Ischemic heart diseases and Dyslipidemia

Color Index	IMPORTANT	NOTES	GOLD	EXTRA

OBJECTIVES

1. CVD risk factors and assessment tools
2. Cardiovascular diseases.
3. Dyslipidemia and introduction to new guidelines on lipid management.

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Primary prevention of CVD

The achievement and maintenance of good health is being emphasized in programs from The American Heart Association that promote seven ideal cardiovascular health metrics, including:
not smoking, *being physically active*, *controlling blood pressure*, *controlling blood glucose*, *controlling total cholesterol*, *being normal in weight* and *eating healthy diet*.

CVD risk factors

Modifiable risk factors	Non-modifiable risk factors	Emerging risk factors
Cigarette and tobacco smoking	Age	Elevated high-sensitivity C-reactive protein
High blood cholesterol	Gender	Coronary artery calcification
High blood pressure	Family history of CVD	Elevated lipoprotein A
Physical inactivity	--------	Homocysteine
Obesity	--------	Fibrinogen
Diabetes	--------	--------

C-reactive protein

- A person's baseline level of inflammation as assessed by the plasma concentration of CRP.
- It predicts the long-term risk of a first MI.

If a patient with chest pain and CRP level is:
Between 3 to 10: that indicate the patient is at high risk of developing an attack.
Above 10: that indicate that the patient is having an acute attack.

The Framingham risk score (FRS)

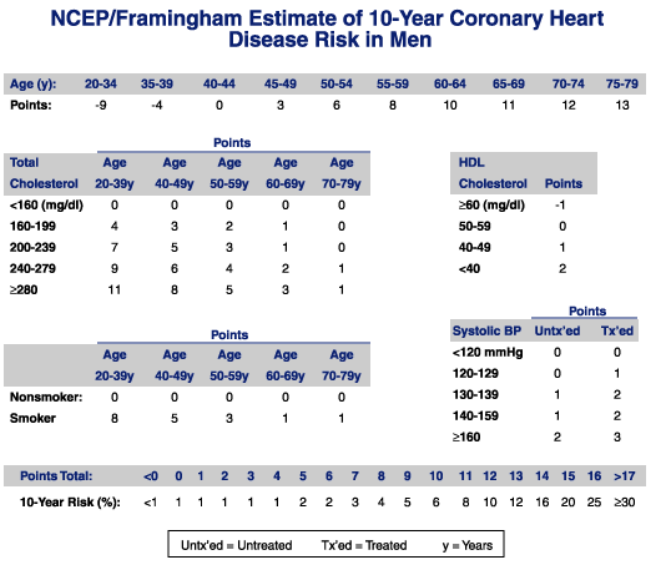
- Scoring system used to calculate patients' risk of coronary events.
- The Framingham study first introduced the term *Risk Factors* to the medical literature.
- *Age*, *Smoking status*, *Systolic BP*, *HTN treatment*, *Total cholesterol levels* and *HDL-C levels* are all used to assess the cumulative risk

Cases in which you don't need FRS?

Patients who already have high risk due to other diseases:

- Stroke.
- Bypass surgery or balloon angioplasty.
- Type 2 DM.
- Kidney diseases.
- Abdominal aortic aneurysm.
- Familial hypercholesterolemia.
- Peripheral artery disease.
- Carotid artery diseases.

NCEP/Framingham Estimate of 10-year coronary heart disease risk in men



NCEP/Framingham Estimate of 10-Year Coronary Heart Disease Risk in Men

Age (y):	20-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79
Points:	-9	-4	0	3	6	8	10	11	12	13

	Points				
Total Cholesterol	Age 20-39y	Age 40-49y	Age 50-59y	Age 60-69y	Age 70-79y
<160 (mg/dl)	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
≥280	11	8	5	3	1

HDL Cholesterol	Points
≥60 (mg/dl)	-1
50-59	0
40-49	1
<40	2

	Points				
	Age 20-39y	Age 40-49y	Age 50-59y	Age 60-69y	Age 70-79y
Nonsmoker:	0	0	0	0	0
Smoker	8	5	3	1	1

	Points	
Systolic BP	Untx'ed	Tx'ed
<120 mmHg	0	0
120-129	0	1
130-139	1	2
140-159	1	2
≥160	2	3

Points Total:	<0	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	>17
10-Year Risk (%):	<1	1	1	1	1	1	2	2	3	4	5	6	8	10	12	16	20	25	≥30

Untx'ed = Untreated Tx'ed = Treated y = Years

NCEP/Framingham Estimate of 10-year coronary heart disease risk in men

Estimate of 10-Year Risk of CHD for Men and Women (Framingham Point Scores)

Age, y	Points M	Points F
20–34	–9	–7
35–39	–4	–3
40–44	0	0
45–49	3	3
50–54	6	6
55–59	8	8
60–64	10	10
65–69	11	12
70–74	12	14
75–79	13	16

HDLC, mg/dL	Points M	Points F
≥ 60	–1	
50–59	0	
40–49	1	
< 40	2	

SBP, mm Hg	Points Untreated M	Points Untreated F	Points Treated M	Points Treated F
< 120	0	0	0	0
120–129	0	1	1	3
130–139	1	2	2	4
140–159	1	3	2	5
≥ 160	2	4	3	6

TCHOL, mg/dL	Points Age 20–39 y M	F	Age 40–49 y M	F	Age 50–59 y M	F	Age 60–69 y M	F	Age 70–79 y M	F
< 160	0	0	0	0	0	0	0	0	0	0
160–199	4	4	3	3	2	2	1	1	0	1
200–239	7	8	5	6	3	4	1	2	0	1
240–279	9	11	6	8	4	5	2	3	1	2
≥ 280	11	13	8	10	5	7	3	4	1	2

Tobacco	Points Age 20–39 y M	F	Age 40–49 y M	F	Age 50–59 y M	F	Age 60–69 y M	F	Age 70–79 y M	F
Nonsmoker	0	0	0	0	0	0	0	0	0	0
Smoker	8	9	5	7	3	4	1	2	1	1

Point Total and 10-Year Risk, %			
M		F	
< 0	< 1	< 9	< 1
0	1	9	1
1	1	10	1
2	1	11	1
3	1	12	1
4	1	13	2
5	2	14	2
6	2	15	3
7	3	16	4
8	4	17	5
9	5	18	6
10	6	19	8
11	8	20	11
12	10	21	14
13	12	22	17
14	16	23	22
15	20	24	27
16	25	≥ 25	≥ 30
≥ 17	≥ 30		
Total____	Male % risk____	Total____	Female % risk____

