تفريغ سول أكاديمي

اسم المادة: Therapy

المحاضرة: Dyslipidemia Part 2

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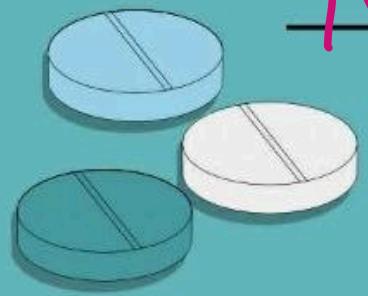

❖ Bile Acid Resins (BARs)

هما not absorbale وهما يرتبطو الbile acide الموجوده بالintestin فبالتالي الliver بصير بده يصنع bile acide لانه صار في deplation فيها ومن وين بتصنع الbile acid بالliver؟من الcholesterol فبده cholesterol لانه hepatic pool cholesterol قلت يزيد cholesterol لانه صار الهliver بالconsumption فشو رحيعمل ؟رحيزي الhepatic LDL receptor الموجوده بالliver حيث بده ياخذ الLDL الموجود بالblood وهيك رح يزيد الLDL CATABOLISM وهيك بنزل cho.esterol بالدم وهذا الاشي الي صار ممكن يزيد الhepatic VLDL production (يعني triglyceride) وهذا الاشي ممكن يأدي للtriglyceridemia بالناس الي عندهم combined hyperlipidemia عشان هيك ما بقدر اعطيهم كوmono therapy الا اذا كان الTG تحت الـ200 فاذا كان الTG high او very high ما بنعطو monotherapy وبنعذيهم other agent مع combination لانه بنخاف انهم يرفعو الTH

- ✓ Their primary action is to bind bile acids in the intestinal lumen, and markedly increasing excretion of acidic steroids in the feces (stimulates hepatic synthesis of bile acids from cholesterol).
- ✓ The increase in hepatic cholesterol biosynthesis may be paralleled by increased hepatic VLDL production and, consequently, bile acid resins may aggravate hypertriglyceridemia in patients with combined hyperlipidemia. ↓ LDL 15-30%, no effect or ↑ TG, ↑ HDL 3-5%
- ✓ These agents should not be used as monotherapy in patients with triglyceride levels > 250 mg/dL. They may be combined with nicotinic acid or statins.

اذا الstatin كانت لحالها غير كافيه لتنزل الCholesterol او مع الniacin ك complementary action لانه الniacin inhibit cholesterol synthesis والbile acid inc catabolism of LDL وطبعا بهاي الحاله بساعدونا ،وبرضه بياخذوه مع الnicotinic acid بعمل على تقليل الTG ومافي مشكله مع الbile acid انه ممكن يرفع الTG بهاي الحاله

في reference تعتقد انه ما ناخذه الا اذا كانت الTG اكثر من ٥٠٠

- ✓ GI complaints of constipation, bloating, epigastric fullness, nausea, and flatulence are most commonly reported. ← همه bulky agent وبنعطو بجرعات عالية عشان هيك همه مزعجين فعليا للpatient
- ✓ The adverse effects can be managed by increasing the fluid intake, modifying the diet to increase bulk, and using stool softeners.
- ✓ The other major limiting complaint is the gritty texture and bulk; these problems may be minimized by mixing the powder with orange drink or juice.

الهم مشكله ثانيه وهي الgritty texture وبكون ملمسها زي الحبيبات

اذا اعطيت الbile acid بجرعات عالية مثلا زي الcholestyeamin الdose الها بين ال4-24 g فأنا بو اعطيت المريض جرعة اكبر من 15g رح تعمل هال side effect و هو انه يقلل الabsorption of
fact-solublevit (AKED) وبرضه 2,3و GI obstruction وهاي غالبا بتكون بالchildren(انا هيك سمعتها)وبرضه تقلل الbioavalability للacidic drg

- ✓ Other potential adverse effects: impaired absorption (with high doses) of fat-soluble vitamins A, D, E, and K; hypernatremia and hyperchloremia; GI obstruction; and reduced bioavailability of acidic drugs as coumarin anticoagulants, nicotinic acid, thyroxine, acetaminophen, hydrocortisone, hydrochlorothiazide, loperamide, and possibly iron.

لانهم هما مش absorbable وبعملو impaire للabsorption
لكثير ادويه يفضل اعطي اي دوا ثاني من befoure 1to 2houre
اعطاء الbile acideاو بعد 4-6 houre من اعطاء الbile acid

- ✓ Drug interactions may be avoided by alternating administration times with an interval of 6 hours or greater between the bile acid resin and other drugs.

- ✓ Colestipol may have better palatability because it is odorless and tasteless.

الcolestipol المريض بتحمله
المريض اكثر(palatability) لانه

bile acid Resin

- ✓ BARs are increasingly used in combination with other drugs, as low doses are tolerated well and they work in a complementary fashion with other agents.

اذا بنستخدم الBAR مع ادويه ثانيه يعني بعمل combination(حكيت عنها بالسلايد الي قبل) بقدر
استعمل الBAR بlow dose ورح تكون more tolerated

- ✓ Currently available BARs include the following:
  - Cholestyramine: 4– 24 g/ d PO in divided doses before meals.
  - Colestipol: tablets, 2– 16 g/ d PO; granules, 5– 30 g/ d PO in divided doses before meals.
  - Colesevelam: 625 mg tablets, three tablets PO bid or six tablets PO daily (maximum of seven tablets daily) with food, or one packet of oral suspension daily.

Niacinال بزبط للmix hyperlipidemia حيث بنزل الtriglycerideوبنزل الcholecsterol

بدرجات منيحة وزي ما حكينا انه في complemantry action مع الbile acid resin(حكينا انه بزيد monotherapy وبقدر استخدمه synthesis of LDL بقلل الniacin وال (LDL للcatabolisimال

❖ Niacin

✓ Niacin (nicotinic acid) may also be used in primary hypercholesterolemia in combination with bile acid resins (complementary action) or as monotherapy for this disorder.

VLDLال بالاخر بده يتحول لLDL فالnicin بقلل من synthesis of VLDL وبالتالي بقلل الLDL

✓ Niacin reduces the hepatic synthesis of VLDL, which, in turn, leads to a reduction in the synthesis of LDL. ↓ LDL 5-25%, ↓ 20-50% TG, ↑ HDL 15-35%

اكثر واحد من الanti.ipidemic drug برفع الHDL

✓ Niacin also increases HDL by reducing its catabolism.

✓ The principal use of niacin is for mixed hyperlipemia or as a second-line agent in combination therapy for hypercholesterolemia.

حكينا انه بالhypercholesteralemia بكون الStatin هو first line فاذا الpateint ما استفاد على الstatin او كان statin ممكن استخدم الin-tolareable second line agent الي هو الNiacin بس انتبهو انه اذا بدنا نستعمل Niacin مع الstatin

اشي ممكن بس هذا الاشي بزيدال risk of liver toxicity والmyopathy as combination

بقدر استخدمه ك first line therapy of hypertriglyceremia او كalternative of triglycerdemie

✓ It is also considered to be the first-line agent or an alternative for hypertriglyceridemia treatment.

