the incidence of complications and drug side effects are higher.
- Statin therapy is effective for the prevention of ASCVD in older patients, thus it is the drug of choice. It should be initiated at low doses and up titrated gradually to the desired LDL goal.
- Intermediate dose of statin is reasonable in the elderly because there is a higher risk of side effects with high statin doses.
- Primary prevention of ASCVD in the elderly patients is indicated only when their cardiovascular risk is at least intermediate/high.
- Insufficient evidence to support targets for primary prevention in older patients, LDL-C target < 100 mg/dl may seem reasonable.
- Frailty, polypharmacy and muscle symptoms are factors to consider in older patients.
- Statins are recommended for older people with ASCVD in the same way as for younger patients.
- Initiation of statin treatment for primary prevention in older people aged ≥ 70 may be considered, if at high risk or above.
Chapter 6

When and how to treat Hypertriglyceridemia?

- Hypertriglyceridemia is defined as fasting serum triglyceride (TG) level ≥200 mg/dL.

- For screening purposes, non-fasting samples are as good as fasting ones.

- CV risk is increased when fasting TGs are >150 mg/dl.

- Use of drugs to lower TGs levels may only be considered in high-risk patients when TGs are >200 mg/dl, and TGs cannot be lowered by lifestyle measures.

- Persistently elevated hypertriglyceridemia (>3 times) is associated with increased cardiovascular risk. Hypertriglyceridemia remains a risk factor for CVD even after achieving LDL targets, they may act directly, or by changing LDL population to small dense more atherogenic particles.

- Management of moderately elevated TG (201-499 mg/dL) is based on finding a secondary cause (obesity, diabetes mellitus, metabolic syndrome) and applying lifestyle modifications (weight reduction, control of hyperglycemia, moderate to high intensity exercise, and reduction of dietary fats and carbohydrates).

- Available pharmacological interventions include statins, fibrates, PCSK9 inhibitors and icosapent ethyl.

Primary prevention

- Statins are indicated for primary prevention of ASCVD in patients with moderate hypertriglyceridemia (≤500 mg/dL) when the 10-year risk of atherosclerotic cardiovascular events is at least intermediate.
- Statins can reduce triglycerides levels by 20-30%.

- Fenofibrates may be considered in high-risk patients with persistently elevated triglycerides (>200 mg/dL) despite statin therapy.

**Secondary prevention**

- Statins are indicated in patients with established ASCVD and hypertriglyceridemia.

- When statins fail to control hypertriglyceridemia in patients with established ASCVD, icosapent (purified eicosapentanoic acid) should be given as it was shown to reduce the cardiovascular mortality.

- Since icosapent ethyl is expensive and non-affordable to most of the Egyptian patients, we may consider adding fenofibrates instead of adding icosapent.

- Dose of icosapent ethyl is 2 g/12 hours.

- Patients with severe hypertriglyceridemia (TG level ≥500 mg/dL) are at a higher risk of pancreatitis. Fibrates, niacin, or omega-3-fatty acids may be considered.

- Adding fenofibrate to statin therapy is safer than adding gemfibrozil because the risk of severe myopathy is lower in the former.

- Studies did not show a cardiovascular prognostic benefit of treating isolated hypertriglyceridemia.
Chapter 7

Non-Pharmacological treatment for dyslipidemia

- Nutritional and dietary therapy, weight loss, exercise, should be used initially in appropriately selected patients to manage dyslipidemia.
- Patients are advised to adopt a diet that is high in fruits and vegetables, whole grains, fish, lean meat, low-fat dairy, legumes, and nuts, with lower intake of red meat, saturated and trans fats, sweets, and sugary beverages (Table 1). Saturated fat should comprise no more than 5%–6% of total calories (5).