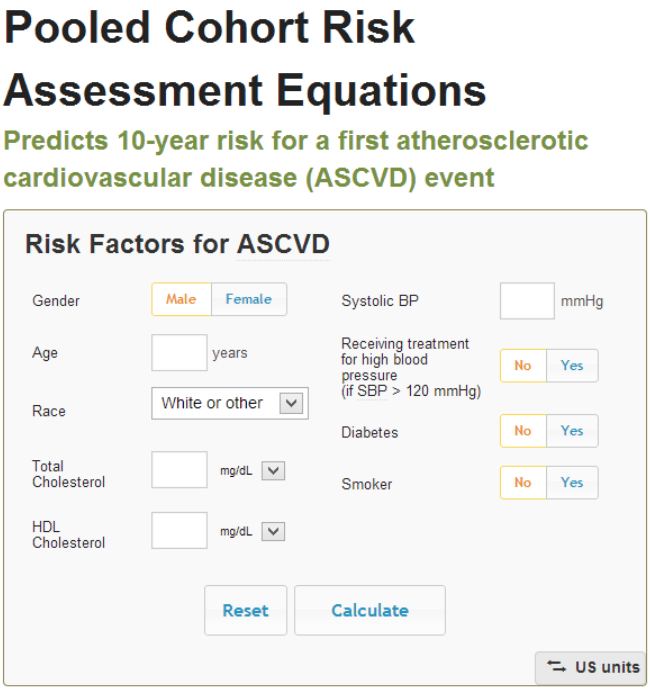
Classification of Patients based on the Framingham risk score (FRS)

Low risk	<10% coronary heart disease risk at 10 years
Moderate	10-20 coronary heart disease risk at 10 years
High	>20% coronary heart disease risk at 10 years

Other CVD risk assessment tools

Pooled Cohort Equation:

Estimated of 12 million to 45 million additional candidates for Statin therapy base in CVD risk estimates.
- Pencina* et al. Estimated 87.4% of men and 53.6% of women ages 60-75 would now be eligible for Statins.
Validation attempts have yielded conflicting results:
- 75%-150% when applied to data from the women's health study and the physician health study.
- Munter* et al. Reported good result in actual vs predicted 5-year risk in contemporary cohort of the REGARDS study.



Observed and expected events for different scores were compared in MESA after 10.2 years follow up

Table 2. Predicted and Observed Events for Each Risk Score

Risk Score	Predicted Events, *n* (%)	Observed Events, *n* (%)	Signed Absolute Difference	Discordance, %*	c-Statistic	Discrimination Slope
Total (*n* = 4227)						
FRS-CHD†	397.6 (9.41)	263 (6.22)	3.18	51	0.68	0.05
FRS-CVD‡	561.3 (13.28)	448 (10.60)	2.68	25	0.71	0.09
ATPIII-FRS-CHD§	288.7 (6.83)	134 (3.17)	3.66	115	0.71	0.06
RRS‖	314.0 (7.43)	323 (7.64)	−0.21	−3	0.72	0.07
AHA-ACC-ASCVD¶	387.2 (9.16)	218 (5.16)	4.00	78	0.71	0.06
Men (*n* = 1961)						
FRS-CHD†	251.1 (12.80)	164 (8.36)	4.44	53	0.69	0.05
FRS-CVD‡	358.7 (18.29)	261 (13.31)	4.98	37	0.71	0.09
ATPIII-FRS-CHD§	218.6 (11.15)	86 (4.39)	6.76	154	0.71	0.05
RRS‖	213.5 (10.89)	196 (9.99)	0.89	9	0.70	0.06
AHA-ACC-ASCVD¶	232.1 (11.84)	125 (6.37)	5.46	86	0.71	0.06
Women (*n* = 2266)						
FRS-CHD†	146.5 (6.47)	99 (4.37)	2.10	48	0.60	0.01
FRS-CVD‡	202.6 (8.94)	187 (8.25)	0.69	8	0.70	0.05
ATPIII-FRS-CHD§	70.2 (3.10)	48 (2.12)	0.98	46	0.67	0.02
RRS‖	100.5 (4.44)	127 (5.60)	−1.17	−21	0.72	0.05
AHA-ACC-ASCVD¶	155.1 (6.84)	93 (4.10)	2.74	67	0.70	0.05

Coronary Artery Disease

Pathogenesis:
CAD is the narrowing of the coronary arteries, decreasing the blood supply to the heart leading to ischemia of the heart muscle.

Etiology:
CAD is mostly due to atherosclerosis.
Atherosclerosis and Thrombosis are the most important pathogenic mechanisms.

Major CAD types

1. Stable angina: due to atheroma.
2. Acute coronary syndrome:
    a. Unstable angina.
    b. Myocardial infarction.

	STEMI	NSTEMI	Unstable angina
ST	Elevated	Normal or decreased	Normal or decreased
Troponin I,T	Elevated for 2 weeks	Elevated	Normal
CK-MB	Elevated for 3 days	Elevated	Normal

Signs and findings of Myocardial Infarction

Positive signs	Negative signs
ST-segment elevation	Normal ECG
New Q wave	Pleuritic, sharp or stabbing chest pain
Chest pain radiating to both arms simultaneously	Pain reproduced on palpitation
Added heart sound	Positional chest pain
hypotension	

Treatment of acute coronary syndrome

- Aspirin (proven to prevent recurrent infarction and decrease mortality).
- Clopidogrel.
- Beta-blocker.
- ACE inhibitors and ARBs (ARBs should. Be used if there is intolerance to ACE inhibitors).
- Nitroglycerin.
- Heparin.
- Statins.

Care following MI

- Risk factors modification.
- Cessation of smoking.
- Control blood sugar and pressure.
- Physical rehabilitation and exercise.
- Long-Term medications:
    - Aspirin, Clopidogrel.
    - Beta-blocker.
    - Aldosterone blockers.
    - ACE inhibitors.

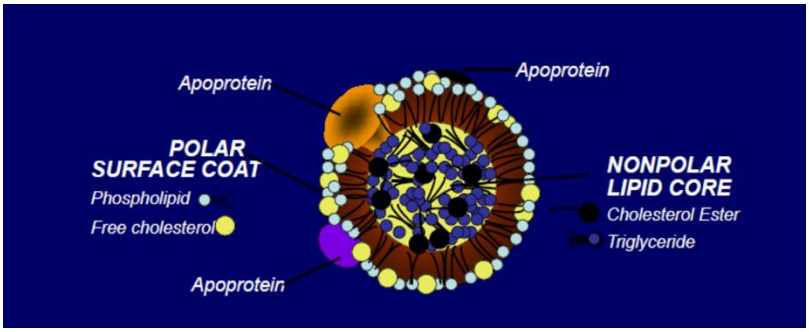
Dyslipidemia

- A disorder of lipoprotein metabolism including lipoprotein over production or deficiency.
- May be manifested by elevation of the total cholesterol, LDL and triglyceride concentration or decrease in the concentration of HDL in the blood.

