
NATIONAL LIPID ASSOCIATION
NLA Recommendations for Patient-Centered Management of Dyslipidemia
Part 1 [DRAFT]
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Abbreviations/Acronyms Used

- Apo = apolipoprotein
- ASCVD = atherosclerotic cardiovascular disease
- CHD = coronary heart disease
- HDL-C = high-density lipoprotein cholesterol
- LDL-C = low-density lipoprotein cholesterol
- NLA = National Lipid Association
- Non-HDL-C = non-high-density lipoprotein cholesterol
- Total-C = total cholesterol

Background

- Various guidelines and recommendations have been issued in the last few years that contain material differences.
- An NLA Expert Panel was formed to prepare a set of consensus recommendations intended to inform, not replace, clinical judgment regarding dyslipidemia management.
- The panel considered evidence from randomized clinical trials, including primary, subgroup and pooled analyses where available, as well as evidence from epidemiological, metabolic, mechanistic and genetic studies.
- The current DRAFT recommendations will enter a comment period to allow input and advice to be obtained from other experts and organizations.

Comment and Publication Process

- We welcome your thoughts and comments on these recommendations. To make a comment go to www.lipid.org/publiccomments. You will have until May 31, 2014 to provide your feedback.
- After comments have been received and considered, an Executive Summary for Part 1 will be published in the *Journal of Clinical Lipidology.*
- A similar process will be followed for Part 2.
- The full report of the NLA Expert Panel (Parts 1 and 2) will be published in the *Journal of Clinical Lipidology*.

NLA's Strategic Plan

- In the past few years, the NLA has moved forward with a strategic plan for a comprehensive set of lipid recommendations, with an expectation for yearly updates as the scientific and clinical evidence evolve.
- Although the release of the recommendations contained herein was accelerated as a result of the release of the ACC/AHA guidelines, the formulation of these recommendations is consistent with the NLA's prior strategic plan.

Part 2

- Part 2 of the NLA Recommendations for Patient-Centered Management of Dyslipidemia is in development and will cover the following topics:
  - Lifestyle therapies
  - Populations with special considerations
    - Children, women and older patients
    - Those with residual risk despite statin therapy
    - Patients with human immunodeficiency virus (HIV)
    - Patients with congestive heart failure (CHF)
  - Other considerations (e.g., adherence)

Guiding Principles/Conclusions

1. An elevated level of atherogenic cholesterol – cholesterol carried by apo B-containing lipoprotein particles (non-HDL-C and LDL-C) – is causally related to the development of atherosclerosis, the key underlying process contributing to most clinical ASCVD events.
2. Reducing elevated levels of atherogenic cholesterol will lower ASCVD risk in proportion to the extent that atherogenic cholesterol is reduced. This benefit is presumed to result from atherogenic cholesterol lowering through multiple modalities, including lifestyle and drug therapies.

Guiding Principles/Conclusions

3. Lifestyle intervention for those with dyslipidemia is central to efforts at ASCVD prevention, whether or not drug therapy is used.
4. The intensity of risk reduction therapy should be adjusted to the patient's absolute risk for an ASCVD event. Atherosclerosis is a process that often begins early in life and progresses for decades before resulting in a clinical ASCVD event. Therefore, both intermediate-term and long-term/lifetime risk should be considered when assessing the potential benefits and hazards of risk reduction therapies.
5. For patients in whom lipid drug therapy is indicated, statin treatment is the primary modality for reducing ASCVD risk.
6. Other ASCVD risk factors should be managed appropriately.

Screening in Adults

- A fasting or non-fasting lipid profile should be measured at least every 5 years, starting at age 20; ideally fasting to allow assessment of LDL-C and triglyceride levels.
  - If non-fasting, focus on non-HDL-C (total-C minus HDL-C) and HDL-C.
- Should be accompanied by an assessment of ASCVD risk factors and risk stratification when indicated (covered later).
- If low-risk, public health recommendations may be applied for those with atherogenic cholesterol levels in the desirable range.
  - LDL-C <100 mg/dL, non-HDL-C <130 mg/dL
  - Re-screen in 5 years, or with changes in risk factors (including weight gain), co-morbidities, new secondary causes of dyslipidemia, ASCVD events in first degree relatives, or other change, based on clinical judgment
- Otherwise, institute therapies and monitoring as outlined in the subsequent slides.

Classifications of Cholesterol and Triglyceride Levels in mg/dL

Non-HDL-C	
<130	Desirable
130-159	Above desirable
160-189	Borderline high
190-219	High
≥220	Very high

HDL-C	
<40 (men)	Low
<50 (women)	Low

LDL-C	
<100	Desirable
100-129	Above desirable
130-159	Borderline high
160-189	High
≥190	Very high

Triglycerides	
<150	Normal
150-199	Borderline high
200-499	High
≥500	Very high

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Targets of Therapy – Atherogenic Cholesterol

- Atherogenic cholesterol (non-HDL-C and LDL-C) levels are the primary targets of therapy. Non-HDL-C is listed first because the panel consensus was that it is a better primary target than LDL-C.
  - More predictive than LDL-C in observational studies and with regard to changes or on-treatment levels in clinical trials.
  - When non-HDL-C and LDL-C are discordant, risk is more closely aligned with non-HDL-C.
  - Elevations in apo B-containing particles, and cholesterol carried by those particles, are considered a “root cause” of atherosclerosis, and of primary importance for prevention.
  - Non-HDL-C testing is universally available, requires no additional cost, and may be measured in the non-fasting state.