Table 1. Nutrient Composition of the Therapeutic Lifestyle Change Diet

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Recommended Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated fat(^a)</td>
<td>&lt;5%–6% of total calories</td>
</tr>
<tr>
<td>Polyunsaturated fat</td>
<td>Up to 10% of total calories</td>
</tr>
<tr>
<td>Monounsaturated fat</td>
<td>Up to 20% of total calories</td>
</tr>
<tr>
<td>Total fat</td>
<td>25%–35% of total calories</td>
</tr>
<tr>
<td>Carbohydrate(^b)</td>
<td>50%–60% of total calories</td>
</tr>
<tr>
<td>Fiber</td>
<td>20–30 g/d</td>
</tr>
<tr>
<td>Protein</td>
<td>Approximately 15% of total calories</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;200 mg/d</td>
</tr>
<tr>
<td>Total calories (energy)(^c)</td>
<td>Balance energy intake and expenditure to maintain desirable body weight/prevent weight gain</td>
</tr>
</tbody>
</table>

\(^a\)Trans fatty acids are another low-density lipoprotein–raising fat that should be kept at a low intake. \(^b\)Carbohydrates should be derived predominantly from foods rich in complex carbohydrates, including grains (especially whole grains), fruits, and vegetables. \(^c\)Daily energy expenditure should include at least moderate physical activity (contributing approximately 200 kcal/d).
Chapter 7. Non-pharmacological treatment

Efforts should be made to replace dietary saturated fat with polyunsaturated and monounsaturated fats, as this has been shown to lower LDL-C and triglycerides. Polyunsaturated fat intake has been shown to promote atherosclerosis regression (6).

- Physical activity, including aerobic and resistance exercise, is recommended in all patients. Regular moderate exercise prevents development and progression of atherosclerosis and benefits dyslipidemia and reduces vascular symptomatology in patients with documented CVD. The mechanism of benefits is derived from maintenance of body weight, blood pressure control, and insulin resistance and dyslipidemia management, all of which promote endothelial stabilization and vascular health.

- For all obese patients (body mass index ≥30) and for overweight patients (body mass index ≥25) who have additional risk factors, sustained weight loss of 3%–5% or greater reduces ASCVD risk.

- Prior to the start of treatment, there should be a risk discussion between the patient and the clinician. Topics for discussion include the following:
  - Potential for ASCVD risk reduction benefits.
  - Potential for adverse effects and drug–drug interactions.
  - Heart healthy lifestyle and nutrition education.
  - Patient preferences.
إرشادات للمرضى

توجد العديد من النصائح والإرشادات التي يوصى بها الأطباء في حال كان الفرد مصابًا بارتفاع مستوى الدهون في الدم أو إذا امتلك العديد من عوامل الخطر التي تؤدي لذلك، بما فيها أتباع نمط حياة صحي؛ يتضمن تناول الغذاء الصحي، والحرص على ممارسة النشاط البدني، بالإضافة إلى الإقلاع عن التدخين، والتخفيض من الإجهاد، والوصول إلى وزن مثالي.

فقدان الوزن الزائد

يرتبط الوزن الزائد بارتفاع خطر وجود نسبة مرتفعة من الكولسترول الضار ونسبة منخفضة من الكولسترول المفيد، لذلك يمكن تحقيق صحة الفرد في حال كان يعاني من الوزن الزائد أو السمنة من خلال السعي للوصول إلى وزن مثالي، وقد وُجد أن خسارة الوزن بنسبة ثلاثة إلى خمسة بالمئة من الوزن الكلي للجسم يخفض نسبة الكولسترول الضار ويرفع نسبة الكولسترول المفيد، وتแจร الإشارة إلى أنه يوصى بفقدان ما نسبته 5-10% من الوزن في غضون 6 أشهر.

ممارسة النشاط البدني

إن ممارسة النشاط البدني باعتدال قد يساهم في رفع مستوى الكولسترول المفيد في الدم، وحقيقةً يوصى بممارسة التمارين الرياضية لمدة ثلاثين دقيقة خمس مرات الأسبوع أو ممارسة التمارين الهوائية الشديدة لمدة عشرين دقيقة ثلاث مرات الأسبوع، وإن ممارسة النشاط البدني لفترات قصيرة عدة مرات في اليوم قد تساهم في فقدان الوزن، ويمكن أن يضمن النشاط البدني المشي لفترة معينة كل يوم.