Types of lipid

Types	Chylomicron	VLDL	LDL	HDL
Made by	Small intestines in the fed stat	The liver from excess dietary carbohydrate and protein along with the chylomicron remnant	The liver "VLDL once it has lost a lot of its TGs"	The liver and small intestine
Absorbed into	The lymph vessels then into the blood	------	------	------
Rich in	TGs	TGs	Cholesterol	------
Function	Transport fats from the intestinal mucosa to the liver	Deliver TGs to body cells	Deliver cholesterol to all body cells	Pick up cholesterol from body cells and take it back to the liver

Lipoprotein structure



Change in lipid guidelines and cholesterol targets

Home » Harvard Health Blog » Cholesterol guidelines update: controversy over heart risk calculator - Harvard

Cholesterol guidelines update: controversy over heart risk calculator

POSTED NOVEMBER 19, 2013, 2:19 PM

Howard LeWine, M.D., Chief Medical Editor
Internet Publishing, Harvard Health Publications

alculator that appears to
mate greatly the risk of heart

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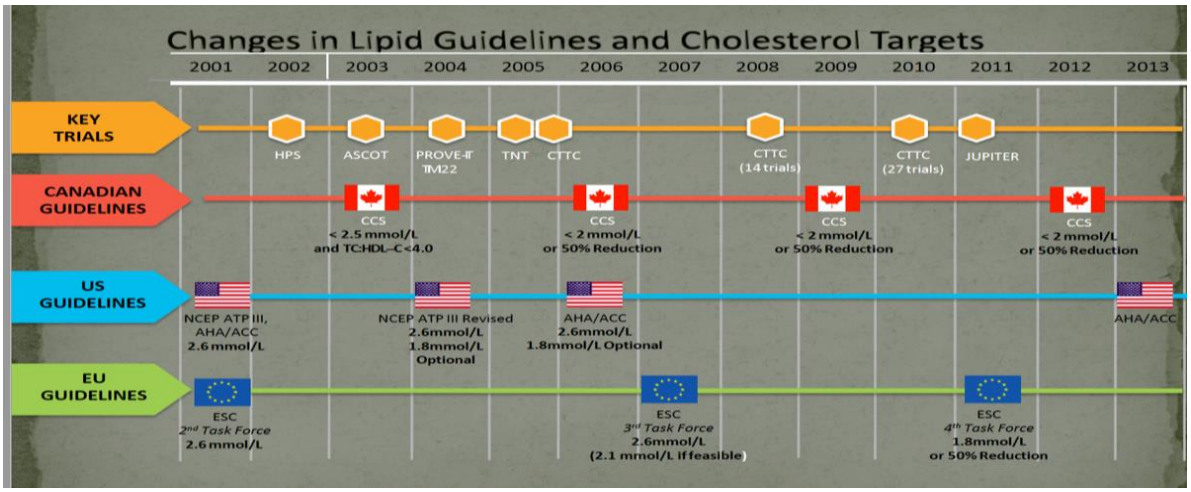
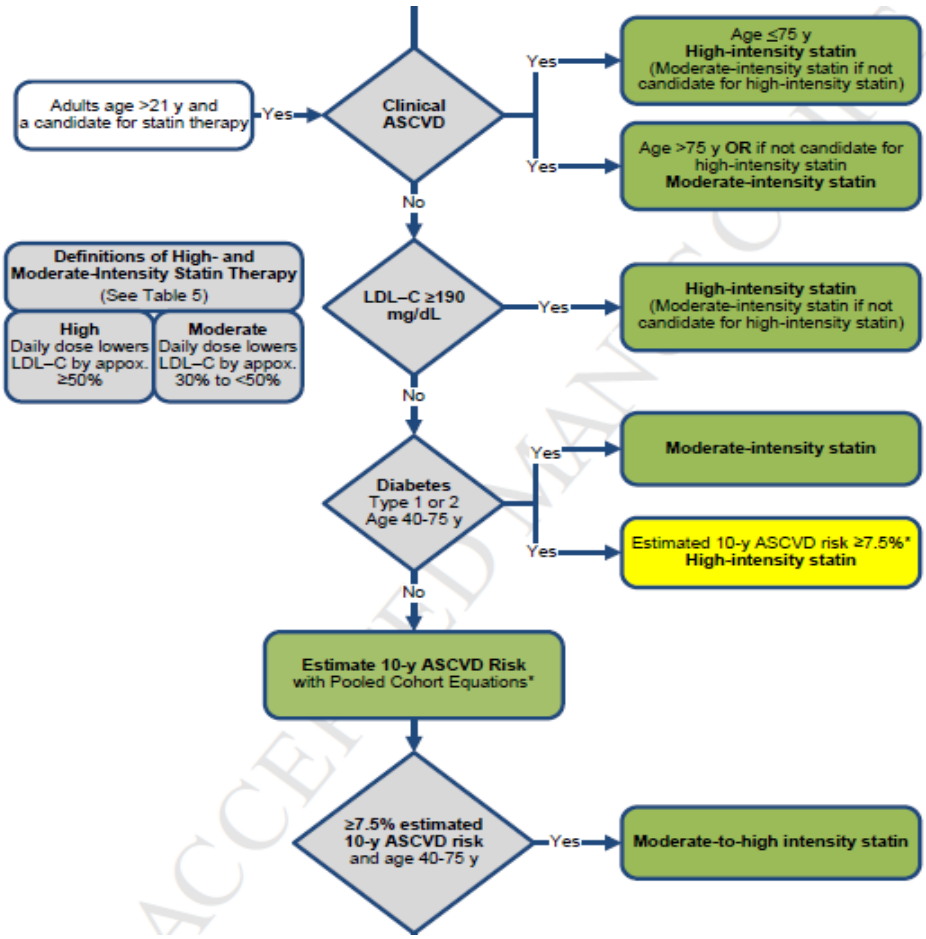
New guidelines may put 13 million more on statins



AHA/ACC vs IAS

AHA/ACC 2013	International atherosclerosis society
• ACC/AHA (elevated from ATP IV/NHLBI efforts) • Recommendations based on what has been shown to reduce risk in RCTs. • Many areas left to clinical judgment where RCT data were not available or limited. • Fire to target	• Apo B-containing lipoproteins is causally associated with ASCVD risk and what lowering “atherogenic cholesterol” (LDL-S and non-HDL-C) will reduce risk • Treat to target



Statin dosing

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

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
Daily dose lowers LDL–C on average, by approximately ≥50%	Daily dose lowers LDL–C on average, by approximately 30% to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40†)–80 mg **Rosuvastatin 20 *(40)* mg**	**Atorvastatin 10 *(20)* mg** **Rosuvastatin (5) 10 mg** **Simvastatin 20–40 mg‡** **Pravastatin 40 *(80)* mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*

ATP III Classification of LDL, total and HDL cholesterol

LDL Cholesterol	
<100	Optimal
100-129	Near optimal/above optimal
130-159	Borderline high
160-189	High
≥190	Very high
Total Cholesterol	
<200	Desirable
200-239	Borderline high
≥240	High
HDL Cholesterol	
<40	Low
≥60	High

LDL cholesterol goals and cut points for therapeutic lifestyle changes and drug therapy in different risk categories