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Targets of Therapy – Apo B

- Apolipoprotein B (apo B) is considered a secondary, optional target for therapy.
  - Strongly associated with ASCVD event risk
  - More predictive power than LDL-C, but not consistently superior to non-HDL-C
  - May be elevated in some individuals who have obtained their non-HDL-C and LDL-C goals, thus a potential contributor to residual risk
  - Optional goals for primary and secondary/very high risk prevention are <90 and <80 mg/dL, respectively

Targets of Therapy – Triglycerides

- An elevated triglyceride level is not a target of therapy *per se*, except when very high (severe).
  - Focus on non-HDL-C simplifies management of triglycerides
- When the triglyceride concentration is ≥500 mg/dL (and especially if ≥1000 mg/dL), reducing the concentration to <500 mg/dL to prevent pancreatitis becomes the primary goal of therapy.

HDL-C

- The level of HDL-C is an important risk indicator and used in risk factor counting and quantitative risk assessment. HDL-C is also a component of the metabolic syndrome.
- HDL-C is not recommended as a target of therapy *per se*, but the level is often raised as a consequence of efforts to reduce atherogenic cholesterol and triglyceride concentrations through lifestyle and drug therapies.

Metabolic Syndrome

- Metabolic syndrome is recognized as a multiplex risk factor for both ASCVD and type 2 diabetes mellitus.
- Insulin resistance appears to be a central pathophysiologic feature of this cluster of interrelated metabolic and hemodynamic disturbances.
- The presence of the metabolic syndrome indicates high potential to benefit from lifestyle therapies, particularly weight loss if overweight/obese and increased physical activity.
  - Successful lifestyle intervention will reduce insulin resistance and improve multiple physiological disturbances that may contribute to risk, including the metabolic syndrome components, as well as indicators of inflammation and thrombogenicity

Major Risk Factors for ASCVD

1. Age
   - Male ≥45 years
   - Female ≥55 years
2. Family history of early CHD
   - <55 years of age in a male first-degree relative, or
   - <65 years of age in a female first-degree relative
3. Current cigarette smoking
4. High blood pressure (≥140/≥90 mm Hg, or on blood pressure medication)
5. Low HDL-C
   - Male <40 mg/dL
   - Female <50 mg/dL

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Other Major ASCVD Risk Factors Not Listed for Risk Factor Counting

- Non-HDL-C and LDL-C
  - Not included because the risk factors counted are used to assess treatment goals for atherogenic cholesterol levels
- Diabetes mellitus
  - Not listed because it is considered a *high* or *very high risk* condition for ASCVD risk assessment purposes

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High or Very High Risk Patient Groups

- Quantitative risk scoring is not necessary for initial risk assessment in patients with the following conditions*:
  - Diabetes mellitus, type 1 or 2
  - Chronic kidney disease, Stage ≥3
  - LDL-C ≥190 mg/dL
  - ASCVD

*Patients in these categories are all at ***high*** or ***very high*** *long-term risk* for an ASCVD event and should be treated accordingly.

Steps in ASCVD Risk Assessment

1. Identify patients with ***very high risk*** conditions.*
   a. ASCVD
   b. Diabetes mellitus with ≥2 other major ASCVD risk factors or end organ damage[1]
2. Identify patients with ***high risk*** conditions
   a. Diabetes mellitus with 0-1 other major ASCVD risk factors
   b. Chronic kidney disease Stage 3 or 4[2]
   c. LDL-C ≥190 mg/dL
3. **Count** major ASCVD risk factors
   a. If 0-1 and no other indicators of higher risk, assign to ***low risk*** category. Consider assigning to a higher risk category based on other risk factors, if known.
   b. If ≥3 major ASCVD risk factors are present, assign to ***high risk*** category.
4. If 2 major ASCVD risk factors, ***risk scoring*** is recommended and additional testing may be useful for some patients.
   a. If <10% 10-year hard CHD risk,[3] assign to ***moderate risk*** category.
   b. If ≥10% 10-year hard CHD risk, assign to ***high risk*** category.
   c. Assign as above, or consider assigning to ***high*** or ***very high*** **risk** category, as appropriate, if other risk indicators are present based on additional testing.

*Further risk assessment is not required in those with very high risk conditions.

Footnotes for Steps in ASCVD Risk Assessment

[1]End organ damage indicated by increased albumin/creatinine ratio (≥30 mg/g), chronic kidney disease (CKD), or retinopathy.

[2]For patients with CKD Stage 3 (glomerular filtration rate [GFR] 30-59 mL/min/1.73 m^2) or Stage 4 (GFR 15-29 mL/min/1.73 m^2) risk calculators should not be used because they may underestimate risk. Stage 5 CKD (or on hemodialysis) is a very high risk condition, but results from randomized, controlled trials of lipid-altering therapies have not provided convincing evidence of reduced ASCVD events in such patients. Therefore, no treatment goals for lipid therapy have been defined for Stage 5 CKD.