الابتعاد عن التدخين

يعتبر التدخين أحد عوامل الخطرة التي تؤدي إلى الإصابة بأمراض القلب، حيث يخفض التدخين من مستوى الكولسترول المفيد، وحقيقةً أن الإقلاع عن التدخين فوائد جمعة سواء كانت لحظية أو طويلة الأمد؛ إذ تبدأ مستويات الكولسترول المفيد بالارتفاع في غضون ساعات قليلة من الإقلاع عنه، كما أن ذلك يقلل من خطر الإصابة بنوبة قلبية؛ لما للكولسترول المفيد من دور في الحماية من الإصابة بأمراض القلب؛ خاصة لدى النساء؛ اللائي عادة ما يكون لديهن مستويات أعلى من الكولسترول من تلك التي لدى الرجال؛ وبسبب التنبؤ أن الدراسات لم تثبت تأثير التدخين على رفع الكولسترول الضار (LDL) بعد بشكل قاطع.
التخفيض من الإجهاد

إن الإجهاد من أهم الأمور التي تؤثر سلباً على جسم الإنسان من نواحي عدة؛ منها أنّه قد يرفع من مستويات الكوليسترول، وقد يحدث ذلك بطريقة بيولوجية مباشرة أو طريقة غير مباشرة من خلال تبني عادات غير صحية كوسيلة للتعامل، وفي الواقع يعد التحكم بالإجهاد أمرًا فريديًا؛ حيث يتفاعل الناس بطرق متنوعة مع الضغوطات المختلفة، كما أنّ تجاربهم السابقة أيضًا تأثير على كيفية استجابتهم، ويمكن إتباع العديد من النصائح والإرشادات للتحكم بالإجهاد، والتي يمكن بيانها فيما يلي:

- اتباع نظام غذائي صحي غني بالفاكهة والخضروات.
- ممارسة التمارين الرياضية بشكل دوري.
- ممارسة الأنشطة التي تركز على التأمل والاسترخاء.
- المحافظة على نظام حياة صحي يزن ما بين العمل والأمور الحياتية الأخرى.
- طلب المساعدة من الآخرين في القيام ببعض الأمور كالأعمال المنزلية.
- قضاء بعض الوقت مع الأصدقاء والعائلة، إضافة إلى تخصيص وقت لممارسة الأمور المحببة لدى الشخص.
- تطوير عادات نوم جيدة، مثل عدم أخذ الأجهزة الإلكترونية إلى غرفة النوم.

الفحص الدوري لمستويات دهنيات الدم

يعتبر فحص مستوى البروتينات الدهنية (بالإنجليزية: Lipoprotein Profile) من الفحوصات الادارية المهمة التي ينص عليها الإجراء للحصول على نماذج عام عن صحة الجسم وقياس مستوى الكوليسترول فيه، حيث يتم إجراء هذا الفحص من خلال أخذ عينة دم لتم تحليلها وقياس مستوى الكوليسترول في أنواعه المختلفة بالإضافة إلى مستوى الدهون الثلاثية.