Risk Category	LDL Goal	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (TLC)	LDL Level at Which to Consider Drug Therapy
CHD or CHD Risk Equivalents (10-year risk >20%)	<100 mg/dL	≥100 mg/dL	≥130 mg/dL (100-129 mg/dL: drug optional)*
2+ Risk Factors (10-year risk ≤20%)	<130 mg/dL	≥130 mg/dL	10-year risk 10-20%: ≥130 mg/dL 10-year risk <10%: ≥160 mg/dL
0-1 Risk Factor†	<160 mg/dL	≥160 mg/dL	≥190 mg/dL (160-189 mg/dL: LDL-lowering drug optional)

* *Some authorities recommend use of LDL-lowering drugs in this category if an LDL cholesterol <100 mg/dL cannot be achieved by therapeutic lifestyle changes. Others prefer use of drugs that primarily modify triglycerides and HDL, e.g., nicotinic acid or fibrate. Clinical judgment also may call for deferring drug therapy in this subcategory.*

† *Almost all people with 0-1 risk factor have a 10-year risk <10%, thus 10-year risk assessment in people with 0-1 risk factor is not necessary.*

Etiology of dyslipidemia

- **Primary causes:**
  - Primary causes are single or multiple gene mutations that result in either overproduction or defective clearance of TG and LDL cholesterol, or in underproduction or excessive clearance of HDL.
- Examples:
  - Familial hypertriglyceridemia.
  - Familial hypercholesterolemia.
  - Familial combined hyperlipidemia.
  - Polygenic hypercholesterolemia.

- **Secondary causes:**
  - Contribute to most cases of dyslipidemia.
  - The most important secondary causes in developed countries is a sedentary life style with excessive dietary intake of saturated fat, cholesterol and trans fats.
- Examples:
  - Diabetes mellitus.
  - Alcohol overuse.
  - Chronic kidney disease.
  - Hypothyroidism.
  - Primary biliary cirrhosis and other cholestatic liver diseases.
  - Drugs such as: thiazides, Beta-blocker, retinoids, highly active antiretroviral agents, estrogen and progesterone and glucocorticoids.
  - Smoking

Common secondary causes of dyslipidemia

Affected lipid	Conditions
High Total cholesterol and LDL-C	Hypothyroidism
	Nephrosis
	Dysgammaglobulinemia (SLE, multiple myeloma)
	Cholestatic diseases of the liver due to abnormal lipoprotein as in primary biliary cirrhosis.
	Protease inhibitors for treatment of HIV infection
High triglycerides and VLDL-C	Chronic renal failure
	Type 2 DM
	Obesity
	Excessive alcohol intake
	Hypothyroidism
	Anti-hypertensive medications (thiazides and beta blockers)
	Corticosteroids (or sever stress)
	Oral estrogen, contraceptives, pregnancy
	Protease inhibitors for HIV infection

Table 6.

Secondary Causes of Hyperlipidemia Most Commonly Encountered in Clinical Practice

Secondary Cause	Elevated LDL-C	Elevated Triglycerides
Diet	Saturated or *trans* fats, weight gain, anorexia nervosa	Weight gain, very-low-fat diets, high intake of refined carbohydrates, excessive alcohol intake
Drugs	Diuretics, cyclosporine, glucocorticoids, amiodarone	Oral estrogens, glucocorticoids, bile acid sequestrants, protease inhibitors, retinoic acid, anabolic steroids, sirolimus, raloxifene, tamoxifen, beta blockers (not carvedilol), thiazides
Diseases	Biliary obstruction, nephrotic syndrome	Nephrotic syndrome, chronic renal failure, lipodystrophies
Disorders and altered states of metabolism	Hypothyroidism, obesity, pregnancy*	Diabetes (poorly controlled), hypothyroidism, obesity; pregnancy*

Sign and symptoms of dyslipidemia

- Dyslipidemia itself usually is asymptomatic but can lead to symptomatic vascular disease including *peripheral arterial diseases* and *coronary artery disease*.
- High levels of TGs (>1000 mg/dl) can cause *acute pancreatitis*.
- High levels of LDL can cause: *Eyelid xanthelasmas*, *Arcus corneae*, *Tendinous xanthoma* commonly at the Achilles, Elbow and knee tendons as well as over the metacarpophalangeal joints.

Overview of primary and secondary ASCVD prevention

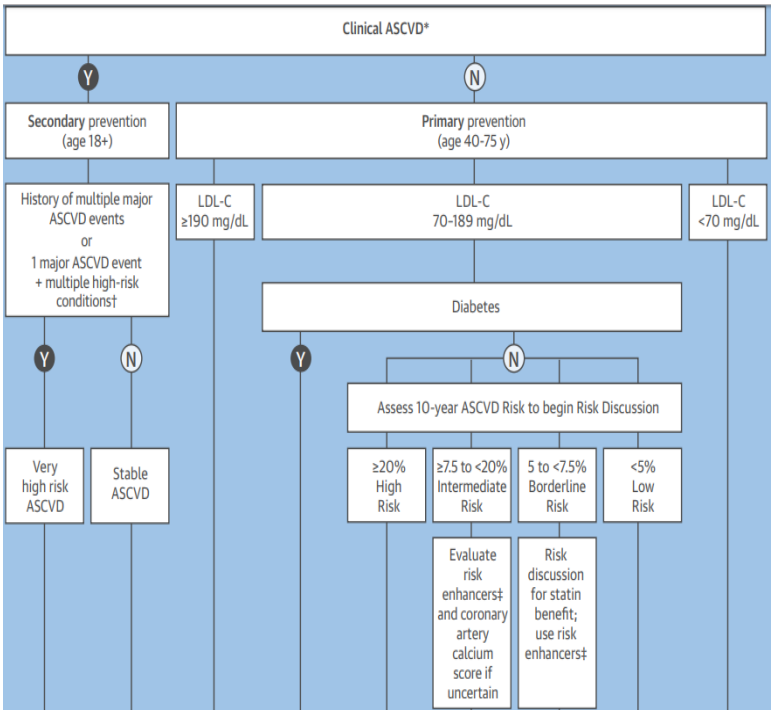
Grundy SM, et al.
2018 Cholesterol Clinical Practice Guidelines