[3]The calculation for 10-year hard CHD event risk of ≥10% is based on the National Cholesterol Education Program Adult Treatment Panel III Framingham Risk Score. Clinicians may prefer to use other risk calculators, but should be aware that these vary in the clinical outcomes predicted (e.g., CHD events, ASCVD events, cardiovascular mortality); the risk factors included in their calculation and the timeframe for their prediction (e.g., 5 years, 10 years, or long-term or lifetime). Such calculators provide only an approximate risk estimate and require clinical judgment for interpretation.

Criteria for ASCVD Risk Categories

Risk Category	Criteria
Low	▪ 0-1 major ASCVD risk factors ▪ Consider other risk indicators, if known
Moderate	▪ 2 major ASCVD risk factors ▪ Quantitative risk scoring recommended ▪ Consider other risk indicators

High	▪ ≥3 major ASCVD risk factors
	▪ Diabetes mellitus (Type 1 or 2)
	  ▪ 0-1 other major ASCVD risk factors, and
	  ▪ No evidence of end-organ damage
	▪ Chronic kidney disease Stage 3 or 4
	▪ LDL-C ≥190 mg/dL
	▪ ≥10% 10-year hard CHD event risk

Very High	▪ ASCVD
	▪ Diabetes mellitus (Type 1 or 2)
	  ▪ ≥2 other major ASCVD risk factor(s) or
	  ▪ Evidence of end-organ damage

Treatment Goals and Levels to Consider Drug Therapy According to Risk Category

Risk Category	Treatment Goal	Consider Drug Therapy
	Non-HDL-C (LDL-C) mg/dL	
Low	<130 (<100)	≥190 (≥160)
Moderate	<130 (<100)	≥160 (≥130)
High	<130 (<100)	≥130 (≥100)
Very High	<100 (<70)	≥100 (≥70)

For patients with ASCVD or diabetes mellitus, consideration should be given to use of moderate or high-intensity statin therapy, irrespective of baseline atherogenic cholesterol levels.

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Criteria for ASCVD Risk Assessment, Treatment Goals, Levels to Consider Drug Therapy

Risk Category	Criteria	Treatment Goal	Consider Drug Therapy
		Non-HDL-C (LDL-C) mg/dL	
Low	▪ 0-1 major ASCVD risk factors ▪ Consider other risk indicators, if known	<130 (<100)	≥190 (≥160)
Moderate	▪ 2 major ASCVD risk factors ▪ Quantitative risk scoring recommended ▪ Consider other risk indicators	<130 (<100)	≥160 (≥130)

High	▪ ≥3 major ASCVD risk factors
	▪ Diabetes mellitus* (Type 1 or 2)
	  ▪ 0-1 other major ASCVD risk factors, and
	  ▪ No evidence of end-organ damage
	▪ Chronic kidney disease Stage 3 or 4
	▪ LDL-C ≥190 mg/dL
	▪ ≥10% 10-year hard CHD event risk
		<130 (<100)	≥130 (≥100)

Very High	▪ ASCVD*
	▪ Diabetes mellitus* (Type 1 or 2)
	  ▪ ≥2 other major ASCVD risk factor(s) or
	  ▪ Evidence of end-organ damage
		<100 (<70)	≥100 (≥70)

For patients with ASCVD or diabetes mellitus, consideration should be given to use of moderate or high-intensity statin therapy, irrespective of baseline atherogenic cholesterol levels.

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Criteria for Classification of ASCVD

- Myocardial infarction or other acute coronary syndrome
- Coronary or other revascularization procedure
- Transient ischemic attack
- Ischemic stroke
- Atherosclerotic peripheral arterial disease
- Other atherosclerotic diseases such as:
  - Renal atherosclerosis
  - Aortic aneurysm secondary to atherosclerosis
  - Carotid plaque
- Evidence of atherosclerosis from imaging studies such as:
  - Coronary or computed tomography angiography
  - Stress echocardiography or nuclear imaging
  - Coronary artery calcium score ≥300 Agatston units, or ≥75th percentile for age, sex and ethnicity

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Risk Indicators (Other Than Major ASCVD Risk Factors) That Might Be Considered For Risk Refinement

1. A severe disturbance in a major ASCVD risk factor, such as multi-pack per day smoking, strong family history, severe hypertension or severely depressed HDL-C
2. Indicators of subclinical disease, particularly coronary artery calcium
   - ≥300 Agatston units or ≥75th percentile for age, sex and ethnicity is considered evidence of ASCVD
3. Long-term ASCVD risk ≥40%
   - Lloyd-Jones 2006 Framingham risk calculator
4. High-sensitivity C-reactive protein ≥2.0 mg/L
5. Apolipoprotein B ≥120 mg/dL or LDL particle concentration ≥1600 nmol/L
6. Lipoprotein (a) ≥50 mg/dL (protein) using an isoform insensitive assay
7. Urine albumin / creatinine ratio ≥30 mg/g

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Criteria for Clinical Identification of Metabolic Syndrome
(Any 3 or More of the Listed Components)