ومن الجدير بالذكر أن التوصيات بشأن العمر الذي ينص البديل فيه بإجراء هذا الفحص والفرصة الزمنية التي يجب عادةّ تكريم الفحص مختلفًا من مكان لأخر، ولكن عادةً ما ينصب في إجراء الفحص كل خمس سنوات تقريبًا، وتقل هذه الفترة للأفراد الذين يمتلكون مستويات دهون قريبة من تلك التي تتطلب علاجًا، في حين تزداد الفترة للأفراد الذين تكون مستويات الدهون لديهم طبيعية عند إجراء الفحص بشكل متكرر وفي نفس الوقت لا يملكون خطرًا مترادًا لارتفاع هذه المستويات، ومن أكثر التوصيات شيوعًا للفحص الدوري لدهنيات الدم ما يأتي:
البدء بالإجراء الفحص الدوري لدهنيات الدم كل خمس سنوات من عمر 35 سنة للذكور و45 سنة للإناث في حال كان الشخص غير معرض للإصابة بأمراض القلب والشرايين. البدء بالإجراء الفحص الدوري لدهنيات الدم في عمر ما بين 25-30 عامًا للذكور وما بين 30-35 عامًا للإناث في حال كان الشخص معرضًا لأحد عوامل الخطر الأخرى للإصابة بأمراض القلب والشرايين؛ مثل الإصابة بالسمنة، والإصابة بمرض السكري، والإصابة بارتفاع ضغط الدم: وفي حالة التدخين، بالإضافة إلى وجود تاريخ عائلي للإصابة بأمراض القلب والشرايين.

علاج ارتفاع مستوى الدهون في الدم طبيعيًا بفقدان الوزن الزائد:

ممارسة الرياضة بشكل منتظم طريقة رائعة لتحقيق التوازن في مستوى الكوليسترول في الدم، حتى لو كنت بديعاً، وإذا كنت بديعاً ثم خسرت ما لا يقل عن 5-10% من الدهون في الجسم فإنه يساعد على خفض حمض الLDL أو الكوليسترول الضار بنسبة كبيرة، ويمكن للأشخاص الذين ي كذلك يتم إضافة نباتات HDL أو الكوليسترول المفيد مما يساعد على إبقاء قليل وأجزاء أخرى من جسمك بنشاط وصحة.

ليس عليك بالضرورة الذهاب إلى صالة الألعاب الرياضية، والعمل بها لضع سعات، ولكن يمكنك ممارسة التمارين المنتظمة التي تشمل على المشي السريع لمدة 30-45 دقيقة لمنع ارتفاع الكوليسترول في الجسم، وأيضاً يمكن عدم قضاء هذا الوقت (30-45 دقيقة) دفعة واحدة، ويمكن تقسيمها 3-4 مرات في اليوم من خلال قضاء 10 دقائق في كل مرة.

- تجنب الإفراط في تناول الأطعمة ذات الدهون عالية مثل الزيت، وكذلك تجنب الأطعمة السريعة التي تعد العدو الأول للمرضى الكوليسترول لاحتوائها على دهون مشبعة تساهم في ارتفاع نسبة الكوليسترول الضار في الجسم.

- تناول الأسماك مرتين أسبوعياً على الأقل لاحتوائها على مادة "أوميجا 3" التي تساهم في خفض نسبة الكوليسترول.

- تجنب الأطعمة المقلية قبل الإمكان واعتماد طريقة "الشيع" للتخلص من أي دهون في الدجاج والسمك على سبيل المثال.

- تناول الفاكهة والخضروات التي تحتوي على الألياف ومضادات الأكسدة، فهي صحيحة بشكل عام للجسم ولا ترفع مستويات السكر في الدم بشكل الزائد عن الحد.

- تجنب تناول النحوس الحمراء قبل الإمكان ومنتجات الألبان التي تحتوي على معدلات مرتفعة من الدهون والاستعاضة عنها بأشكال الأطعمة منخفضة من الدهون.

- تجنب تناول صفار البيض قبل الإمكان وكذلك تجنب تناول الجبن البقري الذي يحتوي على نسبة كبيرة من الدهون.
زيادة الكولسترول في الدم

الغذية يجب تجنبها

(الغذية الغنية بالكولسترول والأحماض الدهنية المشبعة)