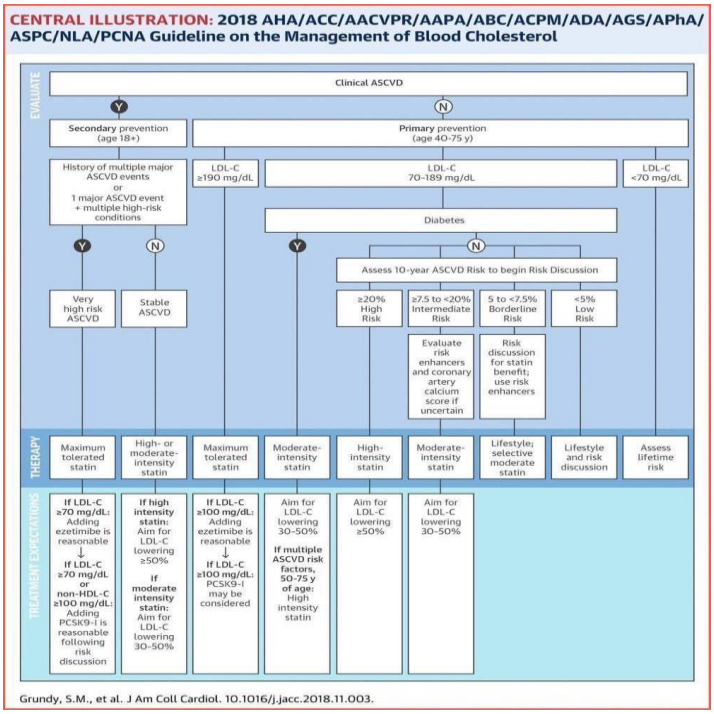
2018
AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA
Guideline on the Management of Blood Cholesterol

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Recommendations for Measurements of LDL-C and Non–HDL-C
Referenced studies that support recommendations are summarized in Online Data Supplement 1.

COR	LOE	Recommendations
I	B-NR	1. In adults who are 20 years of age or older and not on lipid-lowering therapy, measurement of either a fasting or a nonfasting plasma lipid profile is effective in estimating ASCVD risk and documenting baseline LDL-C (S2.2-1–S2.2-6).
I	B-NR	2. In adults who are 20 years of age or older and in whom an initial nonfasting lipid profile reveals a triglycerides level of 400 mg/dL (≥4.5 mmol/L) or higher, a repeat lipid profile in the fasting state should be performed for assessment of fasting triglyceride levels and baseline LDL-C (S2.2-1–S2.2-4).
IIa	C-LD	4. In adults who are 20 years of age or older and without a personal history of ASCVD but with a family history of premature ASCVD or genetic hyperlipidemia, measurement of a fasting plasma lipid profile is reasonable as part of an initial evaluation to aid in the understanding and identification of familial lipid disorders.





Major ASCVD Events
Recent acute coronary syndrome (within the past 12 months)
History of myocardial infarction (other than recent acute coronary syndrome event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ankle brachial index <0.85, or previous revascularization or amputation)

High-Risk Conditions
Age ≥65 years
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or PCI outside of the major ASCVD event(s)
Diabetes Mellitus
Hypertension
Chronic kidney disease (eGFR 15-59 mL/min/1.73 m^2)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL (≥2.6 mmol/L)) despite maximally tolerated statin therapy and ezetimibe
History of congestive heart failure

Diabetes mellitus in adults

Diabetes-specific Risk Enhancers That Are Independent of Other Risk Factors in Diabetes

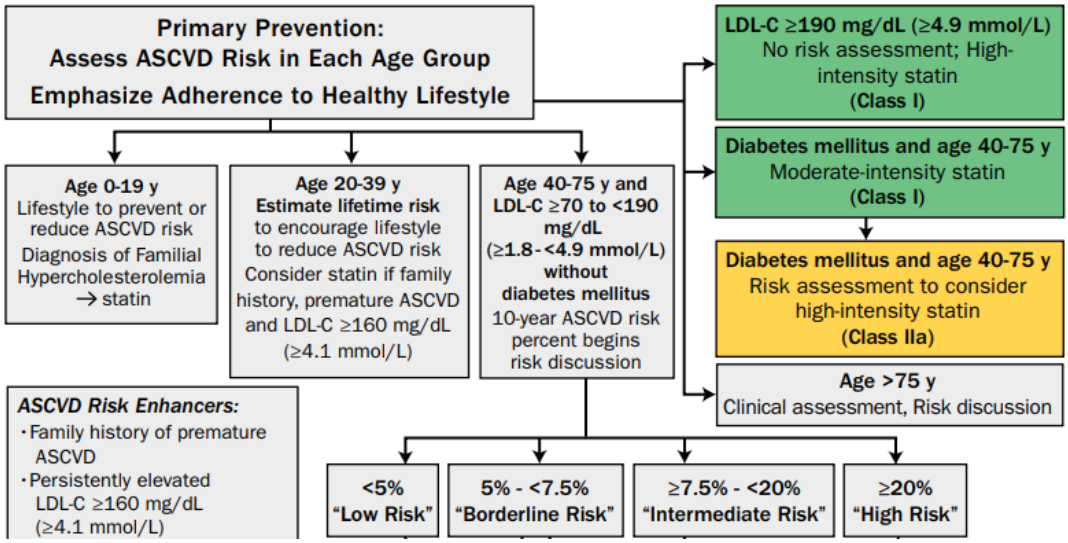
Table 5

- Long duration (≥10 years for type 2 diabetes or ≥ 20 years for type 1 diabetes)
- Albuminuria ≥30 mcg albumin/mg creatinine
- eGFR <60 ml/min/1.73 m^2
- Retinopathy
- Neuropathy
- ABI <0.9

Severe Hypercholesterolemia [LDL-C ≥190 mg/dL (≥4.9 mmol/L)]

Primary prevention over the life span

Primary Prevention



Risk-enhancing Factors for Clinician-Patient Risk Discussion

- **Family history of premature ASCVD;** (males <55 years; females <65 years)
- **Primary hypercholesterolemia** (LDL-C 160-189 mg/dL (4.1- 4.8 mmol/L); non-HDL-C 190-219 mg/dL (4.9-5.6 mmol/L).
- **Metabolic syndrome** (increased waist circumference, elevated TG (>175 mg/dL, elevated BP, elevated glucose, low HDL-C (<40 mg/dL in men, <50 mg/dL in women) are factors; tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15- 59 ml/min per 1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions** such as psoriasis, rheumatoid arthritis (RA) or human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS)
- **History of premature menopause (before age 40) and history of pregnancy-associated conditions that increase later ASCVD risk such as pre-eclampsia**

- **High-risk ethnicities** (e.g. South Asian ancestry)
- **Lipid/Biomarkers:** Associated with increased ASCVD risk

  -Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dl);

  -If measured:

  - **High-sensitivity C-reactive protein** - (≥2.0 mg/L)
  - **Elevated lipoprotein (a)** - A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥ 50 mg/dL or ≥125 nmol/L constitutes a risk enhancing factor especially at higher levels of Lp(a).
  - **Elevated apo B ≥130 mg/dL** - A relative indication for its measurement would be triglyceride ≥ 200 mg/dL. A level ≥ 130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk enhancing factor.
  - **ABI <0.9**

Primary prevention over the life span

Summary of Recommendations - Screening Men

Population	Recommendation	Grade (What's This?)
Men 35 and Older	The USPSTF strongly recommends screening men aged 35 and older for lipid disorders.	A
Men 20-35 at Increased Risk for CHD	The USPSTF recommends screening men aged 20-35 for lipid disorders if they are at increased risk for coronary heart disease.	B