✓ Nicotinic acid is usually administered in two or three doses a day, with the exception of the extended release product Niaspan®, which is administered as a single dose at bedtime.

بالعاده الextended release niacin تساوي dose اله500mg at bedtime وبعد شهر نرفعه كمان 500mg ونضل نرفع لحتى نوصل الmax dose وهي ال2000mg(or 2g) تقريبا كل شهر نرفعها 500mg

الimmedate formulation بنعطوا بين (1-3)g ك devided dose وكل ما زدنا الdose زادت الsiderffectوالدكتوره بهمها تعرفو الNIACIN موجود ب3 formulation(immediate,extended ,sustaind release)

- ✓ Niacin has many adverse drug reactions that occur commonly.

cutaneous flushing oe ال وهذا الاشي كثير مزعج tumbling sensation و warm,itching بصير الجلد لونه red وبكون في
ithching كيف بقدر اتغلب على هاي المشكله ؟عن طريق اعطاء aspirin mg قبل30 min من الniacin ingestion هيك بقل
duration and intensity of flushingللincidance هو فعليا بقلل الithcing بس ما بقلل الflushing

يفضل نتجنبهم لانه بعملو worsing للflushing

- ✓ Cutaneous flushing and itching appear to be prostaglandin mediated and can be reduced by aspirin 325 mg given shortly before niacin ingestion. Concomitant alcohol and hot drinks may magnify flushing and pruritus with niacin and they should be avoided at the time of ingestion.

dosage form (immediate,sustiend,extended)ال وهذا الحكي بختلف باختلاف subsequance metabolisimوال rate of absorptionبال علاقة الهم Niacin بعملهم الي hepatotoxicityوال flushingال بصير رح
toxic metabolism ofوال weast productبال او اله علاقه liverبال catabolisim بصير اله niacinبتصير بسبب انه hepatic toxicityوال metabolism عليه ودصير liver للوبعدين بروح niacin للabsorption

niacin

- ✓ Flushing seems to be related to rising plasma concentrations of niacin; taking the dose with meals and slowly titrating the dose upward may minimize these effects.

أذا اخذته مع الmeal رح يقل الflushing واذا كان الsustaind release برضه رح يقلل الflyshing،همولما عملو الcontrol study لاحظو انه مافي اختلاف بالside
effectبين الimmediate releaseوال sustind release بس من التجربه بعض الpatient برتاحوا على الSustainde والflushing بكون اقل

- ✓ Sustained release products may minimize these complaints in some patients.

Niacinبرضه ال،active peptic ulcer diseaseمع should be avoided هيك عشانpeptic ulcerلل activate رح يعمل Niacin واخذ اذا المريض عنده peptic ulcer
فالمفروض ننتبه على هاي الاشياء should be avoided with gout ,with uncontrolled diabetic

- ✓ Potentially important laboratory abnormalities occurring with niacin therapy include elevated liver function tests, hyperuricemia, and hyperglycemia.

- ✓ Recent experience with niacin in diabetes suggests that some diabetic patients do not have worsened glycemic control with dose-titration and sustained-release products.

حكينا انه الsustained release بقلل من الflushing وبرضه يقلل من
ال risk of hyperglycemic (او glycemic imparment)

- ✓ With less than 3 grams per day, the degree of liver function test elevation is generally not marked and often transient, and a temporary reduction in dosage frequently corrects the problem (contraindicated in patients with active liver disease).

niacin contraindicatedال،g(3-1) بنعطى immediate releaseال
with active liver disease(زي ال statin) بس بنعطى مع الناس الي
chronic liver disease عندهم

- ✓ Niacin-associated hepatitis is more common with sustained-release preparations (more expensive), and their use should be restricted to patients intolerant of regular-release products (should always be used first).

حكينا انه الsustained بعمل اقل flushing واقل hyperglycemic وهي more expensive(اغلى)وبرضه الhepatitis بكون معها اكثر لانه كانه
احنا بنعرض الliver للniacin لفتره اطول لانه sustained release، فاذا بدي ابلش الniacin مع مريض ببلش معه ب -immediat(regular
release) وب low dose ومع الmeal ونعمل monitor ingالل blood glucos e ونعطي uric acidوالل وخصوصا aspirin befoure. Dos
بال first coupled doses بفإذا المريض ما تحمل الimmediate بنزوح للsustianed بس لازم يضل ببالنا انه بزيد الrisk of hepatic toxicity

Peptic ulcer

- ✓ Preexisting gout and diabetes may be exacerbated by niacin; these patients should be monitored more closely and their medication titrated appropriately.

- ✓ Dry eyes and other ophthalmologic complaints are also occasionally noted.

الniacinممكن يعمل مثل ocular problem
الblind vision وeyelide edemaممكن يأثر على
eye browالحواجب) وعلى الeyelashes

- ✓ Niacin may magnify the hypotensive effects of vasodilators.

الniacinالهر vasodilator effect فما بعطيه مع الناس الي عندهم HTN
الNiacin عنده مشاكل كثير وهو دوا مش مرحب فيه من قبل المريض وهو مزعج فعليا

❖ Ezetimibe

الEzetimibe بشتغل على ال cholesterol absorption حيث بعمل inhibition of cholesterol absorption in intestine حيث بقلل الLDL-C بنسبه 25% لما يعمل combination مع ال statin وبقلل ال LDL-C بنسبه 18% لما يكون monotherapy(لحاله)

- ✓ Ezetimibe is currently the only available cholesterol-absorption inhibitor.
- ✓ Ezetimibe may provide an additional 25% mean reduction in LDL-C when combined with a statin and provides an approximately 18% decrease in LDL-C when used as monotherapy.
- ✓ The recommended dosing is 10 mg PO once daily. No dosage adjustment is required for renal insufficiency and mild hepatic impairment or in elderly patients.
- ✓ SEs are infrequent: GI symptoms (e.g., diarrhea, abdominal pain) and myalgias.
- ✓ A clinical outcome trial showed decreased reduction of CV events with the combination of simvastatin and ezetimibe compared with placebo in patients with chronic renal failure.
- ✓ It is useful in patients with FH (Familial → hypercholesterolemia) who do not achieve adequate LDL-C reductions with statin therapy alone.

هو add-on therapy لما الstatin ما يوصل الي بدنا اياه لما يكون لحاله reduction

اكي قبل كانوا لا
Primary hypercholesterolemia

- **Combined hyperlipoproteinemia** may be treated with statins, niacin, or fibrates **combinations** to lower LDL-C without elevating VLDL and triglycerides.

حكينا في complemantary action خصوصا الBAR ممكن ممكن ترفع الtriglyceride فهيك مع الniacin الوضع بكون ممتاز وهيك مافي riskكبير من الBAR انها ترفع الTG

- ✓ Niacin is the most effective agent and may be combined with a bile acid resin.
- ✓ Bile acid resins alone in this disorder may elevate VLDL and triglycerides, and their use as single agents for treating combined hyperlipoproteinemia should be avoided.

بعض الـ TG ألتر من 200

hypercholesterolemia + hypertriglycermia

- ✓ Ezetimibe could also be used in combination therapy in Type IIb.

LDL VLDL مشكلة الـ

- ❖ **Fibrates**

من هون الدكتورة تقرأ

- ✓ Fibric acid (gemfibrozil, fenofibrate) monotherapy is effective in reducing VLDL.

