# Advancing Lipid Management: Non-Statin Therapies in Primary Care Practice

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# Disclosures

I have relevant relationships with ineligible companies to disclose within the past 24 months:
Insulet (diabetes): Speaker and Consultant

All of the relevant financial relationships listed have been mitigated.

# AI Disclosure

Parts of this presentation (and/or its related materials) were generated using AI and are labeled as such, and the faculty have confirmed and validated this information.

# Learning Objectives

01

### Define hyperlipidemia and identify ASCVD risks

Understand the definitions of hyperlipidemia, recognize manifestations of atherosclerotic cardiovascular disease including underrecognized conditions like peripheral artery disease.

02

### Apply evidence-based LDL goals

Establish appropriate LDL cholesterol targets for different patient populations in both primary and secondary prevention settings.

03

### Implement comprehensive lifestyle interventions

Prescribe evidence-based physical activity and nutrition strategies using structured frameworks like FITT-VP and TAF methods.

04

### Optimize pharmacologic management beyond statins

Select appropriate statin and non-statin therapies based on risk stratification, guideline recommendations, and patient-specific factors.

# Hyperlipidemia and ASCVD

## ASCVD Risk

Elevated blood lipids including LDL cholesterol, total cholesterol, and triglycerides that contribute to atherosclerotic plaque formation.
Increased lipid levels accelerate atherosclerosis, leading to coronary artery disease, cardiovascular death, stroke, and peripheral vascular complications.

## Recognized Manifestations

- Coronary artery disease and myocardial infarction
- Ischemic stroke and transient ischemic attacks
- Angina pectoris
- Heart failure
- Sudden cardiac death

## Underrecognized: Peripheral Artery Disease (PAD)

- PAD affects millions but often goes undiagnosed.
- Symptoms include claudication, leg pain with walking, non-healing wounds, and decreased pulses.
- PAD shares the same risk factors as coronary disease, is a signal of increased risk of major adverse cardiovascular events (MACE) and requires aggressive lipid management.