Summary of Recommendations - Screening Women at Increased Risk

Population	Recommendation	Grade (What's This?)
Women 45 and Older at Increased Risk for CHD	The USPSTF strongly recommends screening women aged 45 and older for lipid disorders if they are at increased risk for coronary heart disease.	A
Women 20-45 at Increased Risk for CHD	The USPSTF recommends screening women aged 20-45 for lipid disorders if they are at increased risk for coronary heart disease.	B

Summary of Recommendations - Screening Young Men and All Women NOT at Increased Risk

Population	Recommendation	Grade (What's This?)
Men 20-35, Women Not at Increased Risk	The USPSTF makes no recommendation for or against routine screening for lipid disorders in men aged 20 to 35, or in women aged 20 and older who are not at increased risk for coronary heart disease.	C

Dyslipidemia, medical therapy and adjustment

Treatment options of dyslipidemia	Lifestyle changes	Physical activity
		Medical nutrition therapy
		Smoking cessation
	Pharmacological therapy	Statins
		Cholesterol absorption inhibitors
		PCSK9 inhibitors
		Fibrates
		Omega-3 (fish oil)
		Niacin
		Bile acid sequestration
		MTP inhibitors
		Antisense apo B oligonucleotide
		Combination therapies

Lifestyle changes

Physical Activity

- **R48.** A reasonable and feasible approach to fitness therapy (i.e., exercise programs that include at least 30 minutes of moderate-intensity physical activity [consuming 4-7 kcal/min] 4 to 6 times weekly, with an expenditure of at least 200 kcal/day) is recommended; suggested activities include brisk walking, riding a stationary bike, water aerobics, cleaning/scrubbing, mowing the lawn, and sporting activities **(Grade A; BEL 1)**.
- **R49.** Daily physical activity goals can be met in a single session or in multiple sessions throughout the course of a day (10 minutes minimum per session); for some individuals, breaking activity up throughout the day may help improve adherence with physical activity programs **(Grade A; BEL 1)**.
- **R50.** In addition to aerobic activity, muscle-strengthening activity is recommended at least 2 days a week **(Grade A; BEL 1)**.

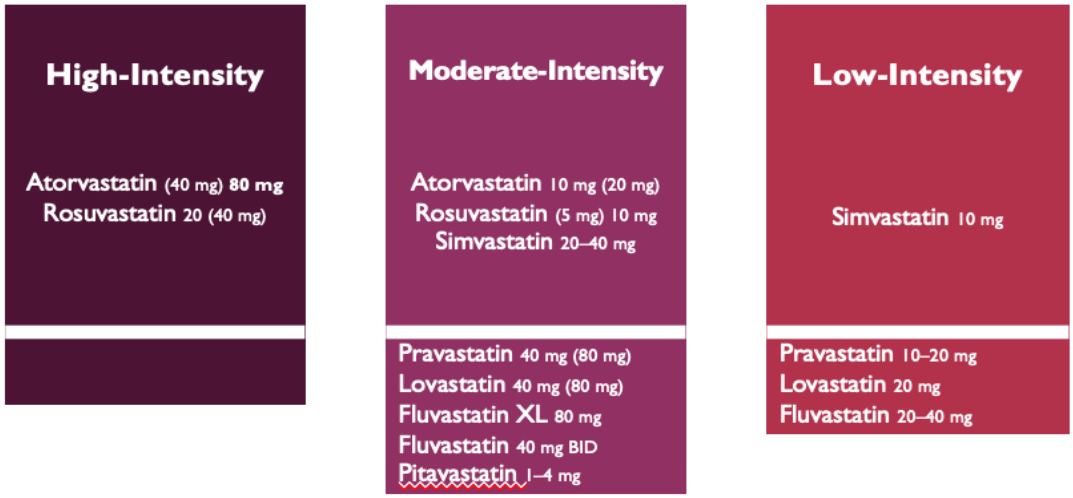
Meical Nutrition Therapy

- **R51.** For adults, a reduced-calorie diet consisting of fruits and vegetables (combined ≥5 servings/day), grains (primarily whole grains), fish, and lean meats is recommended **(Grade A; BEL 1)**.
- **R52.** For adults, the intake of saturated fats, *trans*-fats, and cholesterol should be limited, while LDL-C-lowering macronutrient intake should include plant stanols/sterols (~2 g/ day) and soluble fiber (10-25 g/day) **(Grade A; BEL 1)**.
- **R53.** Primary preventive nutrition consisting of healthy lifestyle habits is recommended in all healthy children **(Grade A; BEL 1)**.

Smoking Cessation

- **R54.** Tobacco cessation should be strongly encouraged and facilitated **(Grade A; BEL 2; upgraded due to potential benefit)**.

Statins



LDL-C Lowering:

- High-Intensity: 50%
- Moderate-Intensity: 30% to 49%
- Low-Intensity: <30%

Cholesterol absorption inhibitors

Agent	Usual recommended starting daily dosage	Dosage range	Method of administration
Cholesterol absorption inhibitors			
Ezetimibe	10 mg	10 mg	Oral
Combination therapies (single-pill)			
Ezetimibe/simvastatin	10/20 mg	10/10 to 10/80 mg	Oral

PCSK9 inhibitors

Agent	Usual recommended starting daily dosage	Dosage range	Method of administration
PCSK9 inhibitors			
Alirocumab	75 mg every 2 weeks	75-150 mg every 2 weeks	SQ
Evolocumab	140 mg every 2 weeks or 420 mg once monthly	Not applicable	SQ

Statin associated side effects

Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Statin-associated muscle symptoms (SAMS)			
Myalgias (CK Normal)	Infrequent (1% to 5%) in RCTs; frequent (5% to 10%) in observational studies and clinical setting	Age, female sex, low body mass index, high-risk medications (CYP3A4 inhibitors, OATP1B1 inhibitors), comorbidities (HIV, renal, liver, thyroid, preexisting myopathy), Asian ancestry, excess alcohol, high levels of physical activity, and trauma	RCTs cohorts/observational
Myositis/myopathy (CK > ULN) with	Rare		RCTs

concerning symptoms or objective weakness			cohorts/observational
Rhabdomyolysis (CK >10× ULN + renal injury)	Rare		RCTs cohorts/observational
Statin-associated autoimmune myopathy (HMGCR antibodies, incomplete resolution)	Rare		Case reports
New-onset diabetes mellitus	Depends on population; more frequent if diabetes mellitus risk factors are present, such as body mass index ≥30, fasting blood sugar ≥100 mg/dL; metabolic syndrome, or A1c ≥6%.	Diabetes mellitus risk factors/metabolic syndrome High-intensity statin therapy	RCTs/meta-analyses