<table>
<thead>
<tr>
<th>المنتجات حيوانية</th>
<th>منتجات نباتية</th>
<th>المنتجات كامل الدسم ومنتجاته</th>
</tr>
</thead>
</table>
| الدهون الحيوانية | الزيوت النباتية المهددة (المجمدة) | السمن 
الزبدة | الزيوت المقطوعة 
زيت النخيل | القشطة، الكريمة 
الأيس كريم | جوز الهند 
الكاكاو |
| الدهون العالقة أو الموجودة بين أنسجة اللحم | كبد الطيرور 
الخ | جلد الطيرور 
الخ | الكبد- الكلاوي- المخ 
السوسات- السجق- اللحوم المكونة 
الضأن- الكباب والكفتة | كبدة الطيرور- البط- الأوز 
الحمام | البطارخ | الحمير | صفار البيض |
نسبة الكوليسترول في بعض الأغذية
بالمليلجرام لكل 100 جرام

<table>
<thead>
<tr>
<th>كمية الكوليسترول (بالميلجرام)</th>
<th>القطعة (بالجرام) أو المقدار</th>
<th>نوع الطعام</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2.000</td>
<td>100 جرام</td>
<td>مخ</td>
</tr>
<tr>
<td>375</td>
<td>100 جرام</td>
<td>الكلاوي</td>
</tr>
<tr>
<td>300</td>
<td>100 جرام</td>
<td>الكبدة</td>
</tr>
<tr>
<td>252</td>
<td>1</td>
<td>صفار البيض</td>
</tr>
<tr>
<td>150</td>
<td>100 جرام</td>
<td>الجمبري</td>
</tr>
<tr>
<td>100</td>
<td>100 جرام</td>
<td>الكابوريا</td>
</tr>
<tr>
<td>84</td>
<td>100 جرام</td>
<td>جبنة شيدر</td>
</tr>
<tr>
<td>67</td>
<td>100 جرام</td>
<td>فراخ</td>
</tr>
<tr>
<td>65</td>
<td>100 جرام</td>
<td>لحم مفري</td>
</tr>
<tr>
<td>50</td>
<td>100 جرام</td>
<td>محار</td>
</tr>
<tr>
<td>14</td>
<td>1 فنجان</td>
<td>لبن كامل النسم</td>
</tr>
</tbody>
</table>
النظام الغذائي لمرضي زيادة الكوليسترول

| الإفطار | 
| --- | --- |
| مختارات من | الإفطار |
| - فول مدمس بالزيت والليمون. | 
| - برتقال - بوسفي - موز - فراولة. | 
| - جبنة قرشف - لبن صويا أو لبن منزوع الدسم. | 
| - بيض بخير. | 
| - بليلة باللبن المنزوع الدسم | 
| - مربى - عسل | 

| الغداء | 
| --- | --- |
| مختارات من | الغذاء |
| - بقول: فول - فاصولياء - لوبية - عدس | 
| - لحم مصنع من الصويا. | 
| - أسماك: تونة معلبة (بعد غسلها من الزيت). | 
| - عيش سمن | 
| - فاكهة: برتقال - موز - نفاح - عنب - بوسفي - فراولة | 

| العشاء | 
| --- | --- |
| مختارات من: | العشاء |
| - لبن منزوع الدسم. | 
| - جبنة قرشف - زبادي من لبن منزوع الدسم | 
| - سلطة خضراء | 
| - عيش سمن | 
| - مكسرات: سوداني - لوز - بندق - عين جمل | 

| تفصيل | 
| --- | --- |
| - برتقال - موز - بوسفي - خيار - طماطم - خس - مكسرات | 

الأكل: مسلوق أو مشوي أو بزيت نباتي (ماعدا زيت النخيل) بدون قدح (في فرن) أو على البخار.

تستخدم الزيوت النباتية (الصويا - ذرة - عبيد الشمس - زيت الزيتون) بدون قدح.
References & suggested readings

1. World Health Statistics 2008: WHO. Available at: https://www.who.int/whosis/whostat/EN_WHS08_TOCintro.pdf


EHS
Dyslipidemia Guidelines

Egyptian Hypertension Society

2021
EHS
Dyslipidemia Guidelines

Egyptian Hypertension Society

2021