↓ LDL 5-20%, ↓ 20-50% TG, ↑ HDL 10-35%

- ✓ Fibrates reduce the synthesis of VLDL and with a concurrent increase in the rate of removal of triglyceride-rich lipoproteins from plasma.
- ✓ Fenofibrate may have fewer drug interactions than gemfibrozil but fenofibrate has been reported to worsen renal function.

- ✓ Fibrates may potentiate the effects of oral anticoagulants and INR should be monitored very closely with this combination.

- ✓ Enhanced hypoglycemic effects are reported to occur when a fibrate is given to patients on sulfonylurea compounds, but the mechanisms for these interactions are not well understood.

- ✓ A myositis syndrome of myalgia, weakness, stiffness, malaise, and elevations in CPK and AST is seen with the fibrates, and it seems to be more common in patients with renal insufficiency.

ممكن يعمل inc liver enzyme وبعمل muscle symptom مشان هيك ا combination من
الfibrate&statin بزيد الrisk of mylagia والliver toxicity ونفس الاشي بال combination
of statin &niacin

الfibrate بزيد من الgallblader ston

- **Hypertriglyceridemia** (lipoprotein pattern types I, III, IV, and V)

TG يكون في ارتفاع بال
chylomicron [Rare] IDL Rare hypertriglyceridemia [VLDL]
[chylomicron + VLDL] → Very Rare
الناس الي عندها TG عالي بدنا نعالجها بال non-pharmacolgical و treatment و remove secondary causes وممكن بال drug therapy

- ✓ Dietary fat restriction (10%-20% of calories as fat), weight loss, alcohol restriction, and treatment of the coexisting disorder are the basic elements of management.

control of Diabet
No Less consumption of carbohydrate [ما بدنا اكثر من 60 بال Diet]
Simple sugar ما بدنا نستخدم ال
non pharmacoligical وال lifestyle بدنا نحاول نشتغل على ال mangment وممكن حكينا نلجأ للادويه الي بالنقطة الي بعد هاي

- ✓ Drugs useful in hypertriglyceridemia include gemfibrozil or fenofibrate, niacin, and higher potency statins (atorvastatin, rosuvastatin, pitvastatin, and simvastatin).

لانه ال statin ممكن تنزل ال TG لحد 30% بال higher doses فهي نسبه كويسه

- ✓ Gemfibrozil or fenofibrate are the preferred drugs in diabetics because of the effect of niacin on glycemic control unless the newer ER forms are used.

Extended Release
ال fibrate هو المفضل لل diabetic patient

- ✓ Fenofibrate may be preferred in combination with statin therapy since it does not impair statin metabolism and minimizes potential drug interactions.

ال fenofibrate هو افضل اشي ينعطى مع ال statin بسبب

- ✓ Statins may also be used, because they provide modest reductions in triglycerides and modest elevations in HDL.

- ✓ Very high triglycerides are associated with pancreatitis.

يعني 500 واكثر
عشان هيك لازم نعالج الارتفاع بال TG وال risk بزيد لما تكون 1000 واكثر

- ✓ The effects of fish oil on lipoprotein metabolism are mediated through a reduction in VLDL production and suppression of VLDL apolipoprotein B.

VLDLبال main protien احد ال

- ✓ Fish oil supplementation may be most useful in patients with hypertriglyceridemia; however, its role in treatment is not well defined.

Hpertriglyceremia لل high dose of fish oil supplement عادة نستخدم

- ✓ Potential complications of fish oil supplementation as thrombocytopenia and bleeding disorders, have been noted, especially with high doses (eicosapentaenoic acid 15 to 30 g/d); and well-controlled trials are needed to determine if fish oils are safe and effective before their use may be broadly recommended.

الdrug drug interaction لل80%:statin من الادويه بصير الها mtabolism بالCype450 واكثر واحد فيهم هو
isoenzyme 3A4 الatorvstatin lovastatin,simvastatin بال3A4؟metabolism طيب مين همه الagent الي بصير الها
assoiccation with drug drug interactio فهذول metabolite by 3A4 لانهم فاي اشي compete مع ال3A4 او بعملو
inhibition الهم رح يزيد الlevel of these statin
وفي statin بصير الهم metabolisim بالCYP2C9/CYP2C8/2C19 الي هما الpitavastatin,fluvastatin,rousovstatin
برضه اي اشي باثر على هاي الenzyme رح يعمل D-D interaction معهم ولكن هذول اقل من 3A4 لانه معظم الادويه بصير الها
metabolisim بواسطتهم
وفي عنا الpravastatin not metabolite with CYP450 عشان هيك هو اقل واحد بالrisk of drug drug interaction
وتذكرو انه هو من mg(80-40) وهو modarte intencity statin(معرانه هو المفروض high بس على الhogher
dose بكونو modarate وهذا الاشي كويس)

لو واحد عنده hypertriglycermia (بين ال200 وال499طبعا بحكي عن الlipid)يعني High TG هذا يفضل نعالجه بstatin بكون مناسب ،طبعا
الfibrate والniacin option برضه بس الstatin افضل(هيك فهمت من الدكتوره)
طيب اذا كانت الTG عباره عن 500 واكثر يعني الrisk للpanceritits اكبر لازم اعطيه من الprimary agent الي بأثرو على الTG زي الfibrate
والniacin والfish oil at high doses(الي هو الomega3)
اذا المريض كان عنده 10years ASCVD اكثر من 7.5% والTG high(500 واكثر) بهاي الحالهبامكاننا نعطي statin بالبدايه ونضيف fibrate او
niacin او omega3 ولو انه الcombination من الstatin مع الfibrate والniacin بتزيد الrisk of muocitis والliver disease ولكن هو احد
الoption of mangment بهاي الحاله بس الاهم انه انزل الTG تحت ال500 واقلل الrisk ofpanceritits بهاي الحاله

➢ Low HDL cholesterol

- ✓ Low HDL-C is a strong independent risk predictor of ASCVD.
- ✓ Specified goal for HDL-C raising is not available.

ال specific goal مش موجوده انه مثلا لو رفعناها اكثر من 60 رح نقلل ال CV event يعني مافي evidance للموضوع

ممكن يكون سبب

- ✓ Low HDL-C may be a consequence of insulin resistance, physical inactivity, diabetes, cigarette smoking, very high carbohydrate intake, and certain drugs.

د هرمون برضه ممكن يكون السبب فلازم اشتغل عليهم لأحل المشكلة

- ✓ Niacin has the potential for the greatest increase in HDL.
- ✓ Due to the lack of pharmacological agents demonstrating an improvement in clinical outcomes by focusing on raising HDL-C, lifestyle modification remains the preferred approach.

مافي انه اعطي دوا لترفع ال HDL يعني لو الدوا بحل مشكله معينه وكان كان برفع ال HDL رح يرتفع بالمعية ومافي target goal لارفع ال HDL فبشتغل على ال non pharmacoligical

- ✓ Although alcohol consumption has been shown to increase HDL-C, it is not acceptable to recommend this to patients who do not already consume alcohol.