Measure	Categorical Cut Points
1. Elevated waist circumference	≥40 inches (≥102 cm) in men ≥35 inches (≥88 cm) in women
2. Elevated triglycerides	≥150 mg/dL
3. Reduced HDL-C	<40 mg/dL in men <50 mg/dL in women
4. Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)	Systolic ≥130 and/or diastolic ≥85 mmHg
5. Elevated fasting glucose (drug treatment of elevated glucose is an alternate indicator)	≥100 mg/dL

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Metabolic Syndrome – Additional Considerations

- The American Heart Association / National Heart, Lung and Blood Institute guidelines for metabolic syndrome suggest:
  - Waist circumference thresholds of ≥37 inches (≥94 cm) in men and ≥32 inches (≥80 cm) in women as optional cut points for individuals or populations with increased insulin resistance, including those of Asian descent (alternate values have also been published for other groups: http://www.athero.org/download/IASPPGuidelines_FullReport_2.pdf)
- Body mass index ≥30.0 kg/m^2 may be used in place of waist circumference if not available, although waist is preferred
  - Note that body mass index may overestimate adiposity in those with above-average muscle mass
  - An optional cut point of 27.5 kg/m^2 for individuals or populations with increased insulin resistance, including those of Asian descent, may be considered

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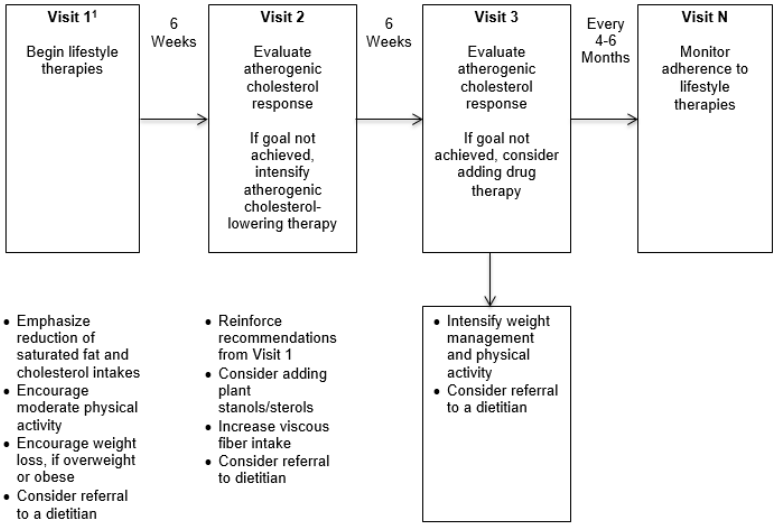
Model of Steps in Lifestyle Therapies



[1]For people at high or very risk for ASCVD in whom drug therapy is indicated, drug treatment may be started concomitantly with lifestyle therapies. For other patients, a trial of lifestyle therapies should be undertaken before initiation of drug therapy.

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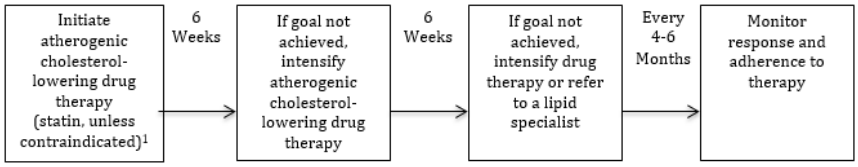
Progression of atherogenic cholesterol-lowering drug therapy



[1]A moderate or high intensity statin should be first-line drug therapy for treatment of elevated levels of atherogenic cholesterol, unless contraindicated. In a patient with very high triglycerides (≥500 mg/dL), a triglyceride-lowering drug may be considered for first-line use to prevent pancreatitis.

Other ASCVD risk factors should be managed appropriately in parallel.

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Intensity of Statin Therapy*

High Intensity Daily dose ↓ LDL-C ≥50%	Moderate Intensity Daily dose ↓ LDL-C 30 to <50%	Low Intensity Daily dose ↓ LDL-C <30%
Atorvastatin 40 (80) mg	Atorvastatin 10 (*20*) mg	*Simvastatin 10 mg*
Rosuvastatin 20 (*40*) mg	Fluvastatin 40 mg bid	*Fluvastatin 20-40 mg*
	Fluvastatin XL 80 mg	Lovastatin 20 mg
	Lovastatin 40 mg	*Pitavastatin 1 mg*
	Pitavastatin 2-4 mg	Pravastatin 10-20 mg
	Pravastatin 40 (*80*) mg	
	Rosuvastatin (*5*) 10 mg	
	Simvastatin 20 (40) mg	

*Individual responses to statin therapy varied in clinical trials and should be expected to vary in clinical practice. Values for LDL-C lowering are approximate averages. Moderate or high intensity statin therapy is preferred unless not tolerated.

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Lifestyle Therapies

- Recommendations will be in general agreement with those of the American Heart Association.
- Specifics will be outlined in Part 2 of the NLA Expert Panel Recommendations.

