



Your heart their lives
The National project for dyslipidemia
management

The Egyptian Consensus of Dyslipidemia Management

Collaborative work between the Egyptian cardiology & diabetology Task Force and the Non-communicable Disease Unit of the Ministry of Health

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Under the supervision of The Ministry of Health
Non communicable disease unit

The Egyptian Consensus of Dyslipidemia Management

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The Egyptian Consensus Of Dyslipidemia Management

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THE RATIONALE OF THIS CONSENSUS

- To highlight the Egyptian view of the new ESC guidelines.
- To improve physician awareness and compliance to recent guidelines.
- To outline gap of evidence for future research.
- To identify frequently asked practical questions and their answers.
- To help reduce cardiovascular burden In Egypt.

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HOW SERIOUS IS THE PROBLEM OF DYSLIPIDEMIA IN EGYPT?

- CVDs are the number one cause of death globally: more people die annually from CVDs than from any other cause.
- Cardiovascular diseases represent 46% of the total mortality in Egypt
- The Egyptian Cardiovascular Risk Factors project in ACS patients showed that 47% of males and 69% of female had premature atherosclerosis.
- One of the major causes and risk factors of CV disease is Dyslipidemia
- 37% of the Egyptian population has high cholesterol level with an overall achievement goal of ONLY 34.4% as per CEPHEUS trial.

3

SCREENING AND RISK ASSESSMENT

Q. When should we screen our Egyptian population for risk factors of CV disease?

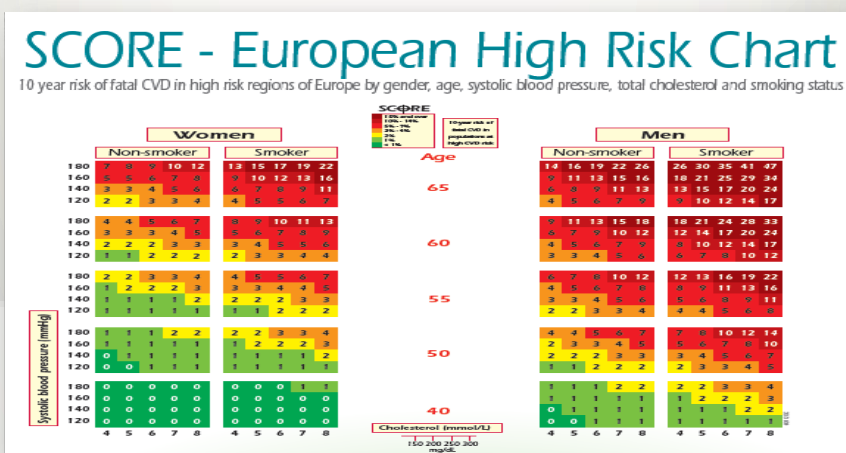
A. Men >40 years old and women >50 years should be considered for CVD risk factors screening and risk estimation of future cardiovascular fatal and nonfatal events using (SCORE) charts of the ESC/EAS Guidelines.

Q. Which SCORE chart to use?

A. We recommend the SCORE chart of high risk regions which is matching the Egyptian population.

Q. Which lipid parameters should be measured?

A. The recommended Laboratory tests used for baseline lipid evaluation are: TC, TGs, HDL-C, LDL-C and non-HDL-C. Non-fasting lipid levels can be used in screening and in general risk estimation. Only Consider fasting samples in severe dyslipidaemia and for follow-up of patients with High TG.



The European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) SCORE chart: 10 years risk of fatal cardiovascular disease in populations at high CVD risk.

Risk levels And Treatment Targets:

VERY-HIGH CV risk: <ul style="list-style-type: none"> • Documented CVD • DM or type-1 DM with target organ damage • Severe CKD: GFR <30 mg/ml/1.73 m² • 10 year risk SCORE ≥10% 	LDL-C target in very high risk: < 70 mg / dl or 50% reduction of the base line start	with high intensity statins
HIGH CV risk: <ul style="list-style-type: none"> • Markedly elevated single risk factor at presentation particular cholesterol (>310 mg/dL) (e.g. in familial hypercholesterolemia) or BP ≥180/110 mmHg. EVEN IF TREATED OR CONTROLLED • 10 year risk SCORE ≥5% and <10% • Moderate CKD: GFR 30-59 mg/ml/1.73 m² 	< 100 mg / dl or 50% reduction of the base line start	with high intensity statins
MODERATE CV risk: <ul style="list-style-type: none"> • 10 year risk SCORE ≥1% and <5% 	< 115 mg/dl and < 100mg/dl is preferred or 40-50% reduction of the base line LDL-c start	with moderate or high intensity statin dosage
LOW CV risk: <ul style="list-style-type: none"> • 10 year risk SCORE <1% 	< 115 mg/dl or 30% reduction of the base line LDL-C	with moderate intensity statin therapy

There is a lack of the evidence that requires future research regarding the percentage of the Egyptian population in different risk categories.