Statin-Associated Side Effects	**Frequency**	**Predisposing Factors**	**Quality of Evidence**
Liver			
Transaminase elevation 3× ULN	Infrequent		RCTs/ cohorts/observational Case reports
Hepatic failure	Rare		
Central nervous system			
Memory/cognition	Rare/unclear		Case reports; no increase in memory/cognition problems in 3 large-scale RCTs
Cancer	No definite association		RCTs/meta-analyses

Statin-Associated Side Effects	Frequency	Predisposing Factors	Quality of Evidence
Other			
Renal function	Unclear/unfounded		
Cataracts	Unclear		
Tendon rupture	Unclear/unfounded		
Hemorrhagic stroke	Unclear		
Interstitial lung disease	Unclear/unfounded		
Low testosterone	Unclear/unfounded		

Management of adverse effects

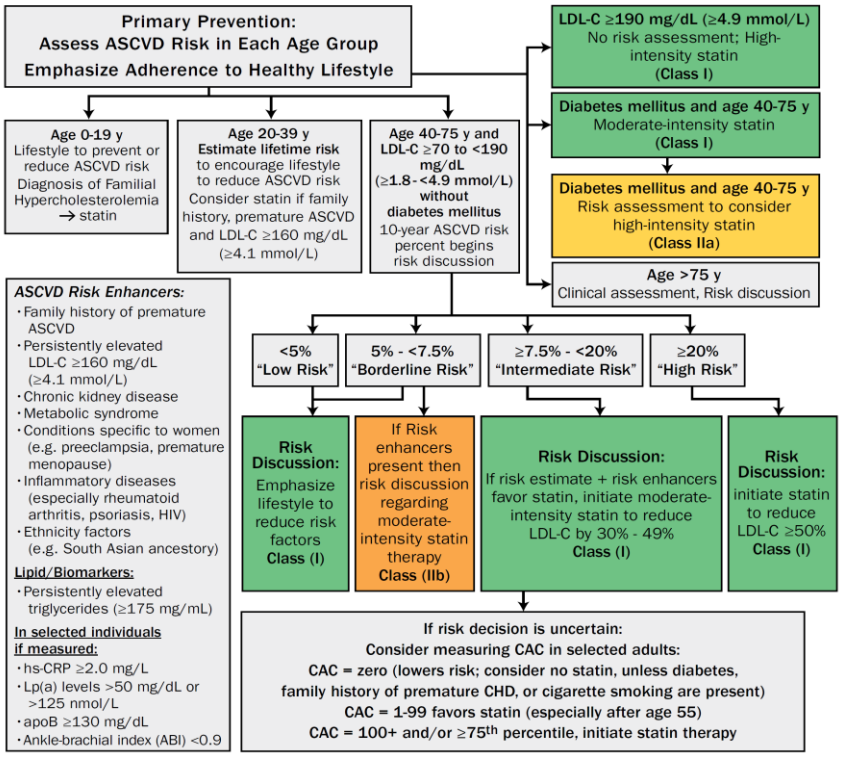
- Mild to moderate muscle spasm:
  - D/C statins until muscle spasm resolve.
  - Re-challenge a lower dose, if the symptoms resume, D/C statins and re-challenge with lower dose of different statin.
  - Gradually titrate to target dose, if symptoms don't resolve after 2 months, assume it is not statin related and resume original statin.
- New onset diabetes:
  - Reinforce lifestyle modification.
- Memory impairment:
  - Consider other potential causes before stopping statin.

Non-statin therapies

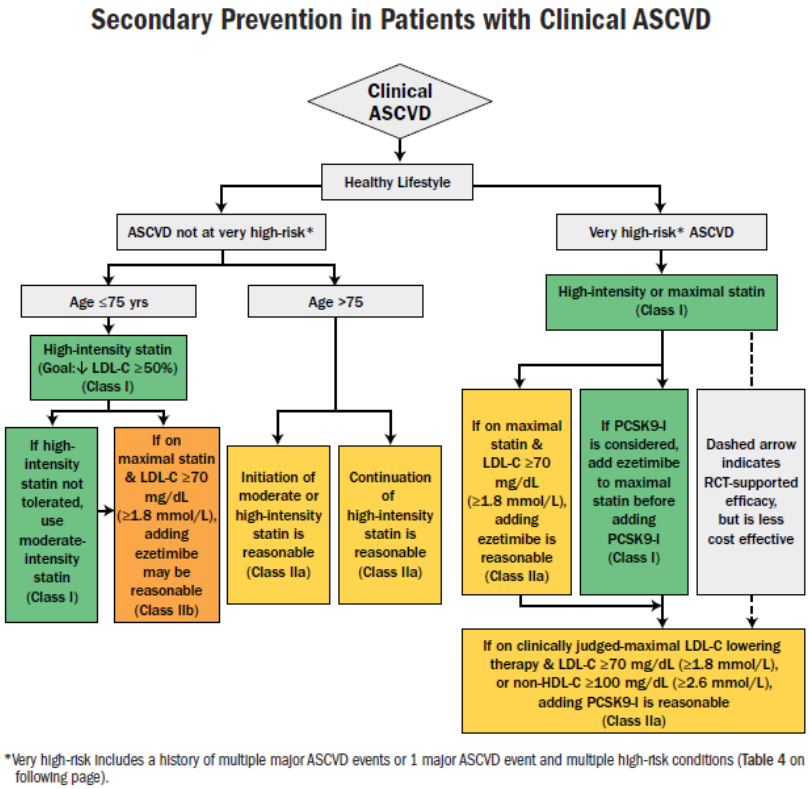
- Non-statin therapies alone or in combination with statin do not provide acceptable risk reduction benefits compared to adverse effect.
- The Non-statin agents include:
  - Zetia.
  - Fibrates.
  - Fish oil.
  - Niacin.
- For the most part, these should be avoided with few exceptions.

Drug Class	Agents and Daily Doses	Lipid/Lipoprotein Effects		Side Effects	Contraindications
HMG CoA reductase inhibitors (statins)	Lovastatin (20-80 mg) Pravastatin (20-40 mg) Simvastatin (20-80 mg) Fluvastatin (20-80 mg) Atorvastatin (10-80 mg) Cerivastatin (0.4-0.8 mg)	LDL HDL TG	↓18-55% ↑5-15% ↓7-30%	Myopathy Increased liver enzymes	Absolute: • Active or chronic liver disease Relative: • Concomitant use of certain drugs*
Bile acid sequestrants	Cholestyramine (4-16 g) Colestipol (5-20 g) Colesevelam (2.6-3.8 g)	LDL HDL TG	↓15-30% ↑3-5% No change or increase	Gastrointestinal distress Constipation Decreased absorption of other drugs	Absolute: • dysbeta-lipoproteinemia • TG >400 mg/dL Relative: • TG >200 mg/dL
Nicotinic acid	Immediate release (crystalline) nicotinic acid (1.5-3 gm), extended release nicotinic acid (Niaspan®) (1-2 g), sustained release nicotinic acid (1-2 g)	LDL HDL TG	↓5-25% ↑15-35% ↓20-50%	Flushing Hyperglycemia Hyperuricemia (or gout) Upper GI distress Hepatotoxicity	Absolute: • Chronic liver disease • Severe gout Relative: • Diabetes • Hyperuricemia • Peptic ulcer disease
Fibric acids	Gemfibrozil (600 mg BID) Fenofibrate (200 mg) Clofibrate (1000 mg BID)	LDL *(may be increased in patients with high TG)* HDL TG	↓5-20% ↑10-20% ↓20-50%	Dyspepsia Gallstones Myopathy	Absolute: • Severe renal disease • Severe hepatic disease

Primary ASCVD prevention



Secondary ASCVD prevention



*Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions (Table 4 on following page).