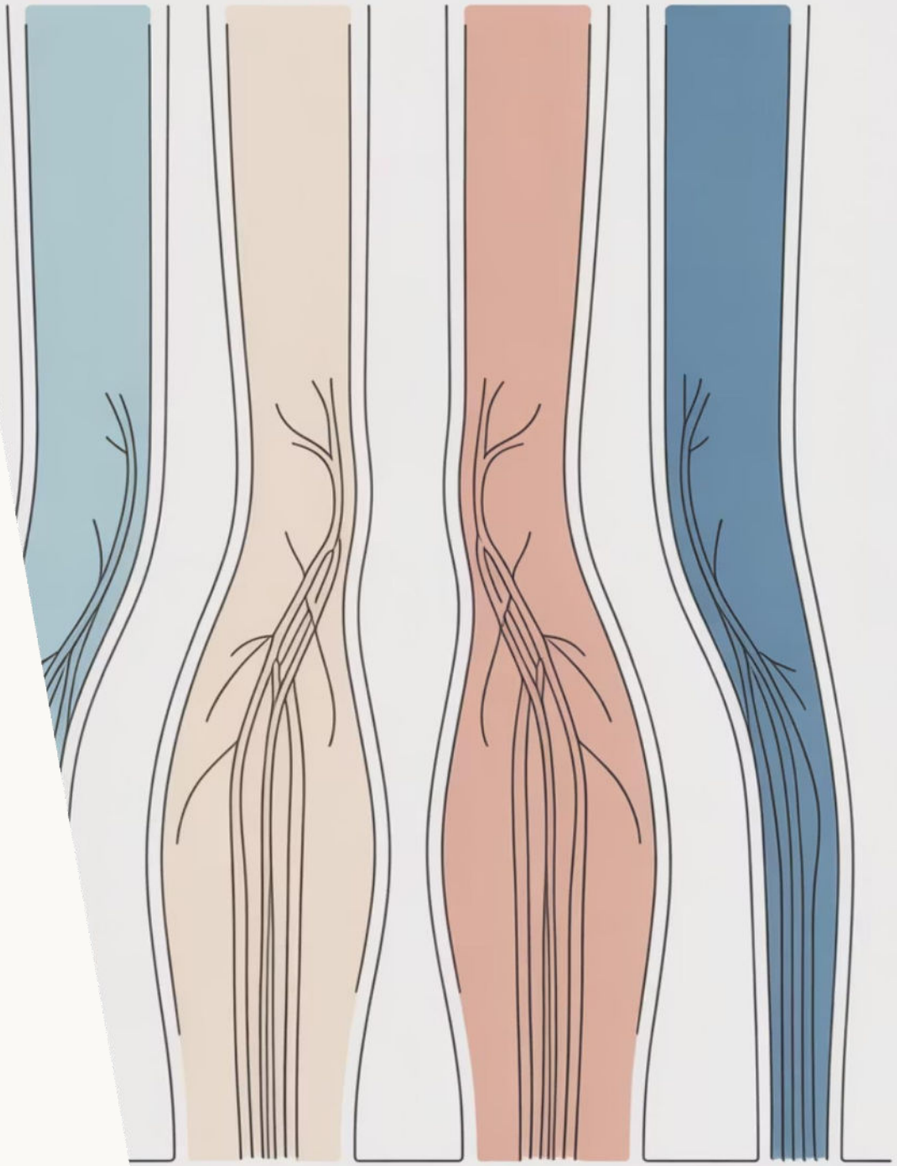


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**Source:** 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease.
https://www.ahajournals.org/doi/10.1161/cir.0000000000000678

# Physical Activity Vital Sign

Physical activity assessment should be incorporated into every clinical encounter. The Exercise is Medicine initiative promotes systematic evaluation and prescription of physical activity as a vital sign for cardiovascular health.

| | | |
|---|---|---|
| **Question 1:** For an average week in the last 30 days, how many days per week did you engage in moderate to vigorous physical activity (like walking fast, running, jogging, dancing, swimming, biking, or other activities that cause a light or heavy sweat)? | _____ | days |
| **Question 2:** On those days that you engage in moderate to vigorous physical activity, how many minutes, on average, do you exercise? | _____ | minutes |
| **Total minutes per week of physical activity (multiply #1 by #2)** | _____ | **minutes per week** |
| Optional Question (particularly important for older adults): | | |
| **Question 3:** During the past month, how many times per week did you do physical activities or exercises to strengthen your muscles? | _____ | days |

## Assess

Ask patients about current activity levels at each visit using standardized questions.

## Advise

Provide specific recommendations based on individual health status and goals.

## Prescribe

Write detailed exercise prescriptions using FITT-VP framework.

**Source:** Exercise is Medicine Physical Activity Vital Sign. Available at: https://www.exerciseismedicine.org; ACSM's Guidelines for Exercise Testing and Prescription, 12th edition

# Aerobic Exercise Recommendations

## Target Guidelines for Adults

Any amount of physical activity provides health benefits.

Most non-pregnant adults should aim for

- **150 minutes of moderate-intensity** aerobic activity per week OR
- **75 minutes of vigorous-intensity** activity per week

## Defining Intensity: The Talk Test

- **Moderate intensity:** Can talk but not sing during activity
- **Vigorous intensity:** Cannot say more than a few words without pausing for breath

## Who Needs Exercise Clearance?

- Cardiovascular disease or high CVD risk
- Renal disease
- Diabetes mellitus

These patients should undergo medical evaluation before starting vigorous exercise programs.

**Important:** Risk is higher with sudden increases in intense activities. Gradual progression is essential for safety.

**Source:** ACSM. Exercise Preparticipation Health Screening. https://pmc.ncbi.nlm.nih.gov/articles/PMC6411298/



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# Resistance Training and Flexibility

## Resistance/Strengthening Exercise

**Goal:** Twice per week minimum

## Flexibility Training

**Frequency:** Encouraged regularly

Stretching and flexibility exercises improve range of motion and reduce injury risk.