Intensity of Statin Therapy

High-Intensity Statin Therapy	Moderate-Intensity Stain Therapy
Lowers LDL-C ↓ ≥50%	Lowers LDL-C 30% to <50%
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

Adapted from Stone NJ, et al. J Am Coll Cardiol. 2013; doi:10.1016/j.jacc.2013.11.002

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ALGORITHM FOR MANAGEMENT OF DYSLIPIDEMIA

Evaluate the Total CV Risk of the subject.

Identify the LDL-C Goal for that risk level

Determine the Percentage Reduction Of LDL-C target to reach

Start with high or moderate intensity statins according to the risk

If the highest tolerated statin dose does not reach the goal, consider
Drug Combinations

Q. Which lipid parameter should be used as a primary target for treatment?

A: LDL-C IS THE PRIMARY TARGET for Treatment. LDL-C target depends on the risk of the patient and the base line LDL-C level.

Q. Should I stop or decrease statin dosage after reaching the target?

A: No. Once statin type and dose is indicated it should be continued indefinitely (Statins for life).

Q: If my patient is at high risk despite low baseline LDL-C, what should I do?

A: Any high risk patient should have a moderate or high intensity statin regardless of the base line LDL-C.

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ROLE OF LIFE STYLE MODIFICATION IN DYSLIPIDEMIA MANAGEMENT:

Healthy diet	<u>The best diet for Egyptians should include:</u> <ul style="list-style-type: none"> • Low amount of trans saturated fats <10% (Fast Food, hydrogenated Fats) • Low amount of carbohydrates < 50-55% • Focus on fibres found in whole grains (30–45 g) per day. • Fruits and vegetables (200- 400 g) per day (2-3 servings). • Oily fish rich in polyunsaturated fats (omega 3&6) twice per week.
	<u>Egyptians should avoid</u> <ul style="list-style-type: none"> • Excess fats in diet • Excess carbohydrates as rice, pasta, starchy vegetables as potatoes. • Sweet carbonted soft drinks
Physical Activity	<ul style="list-style-type: none"> • 2.5 to 5 hours moderate physical activity per week (or 30-60 minutes 5 days a week).
Body weight	<ul style="list-style-type: none"> • Body weight reduction is highly recommended as a way for CV risk reduction. • BMI should not exceed (20-25) • Waist circumference <94 cm (men) <80 cm (women)
Diabetes	<ul style="list-style-type: none"> • Target: HbA1C <7%
Hypertension	<ul style="list-style-type: none"> • Target: BP <130/80 mmHg
Smoking	<ul style="list-style-type: none"> • Should be avoided as it increases the cardiovascular risk

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STATINS IN PRIMARY PREVENTION

Primary prevention People with risk factors who have not yet developed clinically manifest cardiovascular disease. Primary prevention patients should be risk stratified by score chart. Accordingly, they may be high, moderate or low risk patients. The relative risk reduction in primary prevention is about the same as that observed in secondary prevention.

Even among patients without cardiovascular disease, statins reduced the following end points in primary prevention trials:

- All-cause mortality by 14% .
- Combined fatal and non-fatal CVD by 25% .
- Combined fatal and non-fatal CHD events by 27% .
- Combined fatal and non-fatal stroke by 22% .
- Revascularization rates by 38% .

Evidence available to date showed that primary prevention with statins is likely to be cost-effective and may improve patient quality of life.

Q. Do we need high intensity Statins for primary prevention?

A. Yes. Three primary prevention groups must receive high intensity statins:

- Diabetics.
- Familial hypercholesterolemia.
- High/very high risk (10 year risk SCORE \geq 5%, or presence of \geq 3 of the five traditional risk factors: male gender, age $>$ 40, smoking, HTN, elevated cholesterol level).

Q. Should all diabetic patients receive statins?

A. Yes. All diabetic patients above the age of 40 should receive moderate or high intensity statins without risk stratification.