Combination Therapy

يعني افترض انه بدنا نعمل 2 monitoring لازم بين كل وحده والثانيه 6 اسابيع يعني تقريبا 12اسبوعر(يعني 3month)يعني بدي اعطي فتره قبل ما اقرر اعطي another agent

- ✓ Two or three lipoprotein profiles at 6-week intervals should confirm lack of response prior to initiation of combination therapy. → combination تبعت ال

- ✓ In general, a statin and a BAR or niacin with a BAR provide the greatest reduction in total and LDL cholesterol.

- ✓ In particular, familial hypercholesterolemia patients often require combination therapy (two or three drugs) and are managed with surgical therapy (partial ileal bypass), plasmapheresis (LDL-apheresis), and liver transplantation (to replace LDL receptors). 1, 2, 3 → non pharmacological therapy to Familial hypercholesterolemia

  الشي بشبه ال dialysis وبشيلوا ال LDL من ال blood

- ✓ Familial combined hyperlipidemia may respond better to a fibrate and a statin than to a fibrate and a BAR.

  hypertriglyceridemia + hypercholesterolemia

  Fenofibrate ← افضلها الشي وحكينا ليش فوق

الstatinبرفع الlevel لل other druge مثل simvastatin برفع ال digoxin (narrow theraputic index)وبرفع برضه ال warfarin فبزيد ال toxicity الهم وبرضه برفه ال verapmil,amiodarone

➢ Diabetic Dyslipidemia

ال LDL-C مش كتير elevated ولكن نوع الVariant لل LDL بتكون small,dense(pattren B) وهذا more atherogenic اذا بقارنه بال pattren A الي احنا بنعرفه

- ✓ Characterized by hypertriglyceridemia, low HDL-C, and LDL-C that is minimally elevated.
- ✓ Small, dense LDL (pattern B) in diabetes is more atherogenic than larger, more buoyant forms of LDL (pattern A).

بال lab test الي بنعملهم ما بميز بين ال pattren A وال pattren B يعني صح الLDL maily elevated ولكن نوع الcholesterol يعتبر more atherogenic

- ✓ Because the primary target is **LDL-C** in diabetic dyslipidemia, statins are considered by many to be initial drugs of choice.
- ✓ Although the effect of statins on triglycerides and HDL-C abnormalities commonly seen in diabetes is less than with fibrates, studies suggest that they reduce CHD risk significantly.

لعلاجي هما ال statin

➢ Pregnancy

يعني في مشكلة بال safty

- ✓ Cholesterol and triglyceride levels rise progressively throughout pregnancy. Drug therapy is not instituted nor is it usually continued during pregnancy.

- ✓ If the pregnant patient is very high risk, a bile acid resin may considered since there is no systemic drug exposure.

not absorbable يعني ما بتمتص

- ✓ Statins are contraindicated.

- ✓ Dietary therapy is the mainstay of treatment, with emphasis on maintaining a nutritionally balanced diet as per the needs of pregnancy.

اذا بدنا نغير الdiet بدنا ننتبه انه ما بدنانأثر على صحة الام او الجنين
الaltrnative للBAR هو الezetimibeولكن ما عنا data بالنسبه لموضوع
الsafty during pregnancyz بس هو alternative للBAR

1 + 2 → for hyper cholesterolemia

بعد الدكتورة قولت هون

➢ Other agents

1

Mipomersen is an oligonucleotide inhibitor of apolipprotein B-100 synthesis.

- ✓ It is indicated as an adjunct to lipid lowering medications and diet to reduce LDL-C, apolipoprotein B, total cholesterol and non-HDL-C in patients with homozygous familial hypercholesterolemia.
- ✓ The average reduction in LDL-C is ~25% with the most common adverse events being injection site pain (~10%). Mild to moderate elevations in liver enzymes have been reported. → تقريباً 10% وهو hepatotoxic

2

Lomitapide oral capsule is a microsomal triglyceride transfer protein (MTP) inhibitor.

- ✓ Inhibiting MTP reduces the level of cholesterol that the liver and intestines assemble and secrete into the circulation.
- ✓ The average decrease in LDL-C beyond baseline is ~40%.
- ✓ Hepatic steatosis associated with lomitapide may be a risk factor for progressive liver disease including steatohepatitis and cirrhosis. Mild to moderate elevations in liver enzymes have been reported.

hepatotoxic يعني

Alirocumab and evolocumab: A new category of LDL lowering therapy was approved by the FDA in 2015.

- ✓ Their mechanism of action is to inhibit proprotein convertase subtilisin/kexin type 9 (PCSK9).
- ✓ PCSK9 promotes intracellular degradation of hepatic LDL receptor and reduces LDL clearance from the circulation (therefore the drug lower LDL concentrations significantly).
- ✓ Alirocumab and evolocumab are given by SC injection.
- ✓ The typical LDL reduction ranges from about 40% to over 60% with both drugs.
- ✓ The most common adverse effect reported in clinical trials is injection site pain.

بشكل مختصر، إليك آلية عمل أدوية **Alirocumab** و **Evolocumab**:

1. **المشكلة (PCSK9):** يوجد بروتين في الجسم يدمر "مستقبلات الكوليسترول" الموجودة على الكبد. (وكلما دُمّرت هذه المستقبلات، زاد الكوليسترول في دمك).
2. **الحل (الدواء):** هذه الأدوية تُعطل هذا البروتين (**تثبطه**).
3. **النتيجة:** تزيد "مستقبلات الكوليسترول" على سطح الكبد، فتعمل مثل المكنسة التي تسحب الكوليسترول الضار (**LDL**) من الدم بكفاءة عالية.

باختصار: الدواء يحمي "المستقبلات" التي تنظف الدم، مما يؤدي لانخفاض حاد وسريع في مستويات الكوليسترول.

Table 5: Effects of Drug Therapy on Lipids

Drug	Mechanism of Action	Effects	Comment
Cholestyramine, colestipol and colesevelam	↑ LDL catabolism ↓ cholesterol absorption	↓ Cholesterol	Problem with compliance; binds many co-administered acidic drugs immediate release(regularبين محضره انها تكون extended release formulaال release)وبين sutaind releaseال من حيث rate of absorptionوال sub immediateال sequance of metabolisim وهيك بتقلل flushingالي هي مشكله sustaind releaseال والي هيم مشكله hepatotoxcityوبتقلل ال
Niacin	↓ LDL and VLDL ↓ synthesis	↓ Triglyceride ↓ cholesterol ↑ HDL	Problems with patient acceptance; good in combination with bile acid resins; extended release niacin causes less flushing and is less hepatotoxic than sustained release
Gemfibrozil, fenofibrate, clofibrate	↑ VLDL clearance ↓ VLDL synthesis	↓ Triglyceride ↓ cholesterol ↑ HDL	Clofibrate causes cholesterol gall stones; modest LDL lowering; raises HDL; gemfibrozil inhibits the metabolism (glucuronidation) of simvastatin, lovastatin and atorvastatin بتزيد الcholesterolبال bile acidوهذا الاشي بزيد الcalcificationللcholesterol وهذا بعمل