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Drug Therapies – Important Considerations

- Patient-centered therapy: before initiation of pharmacotherapy, the clinician should have a discussion with the patient about treatment objectives and potential ASCVD risk reduction, as well as the potential for adverse effects, interactions with other medications and patient preferences.
- When pharmacotherapy is to be used for lowering atherogenic cholesterol, moderate or high-intensity statin therapy should be the first-line agent. Starting with a moderate dose and titrating as necessary to achieve treatment goals is a reasonable approach.
  - An alternate drug (bile acid sequestrant, cholesterol absorption inhibitor, fibrate or nicotinic acid) may be considered in those with contraindications to statin therapy

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Drug Therapies – Important Considerations (continued)

- A drug targeting triglyceride reduction should be considered for first-line therapy in those with triglycerides ≥500 mg/dL.
  - Triglyceride lowering drug therapies include fibrates, high-dose omega-3 fatty acids and nicotinic acid
  - A statin may be a reasonable first-line agent if the triglyceride concentration is ≥500 mg/dL but <1000 mg/dL, if no history of pancreatitis
- When used, drug therapy should be adequate to attain levels of atherogenic cholesterol (non-HDL-C and LDL-C) that are *below* the goal cut points.
  - For patients with very high baseline levels of atherogenic cholesterol, it may not be possible to achieve goal levels, in which case an alternate goal of reductions of at least 50% for non-HDL-C and LDL-C may be considered.
- At present, no evidence suggests harm associated with LDL-C levels <40 mg/dL, so therapy may be continued in patients with LDL-C <40 mg/dL in the absence of signs of intolerance.

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Drug Therapies – Important Considerations (continued)

- Combination therapy with a statin plus a second agent may be considered for patients who have not reached their treatment goals for atherogenic cholesterol levels, particularly in those at high and very high risk. Generally, the maximally tolerated statin dose should be used before add-on therapy is considered.
- For patients with statin intolerance, reducing the dose of statin, switching to a different statin, and alternate regimens such as every other day statin dosing may be considered.
- For patients who cannot tolerate a statin using the above strategies, alternate agents alone or in combination may be considered.

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Additional Information

- Additional information from the NLA:
  - https://www.lipid.org/practicetools/guidelines/consensus_recommendations
    - Familial Hypercholesterolemia: Screening, Diagnosis and Management of Pediatric and Adult Patients
    - Clinical Utility of Inflammatory Markers and Advanced Lipoprotein Testing: Advice form an Expert Panel of Lipid Specialists
  - https://www.lipid.org/practicetools/guidelines/position_statements

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Common Abbreviations/Acronyms Not Defined in the Tables and Figures

Apo = apolipoprotein

ASCVD = atherosclerotic cardiovascular disease

CHD = coronary heart disease

HDL-C = high-density lipoprotein cholesterol

LDL-C = low-density lipoprotein cholesterol

NLA = National Lipid Association

Non-HDL-C = non-high-density lipoprotein cholesterol

Total-C = total cholesterol

Table A. Classifications of cholesterol and triglyceride levels in mg/dL[1]

Non-HDL-C[2]	
<130	Desirable
130-159	Above desirable
160-189	Borderline high
190-219	High
≥220	Very high
LDL-C	
<100	Desirable
100-129	Above desirable
130-159	Borderline high
160-189	High
≥190	Very high
HDL-C	
<40 (men)	Low
<50 (women)	Low
Triglycerides	
<150	Normal
150-199	Borderline high
200-499	High
≥500	Very high[2]

[1]Non-HDL-C = Total-C minus HDL-C

[2]Severe hypertriglyceridemia is another term used for very high triglycerides in pharmaceutical product labeling.

Table B. Steps in ASCVD risk assessment

1. Identify patients with ***very high risk*** conditions.*
    a. ASCVD
    b. Diabetes mellitus with ≥2 other major ASCVD risk factors or end organ damage[1]
2. Identify patients with ***high risk*** conditions.
    a. Diabetes mellitus with 0-1 other major ASCVD risk factors
    b. Chronic kidney disease Stage 3 or 4[2]
    c. LDL-C ≥190 mg/dL
3. ***Count*** major ASCVD risk factors.
    a. If 0-1 and no other indicators of higher risk, assign to ***low risk*** category. Consider assigning to a higher risk category based on other risk indicators, if known (Table G).
    b. If ≥3 major ASCVD risk factors are present, assign to ***high risk*** category.
4. If 2 major ASCVD risk factors***, risk scoring*** is recommended and additional testing may be useful for some patients (see Table G).
    a. If <10% 10-year hard CHD risk,[3] assign to ***moderate risk*** category.
    b. If ≥10% 10-year hard CHD risk, assign to ***high risk*** category.
    c. Assign or consider assigning to ***high*** or ***very high risk*** category, as appropriate, if other risk indicators are present based on additional testing (Tables F and G).

*Further risk assessment is not required in those with very high risk conditions.

[1]End organ damage indicated by increased albumin/creatinine ratio (≥30 mg/g), chronic kidney disease (CKD), or retinopathy.

[2]For patients with CKD Stage 3 (glomerular filtration rate [GFR] 30-59 mL/min/1.73 m^2) or Stage 4 (GFR 15-29 mL/min/1.73 m^2) risk calculators should not be used because they may underestimate risk. Stage 5 CKD (or on hemodialysis) is a very high risk condition, but results from randomized, controlled trials of lipid-altering therapies have not provided convincing evidence of reduced ASCVD events in such patients. Therefore, no treatment goals for lipid therapy have been defined for Stage 5 CKD.