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STATINS IN SECONDARY PREVENTION

- **Secondary prevention:** People with established CHD, Cerebro-vascular disease or peripheral vascular disease are considered as a very high risk patients without risk stratification and must receive high intensity statins for life. Plethora of evidence clearly proved that statins are effective in secondary prevention for CV events.

8

STATIN SAFETY

A Statin intolerance

- Statin intolerance is a clinical syndrome characterized by:
- The inability to tolerate at least 2 statins EVEN IN LOWEST doses: abnormal laboratory results which are temporally related to statin treatment.
- Reversible upon statin discontinuation, but reproducible by rechallenge with other known determinants being excluded (such as hypothyroidism, interacting drugs, concurrent illnesses, significant changes in physical activity or exercise, and underlying muscle disease).

B Statin-associated muscle symptoms (SAMS)

- Muscle symptoms are the most commonly described adverse effect of statin treatment: muscular pain and tenderness (myalgia) without CK elevation or major functional loss.
- One study suggests that the frequency of muscle-related complaints is 5%.
- In rhabdomyolysis, creatine kinase (CK) levels are elevated at least 10 times, often up to 40 times the upper limit of normal and represents 1–3 cases/100000 patient-years.
- Drugs potentially interacting with statins metabolized by CYP3A4 leading to increased risk of myopathy and rhabdomyolysis (MOST COMMONLY: ALTAZEM, DIGOXIN, AMIODARONE, AZITHROMYCIN).

Consider if statin-attributed muscle symptoms favour statin continuation / reinitiation

Symptomatic & CK < 4X ULN

2-4 weeks washout of statin

Re-challenge statin at same dose or low dose of atorvastatin or Rosuvastatin if SAMS occur.
Consider alternate day or once/twice weekly dosing if SAMS persist.

**CK ≥ 4X ULN +/-
rhabdomyolysis**

6 weeks washout of statin

Start at low dose of atorvastatin or Rosuvastatin if SAMS re-occur.
Consider alternate day or once/twice weekly dosing if SAMS persist.

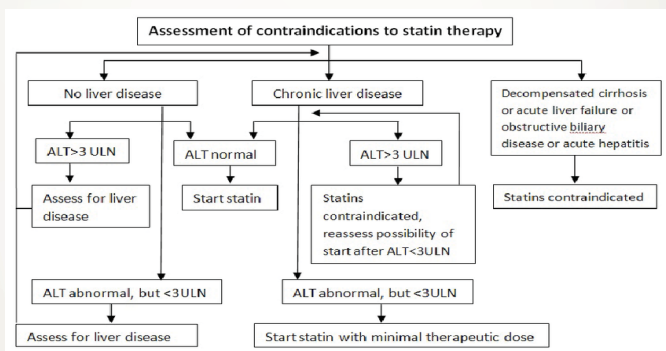
Aim: achieve LDL-C goal with maximally tolerated dose of statin

Q. Can we use the Vitamin D or Coenzyme Q10 to reduce the muscle related adverse events of Statins?

- A. No, The use of supplements such as vitamin D and coenzyme Q10 does not have sufficiently consistent clinical trial evidence to allow for routine recommended use.

C Liver side effects

- Mild elevation of ALT occurs in 0.5–2.0% of patients on statin treatment
- The common definition of clinically relevant ALT elevation has been an increase of three times the upper limit of normal (ULN) on two occasions with statins usage.
- Long-term clinical trial data does not support the incidence of liver failure or liver-related death as being different when comparing statin-treated and placebo administered groups.
- Statins are contraindicated in patients with acute liver failure or decompensated cirrhosis.



Q. Can we use statins in hepatitis C patients?

- A. Yes. The use of statins was associated with a significant 42% reduction in the risk of cirrhosis.

Q. Do we need to check liver enzymes routinely?

- A. Check liver enzymes only at baseline and 3-6 months after treatment, unless symptoms appeared.

Q. What to do for patients with normal liver enzymes that got elevated 2 folds above ULN after initiating statins?

- A. As long as liver enzymes did not exceed 3 folds above ULN, we can continue on statins.

D New onset diabetes mellitus

- Risk for new onset diabetes is higher in the elderly and in the presence of other risk factors for diabetes such as overweight or insulin resistance.
- The number needed to cause one case of diabetes was estimated at 255 over 4 years.
- Overall, the absolute reduction in the risk of CVD in high-risk patients outweighs the possible adverse effects of a small increase in the incidence of diabetes.