Table 5: Effects of Drug Therapy on Lipids			
Drug	Mechanism of Action	Effects	Comment
Simvastatin, Atorvastatin Rosuvastatin	↑ LDL catabolism; inhibit LDL synthesis	↓ Cholesterol	Highly effective in heterozygous familial hypercholesterolemia and in combination with other agents
Ezetimibe	Blocks cholesterol absorption across the intestinal border	↓ Cholesterol	Few adverse effects; effects additive to other drugs
Mipomerson	Inhibitor of Apolipoprotein B-100	↓ Cholesterol	Increase in transaminases, risk of hepatosteatosis and hepatotoxicity; must be given by SQ injection. Only indicated for familial hypercholesterolemia. To be used along with other lipid lowering therapies (statins)

Table 5: Effects of Drug Therapy on Lipids			
Drug	Mechanism of Action	Effects	Comment
Lomitapide	Microsomal triglyceride transfer protein inhibitor	↓ Cholesterol	Hepatotoxicity must be monitored via Juxtapid Risk Evaluation and Mitigation Strategy program. Only indicated for familial hypercholesterolemia. To be used along with other lipid lowering therapies (statins)
Alirocumab **Evolocumab**	PCSK9 inhibitor	↓ Cholesterol, ↓ Lpa	Given by SQ injection, injection site pain, low risk of hepatoxicity

المريض بعبي form معين مشان يعمل monitor
للhepatotoxcity الي ممكن تصير عنده

➢ Evaluation of Therapeutic Outcomes

- ✓ In patients treated for secondary intervention, symptoms of atherosclerotic CVD as angina or intermittent claudication, may improve over months to years. ممكن تتحسن الـ symptom بس بعد فترة طويله

يعني discontinous thrapy ونعمل control للlipid فممكن تخف مع الوقت

- ✓ If patients have xanthomas, these lesions should regress with therapy.

صايم من 12 ساعه او أكثر

- ✓ Lipid measurements should be obtained in the fasted state to minimize interference from chylomicrons, and once the patient is stable, monitoring is needed at intervals of 6 months to 1 year. بتجي من الأكل

انه الواحد يسجل

طريقه منهجيه مش عشوائيه

- ✓ Use of diet diaries enable information about diet to be collected in a systematic fashion and may improve patient adherence to dietary recommendations. يعني يعمل جدول ويشوف هل ماشي هلى الdiet الي كتبه اخصائي التغذيه؟

- ✓ Patients on resin therapy should have a fasting lipid profile (FLP) panel checked every 4 to 8 weeks until a stable dose; triglycerides should be checked at stable dose to insure they have not increased.

لانه اله جرعات عاليه زي الcholesterolamin ممكن توصل 24g باليومب devided dose ففعليا
الtitration dose بكون على فترة طويله فاحنا فعليا بنضل نعمل checlpk لنوصل ال stabel dose

- ✓ Niacin requires baseline LFT, uric acid and glucose; repeat tests are appropriate at doses of 1,000 to 1,500 mg per day.

لما يحس انه اعراض diabete مع الniacin والstatin(ممكن ال statin يعملو diabetic خصوصا لو على high dose)وخصوصا لو المريض بكون عنده risk لل diabete زي الmetabolic syndrom والobesity او عندهم pre dibete بس مع هيك بتضل الbenifit اعلى من الrisk لانه ال statin بتحمي من الrisk of arheroscalarosis وابCVD يعني تحمي الpre event CV event مقابل انها تعمل diabet

- ✓ Symptoms myopathy or diabetes-like symptoms should be investigated and may require CK or glucose determinations; more frequent monitoring in diabetics may be necessary.

كل شهر لشهرين ناخذ FLP ونشوف نغير الجرعة او بعد الinitial dose

- ✓ A FLP 4 to 8 weeks after the initial dose or dose changes with statins is appropriate.

+manufacturing

- ✓ LFTs should be obtained at baseline and periodically thereafter based on package insert information; recognized experts believe that monitoring for hepatotoxicity and myopathy should be symptom triggered.

baseline test عامل وطبعا بكون liver enzyme الbشيك عل symptom اذا في

- ✓ In particular, older patients are more likely to have constipation (bile acid resins), skin and eye changes (niacin), gout (niacin), gallstones (fibrates), and bone/joint disorders (fibrates, statins).

- ✓ Therapy (in elderly) should be started with lower doses and titrated up slowly to minimize adverse effects.

صلاحيه و حطت
مهم تعرفوه

حسب من وين جاي الevidance
بنحدد الclass fecommendation

حكت لو تقرأو التفاصيل رح تعرفو انه
المصطلحات رح تختلف(رح احدد الي حكتهم)

الـ updated صح داخلين
slide

بالملاب بس داخلين بالمادة فلا
تنزل الركيزة شرحهم رح
انزل تقريغهم ان شاء الله

لا تنسوا زملينا اهل الله يرحمه
من دعائكم

CLASS (STRENGTH) OF RECOMMENDATION

CLASS I (STRONG) — Benefit >>> Risk

Suggested phrases for writing recommendations:
- Is recommended
- Is indicated/useful/effective/beneficial
- Should be performed/administered/other
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is recommended/indicated in preference to treatment B
  - Treatment A should be chosen over treatment B

CLASS IIa (MODERATE) — Benefit >> Risk

Suggested phrases for writing recommendations:
- Is reasonable
- Can be useful/effective/beneficial
- Comparative-Effectiveness Phrases†:
  - Treatment/strategy A is probably recommended/indicated in preference to treatment B
  - It is reasonable to choose treatment A over treatment B

CLASS IIb (WEAK) — Benefit ≥ Risk

Suggested phrases for writing recommendations:
- May/might be reasonable
- May/might be considered
- Usefulness/effectiveness is unknown/unclear/uncertain or not well established

CLASS III: No Benefit (MODERATE) — Benefit = Risk
(Generally, LOE A or B use only)

Suggested phrases for writing recommendations:
- Is not recommended
- Is not indicated/useful/effective/beneficial
- Should not be performed/administered/other

CLASS III: Harm (STRONG) — Risk > Benefit

Suggested phrases for writing recommendations:
- Potentially harmful
- Causes harm
- Associated with excess morbidity/mortality
- Should not be performed/administered/other

LEVEL (QUALITY) OF EVIDENCE‡

LEVEL A
- High-quality evidence‡ from more than 1 RCTs
- Meta-analyses of high-quality RCTs
- One or more RCTs corroborated by high-quality registry studies

LEVEL B-R (Randomized)
- Moderate-quality evidence‡ from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

LEVEL B-NR (Nonrandomized)
- Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies
- Meta-analyses of such studies

LEVEL C-LD (Limited Data)
- Randomized or nonrandomized observational or registry studies with limitations of design or execution
- Meta-analyses of such studies
- Physiological or mechanistic studies in human subjects

LEVEL C-EO (Expert Opinion)

Consensus of expert opinion based on clinical experience

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR I and IIa; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

Updated slide

TABLE 35-6

Pharmacokinetic Properties of Statins

Statin	Half-Life (hours)	CYP Enzyme Metabolism	Lipophilic?	Renal Excretion (%)
Atorvastatin	14	CYP3A4	Yes	<2
Fluvastatin	3	CYP2C9	Yes	5
Lovastatin	2-3	CYP3A4	Yes	10
Pitavastatin	12	CYP2C9	Moderately	15
Pravastatin	2	None	No	20
Rosuvastatin	19	CYP2C9	No	10
Simvastatin	2	CYP3A4	Yes	13