[3]The calculation for 10-year hard CHD event risk of ≥10% is based on the National Cholesterol Education Program Adult Treatment Panel III Framingham Risk Score. Clinicians may prefer to use other risk calculators, but should be aware that these vary in the clinical outcomes predicted (e.g., CHD events, ASCVD events, cardiovascular mortality); the risk factors included in their calculation and the timeframe for their prediction (e.g., 5 years, 10 years, or long-term or lifetime). Such calculators provide only an approximate risk estimate and require clinical judgment for interpretation.

Table C. High or very high risk patient groups for whom quantitative risk scoring is not required for assignment of ASCVD risk category

Quantitative risk scoring is not necessary for initial risk assessment in patients with the following conditions:[1]

- Diabetes mellitus, type 1 or 2
- Chronic kidney disease, Stage ≥3
- LDL-C ≥190 mg/dL
- ASCVD

[1]Patients in these categories are all at high or very high long-term risk for an ASCVD event, as outlined in Table E, and should be treated accordingly.

Table D. Major risk factors for ASCVD[1]

1. Age
   - Male ≥45 years
   - Female ≥55 years
2. Family history of early CHD[2]
   - <55 years of age in a male first-degree relative, or
   - <65 years of age in a female first-degree relative
3. Current cigarette smoking
4. High blood pressure (≥140/≥90 mm Hg, or on blood pressure medication)
5. Low HDL-C
   - Male <40 mg/dL
   - Female <50 mg/dL

[1]Levels of non-HDL-C and LDL-C are not listed, because these risk factors are used to assess risk category and treatment goals for atherogenic lipoprotein cholesterol levels. Diabetes mellitus is not listed because it is considered a high or very high risk condition for ASCVD risk assessment purposes.

[2]CHD is defined as myocardial infarction, coronary death or a coronary revascularization procedure.

Table E. Criteria for ASCVD risk assessment, treatment goals for atherogenic cholesterol and levels at which to consider drug therapy

Risk Category	Criteria	Treatment Goal	Consider Drug Therapy
		Non-HDL-C (LDL-C) mg/dL	
Low	• 0-1 Major ASCVD Risk Factors • Consider Other Risk Indicators, if Known	<130 (<100)	≥190 (≥160)
Moderate	• 2 Major ASCVD Risk Factors • Quantitative Risk Scoring Recommended • Consider Other Risk Indicators[1]	<130 (<100)	≥160 (≥130)

High	• ≥3 Major ASCVD Risk Factors
	• Diabetes Mellitus* (Type 1 or 2)[2]
	  ○ 0-1 Other Major ASCVD Risk Factors, and
	  ○ No Evidence of End-Organ Damage
	• Chronic Kidney Disease Stage 3 or 4[3]
	• LDL-C ≥190 mg/dL[4]
	• ≥10% 10-year Hard CHD Event Risk[5]
		<130 (<100)	≥130 (≥100)

Very High	• ASCVD*
	• Diabetes Mellitus* (Type 1 or 2)
	  ○ ≥2 Other Major ASCVD Risk Factor(s), or
	  ○ Evidence of End-Organ Damage[6]
		<100 (<70)	≥100 (≥70)

For patients with ASCVD or diabetes mellitus, consideration should be given to use of moderate or high-intensity statin therapy, irrespective of baseline atherogenic cholesterol levels.			

[1]For those at moderate risk, additional testing may be considered for some patients to assist with decisions about risk stratification. See Tables G and H and text for additional details.

[2]For patients with diabetes plus 1 major ASCVD risk factor, treating to a non-HDL-C goal of <100 mg/dL (LDL-C <70 mg/dL) is considered a therapeutic option.

[3]For patients with chronic kidney disease (CKD) Stage 3 (glomerular filtration rate [GFR] 30-59 mL/min/1.73 m^2) or Stage 4 (GFR 15-29 mL/min/1.73 m^2) risk calculators should not be used because they may underestimate risk. Stage 5 CKD (or on hemodialysis) is a very high risk condition, but results from randomized, controlled trials of lipid-altering therapies have not provided convincing evidence of reduced ASCVD events in such patients. Therefore, no treatment goals for lipid therapy have been defined for Stage 5 CKD.

[4]If LDL-C is ≥190 mg/dL, consider severe hypercholesterolemia phenotype, which includes familial hypercholesterolemia. Lifestyle intervention and pharmacotherapy are recommended for adults with the severe hypercholesterolemia phenotype. If it is not possible to attain desirable levels of atherogenic cholesterol, a reduction of at least 50% is recommended. Risk calculators should not be used in such patients.

[5]The calculation for 10-year hard CHD event risk of ≥10% is based on the National Cholesterol Education Program Adult Treatment Panel III Framingham Risk Score. Clinicians may prefer to use other risk calculators, but should be aware that these vary in the clinical outcomes predicted (e.g., risk for CHD events, ASCVD events, ASCVD mortality, ASCVD events and revascularizations); the risk factors included in their calculation; and the timeframe for their prediction (e.g., 5 years, 10 years, or lifetime). Such calculators provide only an approximate risk estimate and require clinical judgment for interpretation.