E Kidney side effects

- The effect of statin treatment on renal function is still being Debated
- The increased frequency of proteinuria which is in general low and in most cases not higher than that for placebo is of tubular origin and is supposed to be due to reduced tubular reabsorption and not to glomerular dysfunction.

F Neurocognitive Side Effects

Neurocognitive side effects of statins have not been confirmed in analyses of large patient populations or in meta-analyses.

Q. How should we follow up patients on statin therapy?

A. lipids should be tested 8 (\pm 4) weeks after starting treatment AND then annually once a patient has reached the target or optimal lipid level (unless there are adherence problems or other specific reasons for more frequent reviews).

9 NON STATIN THERAPY

- Patients at very high risk, lowering LDL-C to the goal of < 70 mg/dl and/or achieving 50% LDL-C reduction when this goal cannot be reached.
- Patients with statin intolerance
- Patients with Familial hypercholesterolemia



Start with the maximum tolerated dose of statins

Not at goal



Ezetimibe 10 mg or BAS (Colesevelam up to 4.5 gm/day or Cholestyramine up to 24 gm/day) as alternative.

Not at goal



PCSK9 Inhibitors

- The initial dose for alirocumab is 75 mg once every 2 weeks. Patients requiring larger LDL-C reduction ($>60\%$) may be started on 150 mg once every 2 weeks.
- Evolocumab is given 140 mg every 2 weeks or 420 mg once monthly.

- Use the maximum tolerated statins in combination with a Ezetimibe or bile acid sequestrants if the cholesterol goal is not reached or in the case of statin intolerance.
- A- **Ezetimibe**: inhibiting cholesterol absorption at the level of the brush border of the intestine [by interaction with the Niemann-Pick C1-like protein 1 (NPC1L1)]
- If Ezetimibe is used, 10mg/day is the recommended dose. No major side effects but the most frequent are moderate liver enzymes elevation and muscle pain
- B- **Bile acid sequestrants(BAS)**: blocking reabsorption of bile acids from intestinal track leading to increased hepatic consumption of circulating LDL cholesterol through compensatory increase in LDLR activity.
- Colesevelam up to 4.5 gm/day is the newer formulation of bile acid sequestrant and is better tolerated than cholestyramine up to 24 gm/day.
- Side effects: Gastrointestinal (flatulence, constipation and dyspepsia).
- **PCSK9**: proprotein convertase subtilisin/kexin type 9, involved in degradation of LDL-R in liver
- In FH, Mutation in PCSK9 reduce the number of LDL-Rs, decreasing the ability to clear LDL from plasma.
- C. **PCSK9 inhibitors**: monoclonal antibody reduces the degradation of LDL-R and increasing clearance of LDL cholesterol.
- The initial dose for alirocumab is 75 mg once every 2 weeks. Patients requiring larger LDL-C reduction (>60%) may be started on 150 mg once every 2 weeks.
- Evolocumab is given 140 mg every 2 weeks or 420 mg once monthly.
- The initial recommended dose is 420 mg once monthly, up titrated after 12 weeks to 420 mg once every 2 weeks if a clinically meaningful response is not achieved. Patients on apheresis may initiate treatment with 420 mg every 2 weeks to correspond with their apheresis schedule.

PCSK9 inhibitors indications In combination with Maximally tolerated efficacious statin (preferably atorvastatin or rosuvastatin) + ezetimibe		
<ul style="list-style-type: none"> • Patients at very high risk not at LDL-C goal • With documented ASCVD (clinical or unequivocal on imaging, with plaque on coronary angiography or carotid ultrasound) • Patients with a progressive ASCVD [i.e. repeated acute coronary syndromes (ACSs), repeated unplanned coronary revascularizations, or repeated ischaemic strokes within 5 years of the index event] • Diabetic patients with target organ damage or with a major risk factor such as marked hypercholesterolaemia or marked hypertension 	Patients with FH without ASCVD	Patients in any of these groups with statin intolerance

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FAMILIAL HYPERCHOLESTEROLEMIA

Familial Hypercholesterolemia (FH) is an autosomal dominant disorder that causes severe elevations in total cholesterol and low-density lipoprotein cholesterol (LDL-C). It can be either Homozygous or Heterozygous.

In Homozygous FH total cholesterol and LDL-C levels >500 mg/dL with normal triglyceride levels and symptoms consistent with ischemic heart disease, peripheral vascular disease, cerebrovascular disease, or aortic stenosis in early childhood. Corneal arcus may be present and is sometimes circumferential. Articular symptoms such as tendonitis or arthralgias, unusual skin lesions, such as cutaneous xanthomas are present at birth or by early childhood (e.g. palmar xanthomas, tuberous xanthomas; later, tendon xanthomas).