Updated slide

TABLE 35-7

Safety of Lipid-Lowering Therapies

Lipid-Lowering Drug Class	Adverse Effects		Contraindications
	Common/Possible (1%-10%)	Rare/Unlikely (<1%)	
Statins	• Statin-associated muscle symptoms (myalgia/myopathy) • New-onset diabetes mellitus • Transient, mild elevation in transaminase levels	• Rhabdomyolysis • Severe hepatotoxicity	• Pregnancy *in most patients* • Breastfeeding • Decompensated cirrhosis • Acute liver failure
Cholesterol absorption inhibitors	• GI adverse effects • Myalgias (when used with statin) • Elevated transaminase levels (when used with statin)	• Thrombocytopenia	• Pregnancy/breastfeeding • Acute liver failure
Bile acid sequestrants	• GI adverse effects and/or obstruction • Impaired absorption of fat-soluble vitamins • Reduced bioavailability of select drugs	• Ileus • Cholecystitis • Severe hypertriglyceridemia	• History of bowel obstruction • Fasting TG are 300 mg/dL or higher
ACL inhibitors	• Hyperuricemia • Cholelithiasis	• Increased risk of tendon rupture • Increased risk of benign prostate hyperplasia	
PCSK9 mAbs	• Injection-site reactions • Flu-like symptoms post-injection		• Hypersensitivity reaction to alirocumab or evolocumab

Updated slide

Table 35-7
Safety of Lipid-Lowering Therapies

Fibrates	• GI adverse effects • Transient elevation in transaminases • Myalgias (especially when used with statin) • Mild increase in serum creatinine	• Increased risk of gallstones	• Preexisting gallbladder disease • CrCl of 30 mL/min (0.5 mL/s) or lower
Omega-3 PUFA	• GI adverse effects • Eructation • Increased risk of bleeding when used with antiplatelets or anticoagulants • Increased risk of atrial fibrillation or flutter		• Caution in patients with allergy or sensitivity to fish and/or shellfish
Niacin	• Dermatologic effects (flushing/itching) • Increased transaminases • Hyperuricemia • Hyperglycemia	• Increased risk of atrial fibrillation or flutter • Rhabdomyolysis (with statin) • Hepatotoxicity (with statin)	• Active peptic ulcer • Arterial hemorrhage • Persistently elevated transaminase levels
Inclisiran	• Injection-site reactions		• Pregnancy/breastfeeding
Evinacumab	• Infusion-site pruritus • Influenza-like reactions • Rhinorrhea		• Pregnancy/breastfeeding

ACL, adenosine triphosphate-citrate lyase; CrCl, creatinine clearance; mAbs, monoclonal antibodies; PUFA, polyunsaturated fatty acids; SAMS, statin-associated muscle symptoms.

Updated slide

Lipoprotein Goals for ASCVD Risk Reduction

Patient population	LDL-C <100 mg/dL (2.6 mmol/L) Non–HDL-C <130 mg/dL (3.4 mmol/L)	LDL-C <70 mg/dL (1.8 mmol/L) Non–HDL-C <100 mg/dL (2.6 mmol/L)	LDL-C <55 mg/dL (1.4 mmol/L) Non–HDL-C <85 mg/dL (2.2 mmol/L)
Primary prevention	PREVENT-ASCVD <10% • If TG ≥150 mg/dL to 499 mg/dL, apoB goal: <90 mg/dL	PREVENT-ASCVD ≥10% • If TG ≥150 mg/dL to 499 mg/dL, apoB goal: <70 mg/dL	N/A
Severe hypercholesterolemia	**Without** FH, ASCVD risk factors, and subclinical atherosclerosis	**With** FH, ASCVD risk factors, or subclinical atherosclerosis	Severe hypercholesterolemia or HeFH with clinical ASCVD
Diabetes	**Without** ASCVD risk factors or diabetes-specific risk modifiers • apoB goal: <90 mg/dL	**With** ASCVD risk factors or diabetes-specific risk factors • apoB goal: <70 mg/dL	N/A
Subclinical atherosclerosis	CAC = 1–99 AU and <75th percentile for age, sex, and race	• CAC ≥100 to 299 AU or ≥75th percentile for age, sex, race • CAC ≥300 to 999 AU ◦ Optional goal: LDL-C <55 mg/dL, non–HDL-C <85 mg/dL and consider apoB goal <55 mg/dL	CAC ≥1000 AU
Hypertriglyceridemia	<50 y old with no additional risk enhancers	• With clinical ASCVD not at very high risk ◦ apoB goal: <70 mg/dL • Age 40–75 y with ≥1 ASCVD risk factor ◦ apoB goal: <70 mg/dL	With clinical ASCVD at very high risk • apoB goal: <55 mg/dL
Clinical ASCVD	N/A	Not at very high risk • Optional goal: LDL-C <55 mg/dL, non–HDL-C <85 mg/dL and consider apoB goal <55 mg/dL	• At very high risk ◦ apoB goal: <55 mg/dL • With CKD

Figure 1. Lipoprotein Goals for ASCVD Risk Reduction.

apoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; AU, Agatston units; CAC, coronary artery calcium; CKD, chronic kidney disease; FH, familial hypercholesterolemia; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; and TG, triglycerides.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
New	3.3. Measurement of ApoB	N/A	COR 2a: In adults on LLT, particularly those with ASCVD, CKM syndrome, type 2 diabetes, and/or elevated TG, measurement of apoB is reasonable to guide decisions regarding further therapeutic intensification once LDL-C and/or non–HDL-C goals are achieved.
New	3.4. Measurement of Lp(a)	N/A	COR 1: In all adults, measurement of Lp(a) concentration is recommended at least once for ASCVD risk assessment.
New	4.1.5. Dietary Supplements	N/A	COR 3: In individuals with dyslipidemia, the use of dietary supplements is not recommended to lower LDL-C or TG based on limited and inconsistent data and/or limited benefits in lipid-lowering and reduction in ASCVD risk.
New	4.1.6. When to Refer to a Registered Dietitian Nutritionist	N/A	COR 1: In individuals with fasting TG ≥1000 mg/dL (11.3 mmol/L) referral to an RDN is recommended to create an individualized treatment plan aimed at reducing TG and the risk of pancreatitis.
New	4.2.3.2. PREVENT-ASCVD Equations	N/A	COR 1: In adults aged 30 to 79 y without ASCVD or subclinical atherosclerosis and with an LDL-C level between 70 and 189 mg/dL (1.8-4.9 mmol/L), the PREVENT-ASCVD equations should be used to estimate 10-y ASCVD risk, with categorization as having low (<3%), borderline (3% to <5%), intermediate (5% to <10%), or high (≥10%) risk.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
Revised	4.2.3.3. Risk Enhancers	COR 2b: In patients at borderline risk, in risk discussion, the presence of risk-enhancing factors may justify initiation of moderate-intensity statin therapy.	COR 2a: In adults without ASCVD with a borderline 10-y ASCVD risk estimate (3% to <5%) by the PREVENT-ASCVD equations, consideration of risk enhancers is reasonable to personalize risk assessment and the potential benefit of initiating LLT as an adjunct to lifestyle management to reduce ASCVD risk.
New	4.2.3.3. Risk Enhancers	N/A	COR 2a: In adults without ASCVD with a borderline 10-y ASCVD risk estimate (3% to <5%) by the PREVENT-ASCVD equations, if hsCRP is measured and is ≥2 mg/L on 2 successive occasions with no identifiable underlying cause of hsCRP elevation, high-intensity statin therapy can be useful to reduce the risk of ASCVD events.
New	4.2.3.4. Reproductive Risk Markers	N/A	COR 2a: In adults without ASCVD, consideration of reproductive risk markers, such as early menopause (<45 y old) and history of adverse pregnancy outcomes (gestational hypertension, preeclampsia, gestational diabetes, preterm delivery) is reasonable to personalize ASCVD risk assessment when considering the potential benefit of initiating LLT as an adjunct to lifestyle management for primary ASCVD prevention.
Revised	4.2.3.6. Selective Imaging of Subclinical Atherosclerosis	COR 2a: In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone, or initiate statin therapy.	COR 1: In adults at intermediate risk and select adults at borderline risk with no prior ASCVD, if the decision regarding LLT remains uncertain, a CAC score should be used for further risk stratification and to guide the decision to withhold, postpone, or initiate therapy.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
New	4.2.3.7. Management in Primary Prevention in Adults 30 to 79 Years of Age With LDL-C Levels 70 to 189 mg/dL	N/A	COR 1: In adults at low (<3%) 10-y estimated risk for ASCVD who have an LDL-C <160 mg/dL (4.1 mmol/L) and a 30-y risk estimate of <10% (for those aged 30-59 y), counseling on health behaviors is recommended to reduce LDL-C and risk for ASCVD.
New	4.2.3.7. Management in Primary Prevention in Adults 30 to 79 Years of Age With LDL-C Levels 70 to 189 mg/dL	N/A	COR 2a: In adults at low (<3%) 10-y estimated risk for ASCVD but with an LDL-C of 160 to 189 mg/dL (4.1-4.9 mmol/L) or a 30-y ASCVD risk ≥10% (for those aged 30-59 y), a moderate-intensity statin is reasonable to reduce cumulative exposure to atherogenic lipoproteins.
New	4.2.3.7. Management in Primary Prevention in Adults 30 to 79 Years of Age With LDL-C Levels 70 to 189 mg/dL	N/A	COR 2a: In adults at borderline (3% to <5%) 10-y estimated risk for ASCVD risk in whom a decision is made to initiate statin therapy for primary prevention, a moderate-intensity statin is reasonable to achieve ≥30% to 49% LDL-C reduction and to reduce ASCVD risk.
New	4.2.3.7. Management in Primary Prevention in Adults 30 to 79 Years of Age With LDL-C Levels 70 to 189 mg/dL	N/A	COR 1: In adults at intermediate (5% to <10%) 10-y estimated risk for ASCVD, at least a moderate-intensity statin is recommended to achieve ≥30% to 49% LDL-C reduction and to reduce ASCVD risk; for those in the higher end of this risk range, a high-intensity statin is beneficial to further reduce LDL-C by ≥50% and reduce ASCVD risk.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
New	4.2.3.7. Management in Primary Prevention in Adults 30 to 79 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.8-4.9 mmol/L)	N/A	COR 2a: In adults at borderline (3% to <5%) or intermediate (5% to <10%) 10-y estimated risk for ASCVD in whom statin therapy is initiated, it is reasonable to treat to a goal of LDL-C <100 mg/dL (2.6 mmol/L) and non–HDL-C <130 mg/dL (3.4 mmol/L) to reduce ASCVD risk.
New	4.2.3.7. Management in Primary Prevention in Adults 30 to 79 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.8-4.9 mmol/L)	N/A	COR 1: In adults at high (≥10%) 10-y risk for ASCVD in whom LLT is initiated for primary prevention, high-intensity statin therapy is recommended to achieve an LDL-C reduction of ≥50% to reduce the risk of ASCVD.
New	4.2.3.7. Management in Primary Prevention in Adults 30 to 79 Years of Age With LDL-C Levels 70 to 189 mg/dL (1.8-4.9 mmol/L)	N/A	COR 2a: In adults at high (≥10%) 10-y risk for ASCVD in whom a decision to initiate statin therapy is made, it is reasonable to treat to a goal of LDL-C <70 mg/dL (1.8 mmol/L) and non–HDL-C <100 mg/dL (2.6 mmol/L) to reduce ASCVD risk.
New	4.2.3.7. Management in Primary Prevention in Adults 30 to 79 Years of Age With LDL-C Levels 70 to 189 mg/dL	N/A	COR 2a: In adults at high (≥10%) 10-y estimated risk for ASCVD on maximally tolerated statin, it is reasonable to add ezetimibe if a goal LDL-C <70 mg/dL (1.8 mmol/L) and non–HDL-C <100 mg/dL (2.6 mmol/L) is not achieved.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
Revised	4.2.4.3. Severe Hypercholesterolemia With LDL-C ≥190 mg/dL (4.9 mmol/L)	COR 2a: In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher (4.9 mmol/L) who achieve less than a 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of 100 mg/dL or higher (2.6 mmol/L), ezetimibe therapy is reasonable.	COR 1: In adults with severe hypercholesterolemia with an LDL-C ≥190 mg/dL (4.9 mmol/L) and without clinical ASCVD, additional ASCVD risk factors, HeFH, or subclinical atherosclerosis who are on maximally tolerated statin therapy, the addition of ezetimibe, a PCSK9 mAb and/or bempedoic acid is recommended to achieve a goal of LDL-C <100 mg/dL (2.6 mmol/L) and a non–HDL-C goal of <130 mg/dL (3.4 mmol/L) and to reduce ASCVD risk.
Revised	4.2.4.3. Severe Hypercholesterolemia With LDL-C ≥190 mg/dL (4.9 mmol/L)	COR 2b: In patients 30 to 75 y of age with heterozygous FH and with an LDL-C level of 100 mg/dL or higher (2.6 mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered.	COR 1: In adults with severe hypercholesterolemia with LDL-C ≥190 mg/dL (4.9 mmol/L) without clinical ASCVD but with clinical or genetic confirmation of HeFH, additional ASCVD risk factors, or documented coronary calcification, who are on maximally tolerated statin therapy, the addition of ezetimibe, a PCSK9 mAb and/or bempedoic acid to achieve a goal of LDL-C <70 mg/dL (1.8 mmol/L) and non–HDL-C <100 mg/dL (2.4 mmol/L) is recommended to lower LDL-C and reduce ASCVD risk.
New	4.2.4.3. Severe Hypercholesterolemia With LDL-C ≥190 mg/dL (4.9 mmol/L)	N/A	COR 1: In adults with severe hypercholesterolemia with LDL-C ≥190 mg/dL (4.9 mmol/L) with clinical ASCVD, who are on maximally tolerated statin therapy, the addition of ezetimibe, a PCSK9 mAb, or bempedoic acid is recommended to achieve a goal of LDL-C <55 mg/dL (1.4 mmol/L) and non–HDL-C <85 mg/dL (2.2 mmol/L) to lower LDL-C and reduce ASCVD risk.
New	4.2.4.3. Severe Hypercholesterolemia With LDL-C ≥190 mg/dL (4.9 mmol/L)	N/A	COR 2a: In adults with severe hypercholesterolemia with or without clinical ASCVD and LDL-C ≥100 mg/dL (2.6 mmol/L) despite maximally tolerated statin with or without ezetimibe therapy, treatment with inclisiran is reasonable to lower LDL-C.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
Revised	4.2.5. Diabetes in Adults Without Established ASCVD	COR 1: In adults 40 to 75 y of age with diabetes, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated.	COR 1: In adults 40 to 75 y of age with diabetes and without clinical ASCVD, moderate-intensity statin therapy is indicated to achieve ≥30% to 49% reduction in LDL-C and a goal of LDL-C <100 mg/dL (2.6 mmol/L) and non–HDL-C <130 mg/dL (3.4 mmol/L) to reduce ASCVD risk.
Revised	4.2.5. Diabetes in Adults Without Established ASCVD	COR 2a: In adults with diabetes who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more.	COR 2a: In adults 40 to 75 y of age with diabetes who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy to achieve ≥50% reduction in LDL-C and a goal of LDL-C <70 mg/dL (1.8 mmol/L) and non–HDL-C <100 mg/dL (2.6 mmol/L) to reduce ASCVD risk.
Revised	4.2.6. Secondary ASCVD Prevention	COR 1: In patients who are 75 y of age or younger with clinical ASCVD, high-intensity statin therapy should be initiated or continued with the aim of achieving a 50% or greater reduction in LDL-C levels.	COR 1: In adults with clinical ASCVD who are not at very high risk, high-intensity statin therapy should be initiated to achieve ≥50% reduction in LDL-C and a goal of LDL-C <70 mg/dL (1.8 mmol/L) and non–HDL-C <100 mg/dL to reduce the risk of recurrent ASCVD events.
New	4.2.6. Secondary ASCVD Prevention	N/A	COR 2a: In adults with clinical ASCVD who are not at very high risk and on maximally tolerated statin therapy, it is reasonable to add ezetimibe, a PCSK9 mAb, or bempedoic acid (selected based on the degree of LDL-C lowering needed and patient preference) to achieve a goal LDL-C <55 mg/dL (1.4 mmol/L) and non–HDL-C <85 mg/dL (2.2 mmol/L) and to reduce the risk of ASCVD events.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
New	4.2.6. Secondary ASCVD Prevention	N/A	COR 2a: In adults with clinical ASCVD who are at very high risk and on maximally tolerated statin therapy, ezetimibe and/or a PCSK9 mAb should be added (selected based on the degree of LDL-C lowering needed and patient preference) to achieve a goal of LDL-C <55 mg/dL (1.4 mmol/L) and non–HDL-C <85 mg/dL (2.2 mmol/L) and to reduce risk of ASCVD events.
New	4.2.6. Secondary ASCVD Prevention	N/A	COR 2a: In adults with clinical ASCVD who are at very high risk on maximally tolerated statin therapy, it is reasonable to add bempedoic acid to a statin, with or without ezetimibe and/or PCSK9 mAb, to reach an LDL-C goal <55 mg/dL (1.4 mmol/L) and non–HDL-C <85 mg/dL (2.2 mmol/L) to reduce the risk of ASCVD events.
New	4.2.6. Secondary ASCVD Prevention	N/A	COR 2a: In adults with clinical ASCVD who are at very high risk and on maximally tolerated statin therapy with or without ezetimibe, it is reasonable to add inclisiran in those unable to tolerate or obtain evolocumab or alirocumab or have a strong preference for less frequent dosing to achieve an LDL-C goal <55 mg/dL (1.4 mmol/L) and non–HDL-C <85 mg/dL (2.2 mmol/L).
New	4.2.8.4. Management of Dyslipidemia in Persons Planning Pregnancy, During Pregnancy, or While Lactating	N/A	COR 2a: In pregnant individuals with severe fasting hypertriglyceridemia (TG ≥500 mg/dL [5.7 mmol/L]), the use of fibrates (after the first trimester) or high-dose omega-3 ethyl esters is reasonable as an adjunct to lifestyle management to lower TG levels and reduce the risk of pancreatitis.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
New	4.2.8.8. Adults With CKD—Stage 3 or Higher	N/A	COR 1: In adults with CKD stage 3 or higher and clinical ASCVD, LLT with high-intensity statin therapy with or without ezetimibe and/or a PCSK9 mAb is recommended to achieve a ≥50% reduction in LDL-C levels and a goal of LDL-C <55 mg/dL (1.4 mmol/L) and non–HDL-C <85 mg/dL (2.2 mmol/L) to reduce ASCVD risk.
New	4.2.8.9. Persons Living With HIV	N/A	COR 1: In people living with HIV aged 40 to 75 on stable combination antiretroviral therapy, statin therapy is recommended to reduce risk of a first ASCVD event and reduce the rate of coronary atherosclerosis progression.
New	4.2.8.10. Adults With Cancer or History of Cancer	N/A	COR 1: Adult cancer survivors with life expectancy of at least 2 y who otherwise qualify for LLT should be treated similarly to people without history of cancer to reduce the risk of ASCVD events.
New	4.2.9. Management of Hypertriglyceridemia	N/A	COR 1: In adults with clinical ASCVD and LDL-C ≥55 mg/dL (1.4 mmol/L) and non–HDL-C ≥85 mg/dL on maximally tolerated statin with persistently elevated TG levels ≥150 to 999 mg/dL (1.7–11.3 mmol/L), intensification of LDL-C–lowering therapy is recommended to reduce ASCVD risk.