Very High-Risk for Future ASCVD Events*

Table 4

Major ASCVD Events
Recent acute coronary syndrome (within the past 12 months)
History of myocardial infarction (other than recent acute coronary syndrome event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ankle brachial index <0.85, or previous revascularization or amputation)
High-Risk Conditions
Age ≥65 years
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or PCI outside of the major ASCVD event(s)
Diabetes Mellitus
Hypertension
Chronic kidney disease (eGFR 15-59 mL/min/1.73 m^2)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL (≥2.6 mmol/L)) despite maximally tolerated statin therapy and ezetimibe
History of congestive heart failure

*Very High Risk includes a history of multiple major ASCVD events or one major ASCVD event and multiple high-risk conditions.

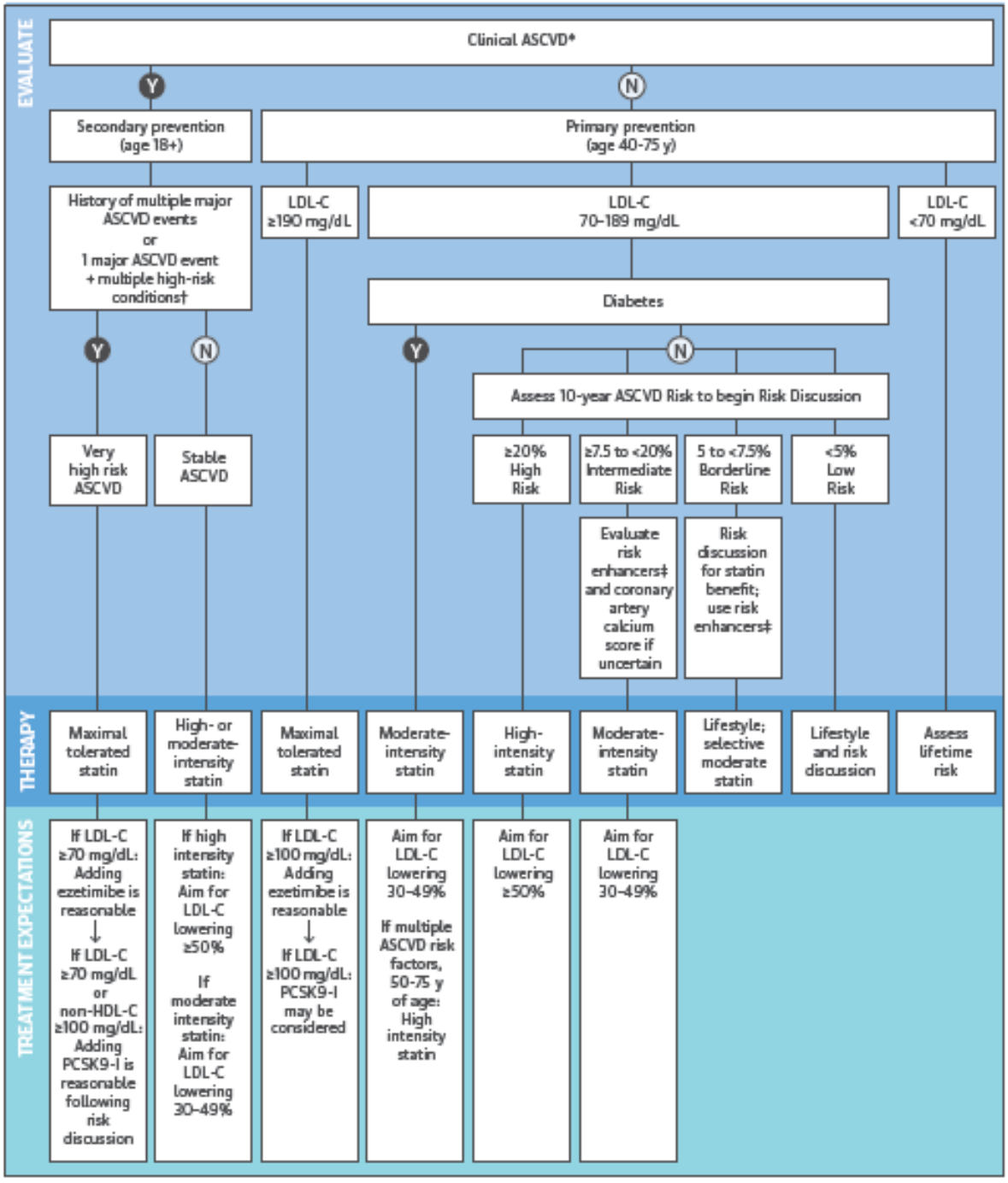
Follow up

- Assess adherence and percentage response to LDL-C lowering medication and lifestyle changes with repeating lipid measurement 4-12 weeks after statin initiation or dose adjustment.
- Repeat every 3-12 months as needed

Summary

Overview of Primary and Secondary ASCVD Prevention

This tool provides a broad overview of the 2018 Cholesterol Guideline.
Please refer to the full guideline document for specific recommendations.



* Clinical ASCVD consists of acute coronary syndromes, those with history of myocardial infarction, stable or unstable angina or coronary other arterial revascularization, stroke, TIA, or peripheral artery disease including aortic aneurysm, all of atherosclerotic origin.

† Major ASCVD events: Recent ACS, history of MI, history of ischemic stroke, symptomatic PAD; High-Risk Conditions: ≥65 y of age, heterozygous FH, hx of HF, prior CABG or PCI, DM, HTN, CKD, current smoking, persistently elevated LDL-C≥100 mg/dL.

‡ Risk Enhancers: Family history of premature ASCVD, persistently elevated LDL-C ≥160 mg/dl, chronic kidney disease, metabolic syndrome, conditions specific to women (e.g. pre-eclampsia, premature menopause), inflammatory disease (especially psoriasis, RA, or HIV), ethnicity (e.g. South Asian ancestry), Lipid/biomarkers; persistently elevated triglycerides (≥175 mg/dL), If measured: hs-CRP ≥2.0 mg/L, Lp(a) levels ≥50 mg/dL or ≥125 nmol/l, apoB ≥130 mg/dL especially at higher levels of Lp(a), ABI <0.9.