Heterozygous FH is usually symptomatic in young adults at age of 20 years. If left untreated, both sexes will develop premature CAD and tendon xanthomas (Achilles tendons, metacarpo-phalangeal extensor tendons) will occur by third decade of life. In more than 60% of patients LDLc level >200 mg/dL Dutch Lipid Clinic Network criteria will help in diagnosis. (Table1)

Management

- Lifestyle changes
- Lipid-lowering therapy should be started as early as possible. Statins up to maximum tolerated dose. Add Ezetimibe or PCSK9 if target can't be reached (LDL-C <100 mg/dl in high risk patients or <70 mg/dl in patients with ASCVD).
- Lipoprotein apheresis should be considered in all patients with HoFH, and starts as soon as possible, ideally by age of 5 years and not later than 8 years of age.

Table1 Dutch Clinic Network Criteria for clinical diagnosis of FH*

Criteria	Score
1) Family history First-degree relative with known premature (men: <55 years; women: <60 years) coronary or vascular disease, or First-degree relative with known LDL-C above the 95th Percentile	1
First-degree relative with tendinous xanthomata and/or arcus cornealis, or children <18 years of age with LDL-C above the 95th percentile	2
2) Clinical history Patient with premature (men: <55 years; women: <60 years) coronary artery disease	2
Patient with premature (men: <55 years; women: <60 years) cerebral or peripheral vascular disease	1
3) Physical examination Tendinous xanthomata	6
Arcus cornealis before age 45 years	4
4) LDL-C levels LDL-C \geq 325 mg/dL	8
LDL-C 251–325 mg/dL	5
LDL-C 191–250 mg/dL	3
LDL-C 155–190 mg/dL	1
5) DNA analysis Functional mutation in the LDLR, apoB or PCSK9 gene	8

Mmol = 38 mg/dl

- A 'definite' FH diagnosis requires >8 points
- A 'probable' FH diagnosis requires 6–8 points
- A 'possible' FH diagnosis requires 3–5 points

* Adapted from 2016 ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force of ESC and EAS Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR)
Alberico L. Catapano et al. Eur Heart J 2016;eurheartj.ehw272

11 HYPERTRIGLYCREDEMIA

- Hypertriglyceridemia (fasting TG level \geq 150 mg/dl) is common ; it is present in 30% of adults
- Very high serum TG levels (> 500 -800 mg/dl) are associated with risk of acute pancreatitis. In this situation triglycerides are the primary target of treatment
- Increased serum TG levels (200-500 mg/dl) are associated with increased risk of cardiovascular disease. However, TG is not a primary target of treatment. Drugs for treatment of hypertriglyceridemia may be considered only in high risk patients who have had achieved their LDL-C goals but who still have elevated TG (> 200 mg/dl) despite life style modification
- Weight reduction, regular physical activity, and restriction of caloric and carbohydrate intake are associated with significant reduction in TG levels.

Very high TG levels (> 500 mg/dl)



Primary objective: lowering of TG levels

- Drug therapy: Fenofibrate & Omega 3 fatty acids (3-5 g/day)
- Rule out 2ry causes: ↑ CHO intake, ↑ saturated FA, uncontrolled DM, hypothyroidism, medications (eg, corticosteroids, estrogens, thiazides, B-blockers)
- Life style modification: weight reduction, physical activity, and restriction of caloric and carbohydrate



Secondary objective: achieve LDL-C target

High TG levels (200-499 mg/dl)



Primary Objective: achieve LDL-C target

- Life style modification + statin therapy



Still TG > 200 mg/dl

Secondary Objective: achieve non-HDL target*

- Life style modification: weight reduction, physical activity, restriction of caloric and carbohydrate
- Drugs to lower TG+ : fenofibrate , omega-3 fatty acid may be added if TG is still high

12 STATINS IN SPECIAL POPULATION

Q. 12 years old girl with homozygous familial hypercholesterolemia. Would you give her statins?

A. Children with FH (HoFH or HeFH) should be considered for lipid-lowering drug treatment as early as possible to a target of LDL < 130mg/dl. Statin treatment is generally started at the age of 8 and 10 years.

Q. 30 years old lady already on statin treatment and got pregnant, how would you manage?

A. She should stop statins and start BAS treatment. Lipid-lowering drugs should not be given when pregnancy is planned. Bile acid sequestrants are the only lipid lowering agents that may be considered during pregnancy and breastfeeding.