What Is New?

Updated slide

New or Revised	Section Title	2018 Recommendation	2026 Recommendation
New	4.2.9. Management of Hypertriglyceridemia	N/A	COR 1: In adults with familial chylomicronemia syndrome and fasting TG ≥1000 mg/dL (11.3 mmol/L), olezarsen (an apoC3 inhibitor) is recommended, as an adjunct to diet, to lower TG levels and reduce the risk of pancreatitis.
New	4.2.9. Management of Hypertriglyceridemia	N/A	COR 1: In adults aged 40 to 75 y without a history of ASCVD or diabetes who have persistently elevated TG levels ≥150 to 499 mg/dL (≥1.7–5.6 mmol/L), it is recommended to estimate 10-y ASCVD risk by the PREVENT equations to guide a benefit-risk discussion regarding further optimization of diet and lifestyle management as well as the potential initiation of statin therapy to reduce ASCVD risk.
New	4.2.10. Approach to Patients With Elevated Lp(a)	N/A	COR 1: In all individuals with elevated Lp(a) (≥125 nmol/L or ≥50 mg/dL), optimal early control of modifiable cardiovascular risk factors is recommended to reduce ASCVD risk.
New	4.2.10. Approach to Patients With Elevated Lp(a)	N/A	COR 1: In individuals with clinical ASCVD and elevated Lp(a) who have not achieved LDL-C and non–HDL-C treatment goals on maximally tolerated statin therapy, the addition of a PCSK9 mAb with proven cardiovascular benefit is recommended to achieve treatment goals and reduce ASCVD risk.

Thank You