[6]End-organ damage indicated by increased albumin/creatinine ratio (≥30 mg/g), CKD or retinopathy.

Table F. Criteria for classification of ASCVD

ASCVD

Myocardial infarction or other acute coronary syndrome

Coronary or other revascularization procedure

Transient ischemic attack

Ischemic stroke

Atherosclerotic peripheral arterial disease

Other atherosclerotic diseases such as:

- Renal atherosclerosis
- Aortic aneurysm secondary to atherosclerosis
- Carotid plaque

Evidence of atherosclerosis from imaging studies such as:

- Coronary or computed tomography angiography
- Stress echocardiography or nuclear imaging
- Coronary artery calcium score ≥300 Agatston units, or ≥75th percentile for age, sex and ethnicity

Table G. Risk indicators other than major ASCVD risk factors that might be considered for risk refinement[1]

1. A severe disturbance in a major ASCVD risk factor, such as multi-pack per day smoking, strong family history, severe hypertension, or severely depressed HDL-C
2. Indicators of subclinical disease, particularly coronary artery calcium (see criteria for ASCVD classification in Table F)
3. Long-term ASCVD risk ≥40%[2]
4. High-sensitivity C-reactive protein ≥2.0 mg/L[3]
5. Apolipoprotein B ≥120 mg/dL or LDL particle concentration ≥1600 nmol/L
6. Lipoprotein (a) ≥50 mg/dL using an isoform insensitive assay
7. Urine albumin/creatinine ratio ≥30 mg/g

[1]The presence of one or more of the risk indicators listed may be considered, in conjunction with major ASCVD risk factors, to reclassify an individual into a higher risk category. Except in the case of evidence of subclinical disease defining the presence of ASCVD, reclassification to a higher risk category is a matter of clinical judgment. Doing so will alter the threshold for consideration of pharmacotherapy and/or the treatment goals for atherogenic cholesterol. Many other ASCVD risk markers are available, but the panel consensus view was that those listed have the greatest clinical utility.

[2]Long-term ASCVD risk to age 80 using the Lloyd-Jones Framingham calculator (http://circ.ahajournals.org/content/113/6/791.full.pdf+html). Clinicians may prefer to use other risk calculators, but should be aware that these vary in the outcome predicted, risk factors included in the calculation, and timeframe for prediction. Such calculators provide only an approximate risk estimate and require clinical judgment for interpretation.

[3]Because of high intra-individual variability, multiple high-sensitivity C-reactive protein (hs-CRP) values should be obtained before concluding that the level is elevated; hs-CRP should not be tested in those who are ill, have an infection, or are injured. If hs-CRP level is >10 mg/L, consider other etiologies such as infection, active arthritis, or concurrent illness.

Table H. Criteria for clinical identification of the metabolic syndrome: any 3 or more of the listed components

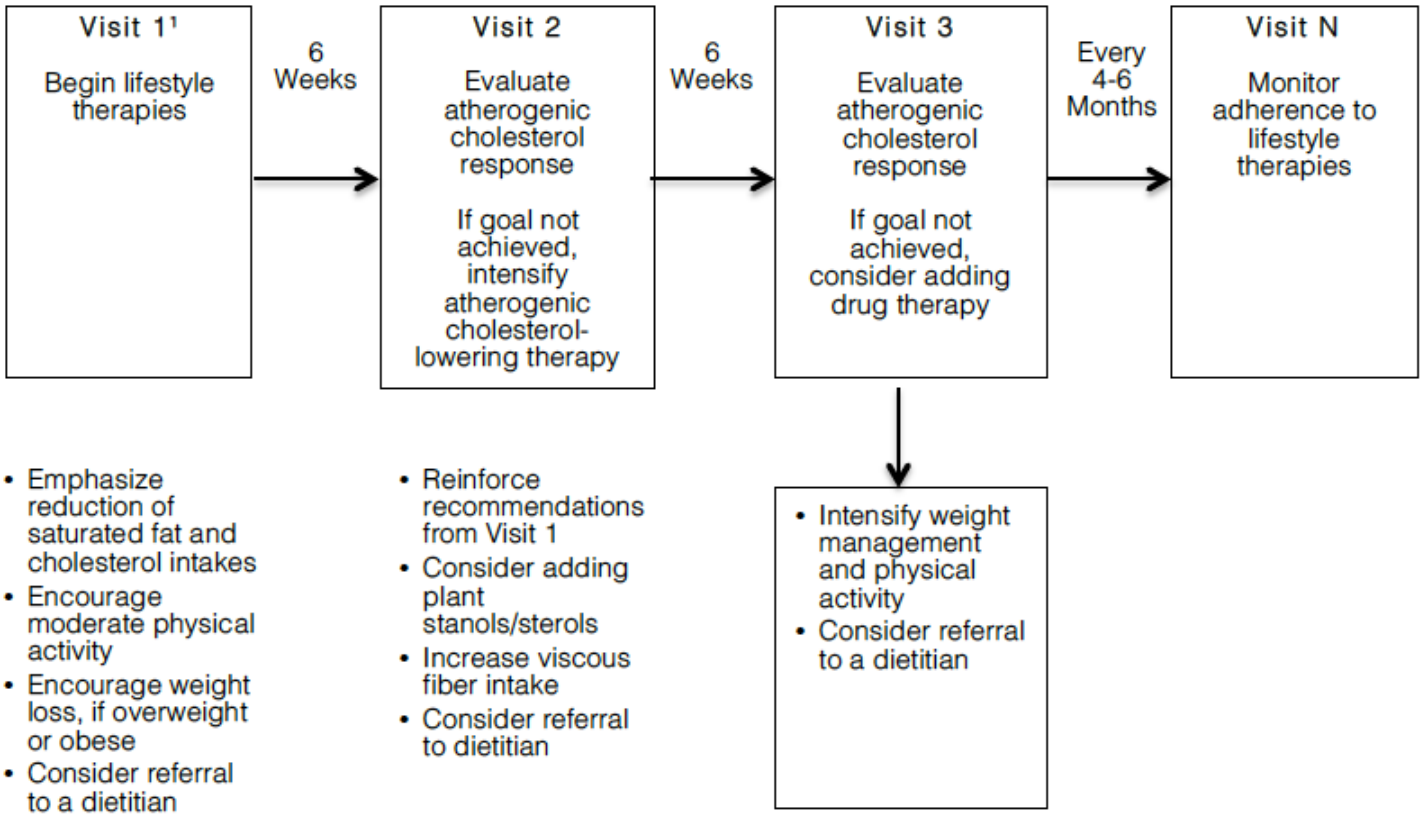
Measure	Categorical cut points
1. Elevated waist circumference[1,2]	≥40 inches (≥102 cm) in men ≥35 inches (≥88 cm) in women
2. Elevated triglycerides	≥150 mg/dL
3. Reduced HDL-C	<40 mg/dL in men <50 mg/dL in women
4. Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)	Systolic ≥130 and/or diastolic ≥85 mm Hg
5. Elevated fasting glucose (drug treatment of elevated glucose is an alternate indicator[3])	≥100 mg/dL