Q. Should we give statins for primary prevention to 49 years old lady with severe hypertension?

A. Statin treatment is recommended for primary and secondary prevention of CAD in women in the same indications as for men.

Q. 80 years lady with acute coronary syndrome, would you give her statins?

A. Statins are recommended for older adults with established CVD in the same way as for younger patients. Statin therapy should be considered even in older adults free from CVD with other risk factors for primary prevention. Lipid-lowering medication should be started at a lower dose and then titrated with caution to achieve target level.

Q. 25 years gentleman with type I DM and microalbuminuria, would you give him statins?

A. In type 1 diabetes and in the presence of microalbuminuria or any other target organ damage, LDL-C lowering (at least 30%) with statins as the first choice is recommended irrespective of the baseline LDL-C level.

Q. 45 years old gentleman with type II DM but no CV disease, would you give him statins?

A. Statins are recommended in patients with type 2 diabetes who are > 40 years of age. The recommended goal for LDL-C is < 70 mg/dL if there is additional one or more other CVD risk factors. The goal for LDL-C is < 100 mg/dL in patients with type 2 diabetes and no additional risk factors and/or evidence of target organ damage.

Q. 70 years old man with non-ischemic dilated cardiomyopathy, would you give him statins?

A. Routine administration of statins in patients with non ischemic HF is not advised. However there is no need for discontinuation if patients are already on this medication. Statins are indicated if HF is due to CAD.

Q. 65 years old gentleman presenting with NSTEMI, would you give him statins even with LDL below 70 mg/dl

A. High-intensity statin is initiated immediately at hospitalization for ACS; aiming to achieve LDL-C goal of <70 mg/dL or a 50% reduction of LDL-C regardless of initial LDL-C values. Moderate intensity statin therapy should be considered in patients at increased risk of adverse effects. If the LDL-C target is not reached with the highest tolerable statin dose, Ezetimibe should be considered, or PCSK9 inhibitors may be considered on top of lipid-lowering therapy. Lipids should be re-evaluated 4–6 weeks after ACS. Routine short pretreatment or loading (on the background of chronic therapy) with high-dose statins before PCI should be considered in elective PCI or in NSTEMI-ACS.

Q. 65 years old gentleman with controlled hypertension and chronic occlusion of anterior tibial artery of right lower limb on Duplex but with no symptoms, would you give him statins?

A. PAD is a very-high-risk condition and lipid-lowering therapy is recommended in these patients. Statin therapy should be considered to prevent the progression of abdominal aortic aneurysm (AAA).

Q. 65 years old lady with controlled hypertension suffered from minor non embolic stroke, would you give her statins?

A. Intensive Statin therapy is recommended in patients with a history of non-cardioembolic ischemic stroke or TIA for secondary prevention of stroke. For patients with high or very high CV risk of stroke statin is recommended for primary prevention to reach established treatment goal.

Diabetic Dyslipidemia introduction

Dyslipidemia is one of the major risk factors for cardiovascular disease in diabetes mellitus.

The prevalence of hypercholesterolemia is not increased in patients with diabetes mellitus, but mortality from coronary heart disease increases exponentially as a function of serum cholesterol levels, and lowering of cholesterol with statins reduces diabetic patients' relative cardiovascular risk.

Although drug therapy for dyslipidemia must be individualized, (almost) all people with diabetes mellitus are candidates for statin therapy.

Hypercholesterolemia and diabetic dyslipidemia are still not effectively treated in many at-risk patients in Egypt as the dyslipidemia goal was reached only for 21.6% of patients with diabetes mellitus and thus initiatives are needed to improve physicians management of lipid abnormalities in the general population and type 2 diabetes in Egypt.

Diabetic dyslipidemia Characteristics

The characteristic features of diabetic dyslipidemia are:

1- High plasma triglyceride concentration

2- Low HDL-cholesterol concentration.

3- Increased concentration of small dense LDL-cholesterol concentration.

Diabetic dyslipidemia is attributed to increased free fatty acid flux secondary to insulin resistance.