**Important note:** Flexibility training does NOT count toward the weekly aerobic or strengthening activity requirement.

**Source:** ACSM. Exercise Preparticipation Health Screening. https://pmc.ncbi.nlm.nih.gov/articles/PMC6411298/

# Exercise Prescription: FITT-VP Framework

Every physical activity prescription should include comprehensive details using the FITT-VP principle. This structured approach ensures clarity and promotes adherence to exercise recommendations.

## Frequency*

How often per week (e.g., 5 days/week)

## Intensity*

Level of effort (moderate or vigorous)

## Time (Duration)*

Minutes per session (e.g., 30 minutes)

## Type*

Specific activities (walking, cycling, swimming)

## Volume

Total amount determined by F × I × T

## Progression

Plan for gradual increases over time

*Included in exercise rx to patient

**Sources:** American College of Sports Medicine (ACSM) and American Heart Association (AHA) Guidelines



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"Focusing on healthy eating patterns that limit saturated fat while increasing un-saturated fat produces more consistent LDL-C lowering than restricting dietary cholesterol."

# Nutrition: ACC/AHA Dietary Recommendations

**Emphasize:**

Vegetables

Fruits

Nuts, legumes, seeds or lean vegetable protein

Whole grains and fiber

Non-fat or low-fat dairy

Unsaturated fat

**Minimize:**

*Trans* fats

Saturated fat (red meat, butter/high-fat milk, tropical oils

Processed meats

Refined carbohydrates

Sugar-sweetened beverages (SSB)

Ultra-processed foods (UPFs)

If consuming meat, pick lean cuts, prioritize fish, avoid ultra-processed meat, keep portions small

**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# Plant-Forward Diets and *Trans* Fats

## Plant-Forward Eating

Diets emphasizing unprocessed whole plant foods naturally limit dietary cholesterol.

These patterns reduce ASCVD risk through multiple mechanisms including:

- Improved lipid profiles
- Reduced inflammation
- Better glycemic control

## *Trans* Fats: Banned But Not Gone

Added trans fats were deemed unsafe for human consumption and forbidden since 2018.

However, ***trans* fats naturally occur in animal products**.

Minimizing animal product consumption reduces *trans* fat exposure.

**Source:** American College of Lifestyle Medicine. Benefits of Plant-Based Nutrition Whitepaper 2025

# The Power of Fiber



## Cardiovascular Protection

Soluble fiber binds cholesterol in the digestive tract, reducing LDL-C absorption and lowering cardiovascular risk.



## Metabolic Benefits

Fiber slows glucose absorption, improving insulin sensitivity and reducing diabetes risk.



## Digestive Health

Both soluble and insoluble fiber promote healthy gut microbiome and reduce colon cancer risk.

**Source:** American College of Lifestyle Medicine. Benefits of Plant-Based Nutrition Whitepaper 2025

# Evidence-Based Dietary Patterns

Multiple dietary approaches have demonstrated cardiovascular benefits. Rather than a specific “one-size-fits-all” diet, focus on **dietary patterns** to improve health. The key is choosing a sustainable pattern that **emphasizes** whole foods and **limits** processed items.

## Vegan or Vegetarian Diet

LDL-C reduction beyond Mediterranean Diet

Greater LDL-C reduction in vegan over vegetarian

## Portfolio Diet

Very low saturated fat, high in plant sterols, soy protein, viscous fibers, and almonds.

Decreases LDL by 28% (comparable to low-dose statin).

## Mediterranean Diet

High monounsaturated to saturated fat ratio.

Emphasizes fruits, vegetables, legumes, whole grains, fish, moderate red wine and dairy, minimal meat and processed foods.

**Sources:** American College of Lifestyle Medicine. Benefits of Plant-Based Nutrition Whitepaper 2025

2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# Portfolio Diet: Specific Components

This dietary pattern is an example of nutritional changes that make substantial lipid-lowering effects.

### Plant Sterols

2 grams daily from fortified foods or supplements. Blocks cholesterol absorption in the intestine.

### Soy Protein

42 grams daily replacing animal protein. Lowers LDL through multiple mechanisms.