[1]American Heart Association/National Heart, Lung and Blood Institute guidelines for metabolic syndrome suggest waist-circumference thresholds of ≥37 inches (≥94 cm) in men and ≥32 inches (≥80 cm) in women as optional cut points for individuals or populations with increased insulin resistance, including those of Asian descent (alternate values have also been published for other groups: http://www.athero.org/download/IASPPGuidelines_FullReport_2.pdf).

[2]Body mass index ≥30.0 kg/m^2 may be used in place of waist circumference if not available, although waist is preferred. Note that body mass index may overestimate adiposity in those with above-average muscle mass. An optional cut point of 27.5 kg/m^2 may be considered for individuals or populations with increased insulin resistance, including those of Asian descent.

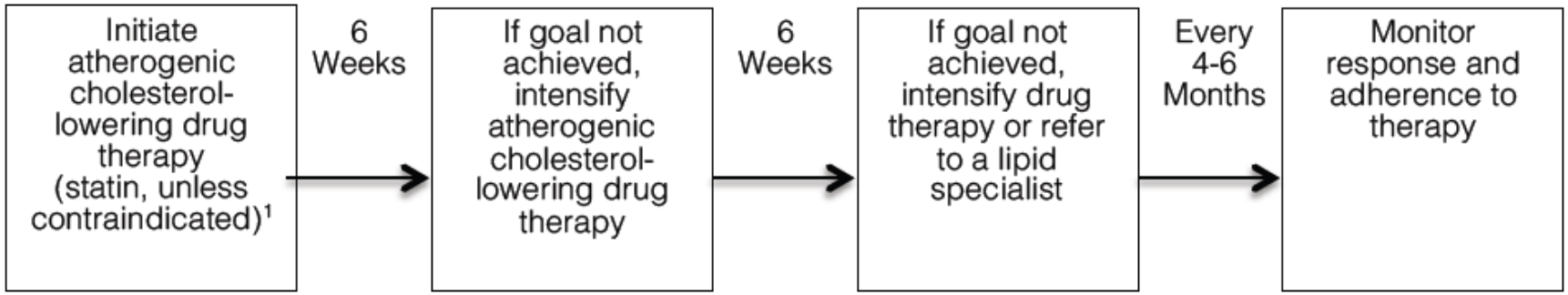
[3]Most patients with type 2 diabetes mellitus will have the metabolic syndrome by these criteria.

Figure 1. Model of steps in lifestyle therapies



[1]For people at high or very risk for ASCVD in whom drug therapy is indicated, it may be started concomitantly with lifestyle therapies. For other patients, a trial of lifestyle therapies should be undertaken before initiation of drug therapy.

Figure 2. Progression of atherogenic cholesterol-lowering drug therapy



[1]A moderate or high intensity statin should be first-line drug therapy for treatment of elevated levels of atherogenic cholesterol, unless contraindicated. In a patient with very high triglycerides (≥500 mg/dL), a triglyceride-lowering drug may be considered for first-line use to prevent pancreatitis. Other ASCVD risk factors should be managed appropriately in parallel.