Evidence behind the diabetic dyslipidemia consensus

- Elevated LDL- cholesterol and low HDL- cholesterol are the classical CV risk biomarkers. However with time it has become clear that targeting LDL-C is beneficial and not HDL-C.
- Use of statin therapy in patients with type 2 diabetes mellitus (T2DM) has been recommended by most clinical guidelines.
- As per the Cholesterol Treatment Trialists (CTT) Collaborators . Participants with diabetes had a 9% reduction in all-cause mortality

while the overall effect was 21% in major vascular events per millimole per liter LDL cholesterol reduction

- American Diabetes Association standards of care recommend moderate or high -intensity statins for all T2DM patients over the age of 40 years as a primary prevention . The choice of regimen should be individualized according to benefits of CVD risk reduction, patient preferences, and safety issues.
- Higher doses of statins are required for the secondary prevention of diabetic patients with coronary artery disease or at increased CVD risk(such as those with abnormal LDL-C levels, smokers, hypertension, or albuminuria) , unless there are patients safety or tolerability concerns.
- At the same time,The latest guidelines from the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) 2018 stated that the lower the LDL cholesterol the better, regardless of where your LDL is to begin with , and targets are very useful as they are strong incentives for both patients and physicians. There is a benefit for lowering LDL-cholesterol levels to 50 mg/dL or even lower.
- The proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor evolocumab decreased major cardiovascular events, but not cardiovascular or all-cause deaths when combined with statins, via lowering LDL cholesterol to a mean of 30 mg/dL . (Odyssey trial indicates that the use of alirocumab q2 weeks significantly reduces ischemic events, including all-cause mortality and MI, among patients with an ACS event within the preceding 1-12 months; 90% were on high dose of a potent statin)
- On the other hand, although there is incremental further risk reduction from adding ezetimibe or a PCSK9 monoclonal antibody, no trial has compared titration with different LDL goals.

Lipid management in diabetes

Screening for dyslipidemia in diabetic patients

1. In adults not taking statins or other lipid-lowering therapy, it is reasonable to obtain a lipid profile at the time of diabetes diagnosis
2. Obtain a lipid profile at initiation of statins or other lipid-lowering therapy, 4–12 weeks after initiation or a change in dose, and annually thereafter as it may help to monitor the response to therapy and inform adherence

Management of dyslipidemia in diabetic patients

- 1-Life style modification for diabetic patients focusing on weight loss (if indicated), increased physical activity should be recommended to improve the lipid profile in patients with diabetes.
 - Nutritional management
You have to help them learn to balance their meals and make the healthiest food choices.

Healthy Food	Food to be avoided
Whole grains are rich in vitamins, minerals, phytochemicals and fiber. Starchy Vegetables The best choices do not have added fats, sugar or sodium. While these foods can be part of healthy diet, they do raise blood glucose. A variety such as: <ul style="list-style-type: none">• Potato• Pumpkin• Green Peas• Corn	Avoid sugary drinks like regular soda, fruit punch, fruit drinks, energy drinks, sports drinks, sweet tea, and other sugary drinks. e.g. <ul style="list-style-type: none">• One 12-ounce can of regular soda has about 150 calories and 40 grams of carbohydrate. This is the same amount of carbohydrate in 10 teaspoons of sugar!• One cup of fruit punch and other sugary fruit drinks have about 100 calories (or more) and 30 grams of carbohydrate.
<u>Protein Foods</u> It depends on how much fat they contain, and for the vegetarian proteins, whether they have carbohydrate	

<p><u>Plant-Based Proteins</u></p> <ul style="list-style-type: none"> • Beans such as black, kidney, and pinto • Bean products like baked beans and refried beans • Hummus and falafel • Lentils such as brown, green, or yellow • Peas such as black-eyed or split peas • Nuts and spreads like almond butter, cashew butter, or peanut butter 	<p><u>Fats</u></p> <p><u>Unhealthy Fats</u></p> <p><u>Saturated Fat include:</u></p> <ul style="list-style-type: none"> • High-fat meats like regular ground beef, hot dogs, sausage and bacon • High-fat dairy products such as full-fat cheese, cream, ice cream and whole milk • Butter • Chocolate • Palm oil and palm kernel oil • Coconut and coconut oil
<p><u>Fish and Seafood</u></p> <p>Try to include fish at least 2 times per week.</p> <ul style="list-style-type: none"> • Fish high in omega-3 fatty acids like Albacore tuna, herring, mackerel, rainbow trout, sardines, and salmon 	<p>Poultry (chicken and turkey) skin</p> <p>The goal for people with and without diabetes is to eat less than 10% of calories from saturated fat. For most people, eating this is about 20 grams of saturated fat per day. That is not much when you consider just one ounce of cheese can have 8 grams of saturated fat.</p>
<p><u>Poultry</u></p> <p>Choose poultry without the skin for less saturated fat and cholesterol.</p> <ul style="list-style-type: none"> • Chicken, turkey 	<p>Foods with 1 gram or less saturated fat per serving are considered low in saturated fat.</p> <p><u>Trans Fat</u></p> <p>It is actually worse than saturated fat and for a heart-healthy diet can raise cholesterol level.</p> <p>Trans fats are produced when liquid oil is made into a solid fat. This process is called hydrogenation. Trans fats act like saturated fats and Sources of trans fat include:</p>

Cheese and Eggs

- Reduced-fat cheese or regular cheese in small amounts
- Cottage cheese
- Whole eggs

Beef, Veal & Lamb

- Lamb: chop, leg, or roast
- Veal: loin chop or roast
- Select or Choice grades of beef trimmed of fat including: chuck, rib, rump roast, round, sirloin, cubed, flank, porterhouse, T-bone steak, tenderloin

Dairy

- Fat-free (skim) or low-fat (1% milk)
- Yogurt (regular or Greek yogurt)
- Some reduced fat cheeses

Healthy Fats**Monounsaturated Fat**

they can lower our bad (LDL) cholesterol. Sources:

- cans, and peanuts
- Olive oil and olives
- Peanut butter and peanut oil
- Sesame seeds

- Processed foods like snacks (crackers and chips) and baked goods (muffins, cookies and cakes) with hydrogenated oil or partially hydrogenated oil
- Some fast food items such as french fries

Cholesterol

It's a good idea to advise your patients to eat less than 300 mg of cholesterol per day.

- Sources of cholesterol include:
- High-fat dairy products (whole or 2% milk, cream, ice cream, full-fat cheese)
- Egg yolks
- Liver and other organ meats
- High-fat meat and poultry skin

- 2- No need for use of CV risk calculator to initiate statin therapy in people with diabetes as diabetes itself confers increased risk for ASCVD
- 3- High-intensity statin therapy should be added to lifestyle therapy for:
 - a. All patients with diabetes and atherosclerotic cardiovascular disease
 - b. Patients with diabetes > 40 years of age with additional CV risk factors (LDL-C > 100 mg/dl. HTN, smoking, CKD or family history of premature CVD).
 - The target is to reach LDL-C <70 mg/dl if the baseline LDL-c >135 mg/dl or to reduce LDL-C by 50% if the baseline LDL-C is <135 mg/dl
- 4- Moderate-intensity statin in addition to lifestyle therapy should be used:

- a. For patients with diabetes aged > 40 years without atherosclerotic cardiovascular disease
- b. Patients with diabetes aged <40 years with additional atherosclerotic cardiovascular disease risk factors
 - The target is to reach LDL-C <100 mg/dl if the baseline LDL-c >200 mg/dl or to reduce LDL-C by 50% if the baseline LDL-C is <200 mg/dl
- 5- High-intensity statin therapy includes Rosuvastatin 20-40 mg or Atorvastatin 40-80 mg. Whereas moderate-intensity statin therapy Rosuvastatin 5–10 mg, Atorvastatin 10-20 mg, Simvastatin 20–40 mg, and Pravastatin 40–80 mg
- 6- In clinical practice, providers may need to adjust the intensity of statin therapy based on individual patient response to medication
- 7- For patients who do not tolerate the intended intensity of statin, the maximally tolerated statin dose should be used.
- 8- For patients with diabetes and atherosclerotic cardiovascular disease, if LDL cholesterol is >70 mg/dL on maximally tolerated statin dose, consider adding ezetimibe.
- 9- Combination therapy (statin/fibrate) is generally not recommended
- 10- Intensify lifestyle therapy and optimize glycemic control for patients with elevated triglyceride levels

Q1-When we should screen for Diabetic Dyslipidemia in children ?

Routine lipid testing is recommended by the American Academy of Pediatrics (AAP) in all children once between the ages of 9 and 11 and again between 17 and 21 years.

Q2-What is the main target for treatment of Diabetic Dyslipidemia?

The main target is THE LDL- C ,followed by THE NON –HDL-C as a secondary target.

Q3-What is the main treatment of Diabetic Dyslipidemia?

The cornerstone treatment of Diabetic Dyslipidemia is statin therapy.

Q4-So, why we should monitor the lipid levels in those patients?

Lab monitoring of lipid pattern is mainly to know:

- Adherence of the patient,
- And, his or her response to treatment.

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