### Viscous Fiber

18 grams daily from oats, barley, psyllium, eggplant, okra, apples, oranges, berries.

### Almonds

45 grams (about 1.5 ounces) daily. Provides healthy fats and additional fiber.

**Source:** American College of Lifestyle Medicine. Benefits of Plant-Based Nutrition Whitepaper 2025

# Mediterranean Diet: Key Features

## Emphasize

- High monounsaturated to saturated fat ratio
- Abundant fruits and vegetables
- Legumes and whole grains
- Nuts and seeds
- Fish and seafood (twice weekly)
- Olive oil as primary fat source
- Moderate red wine with meals (optional)
- Moderate dairy (mainly cheese and yogurt)

## Minimize

- Red meat and processed meats
- Refined grains and sugars
- Processed foods
- Butter and margarine

### Lyon Heart Trial

Mediterranean diet was protective against secondary MI risk for 4 years, independent of other CV risk factors including hypertension and hyperlipidemia (50-70% relative risk reduction).

**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# Foods Associated with CVD Risk

Certain dietary patterns and specific foods consistently demonstrate associations with increased cardiovascular disease risk. Minimizing these foods is as important as emphasizing healthy options.

## Sugar-Sweetened Beverages

SSBs contribute to weight gain, insulin resistance, and increased triglycerides without providing nutritional value. Replace with water, unsweetened tea, or coffee.

## Red and Processed Meats

High in saturated fat and, in processed forms, sodium and preservatives. Associated with increased ASCVD and all-cause mortality.

## Fried Foods

Increase aldehydes and advanced glycation end products. Cooking method matters—baking, stewing, or steaming are healthier alternatives.

**Source:** American College of Lifestyle Medicine.

# Effective Nutrition Counseling: TAF Method

Successful dietary counseling requires specificity. The **TAF method** provides a framework for clear, actionable nutrition recommendations that patients can implement.



## Type of Food

Be specific: "leafy greens" not "vegetables"



## Amount

Provide exact quantities: "1 cup" or "3 ounces"



## Frequency

Specify timing: "per day," "3 times per week"

**Source:** American College of Lifestyle Medicine (ACLM)

# Strategies for Sustainable Dietary Change



## Focus on Addition, Not Restriction

Frame recommendations positively: "Add a serving of vegetables to lunch" rather than "Stop eating fast food." This approach feels empowering rather than punitive.



## Emphasize Swaps Over Avoidance

Suggest alternatives: "Try olive oil instead of butter" or "Choose whole grain bread instead of white bread." Swaps maintain satisfaction while improving nutrition.



## Use SMART Goals

Goals should be Specific, Measurable, Achievable, Relevant, and Time-bound. Example: "I will eat 2 servings of fish per week for the next month."

**Source:** American College of Lifestyle Medicine (ACLM)

# Supplement Misconceptions

Many patients take supplements believing they provide cardiovascular protection. However, evidence does not support the use of most supplements for ASCVD risk reduction.

## Coenzyme Q10

No evidence shows CoQ10 decreases statin-associated myopathies. Not recommended for preventing muscle symptoms with statin therapy.

## Red Yeast Rice

May increase glucose levels without lowering ASCVD risk. Contains variable amounts of statin-like compounds with unpredictable effects and quality.

## OTC Fish Oil/Omega-3

May lower triglycerides but no evidence of lowering ASCVD risk in most populations.

***Important:*** Dietary omega-3 and prescription omega-3 icosapent ethyl show benefit in lowering ASCVD risk.

**Note:** Patients should discuss all supplements with their healthcare provider. Evidence-based therapies should be prioritized.

# Lipid Screening Protocols

The ACC/AHA guidelines provide clear recommendations for when and how to screen for lipid disorders. Early identification enables timely intervention and risk reduction.

### Ages 9-11 Years

1

Universal screening recommended. Identifies familial hypercholesterolemia and other genetic lipid disorders early.

2

### Ages 19-29 Years

Begin screening for hyperlipidemia every 5 years.

### Ages 30-79 Years

3

Regular screening with risk assessment. Use PREVENT calculator for 10-year and 30-year risk estimation

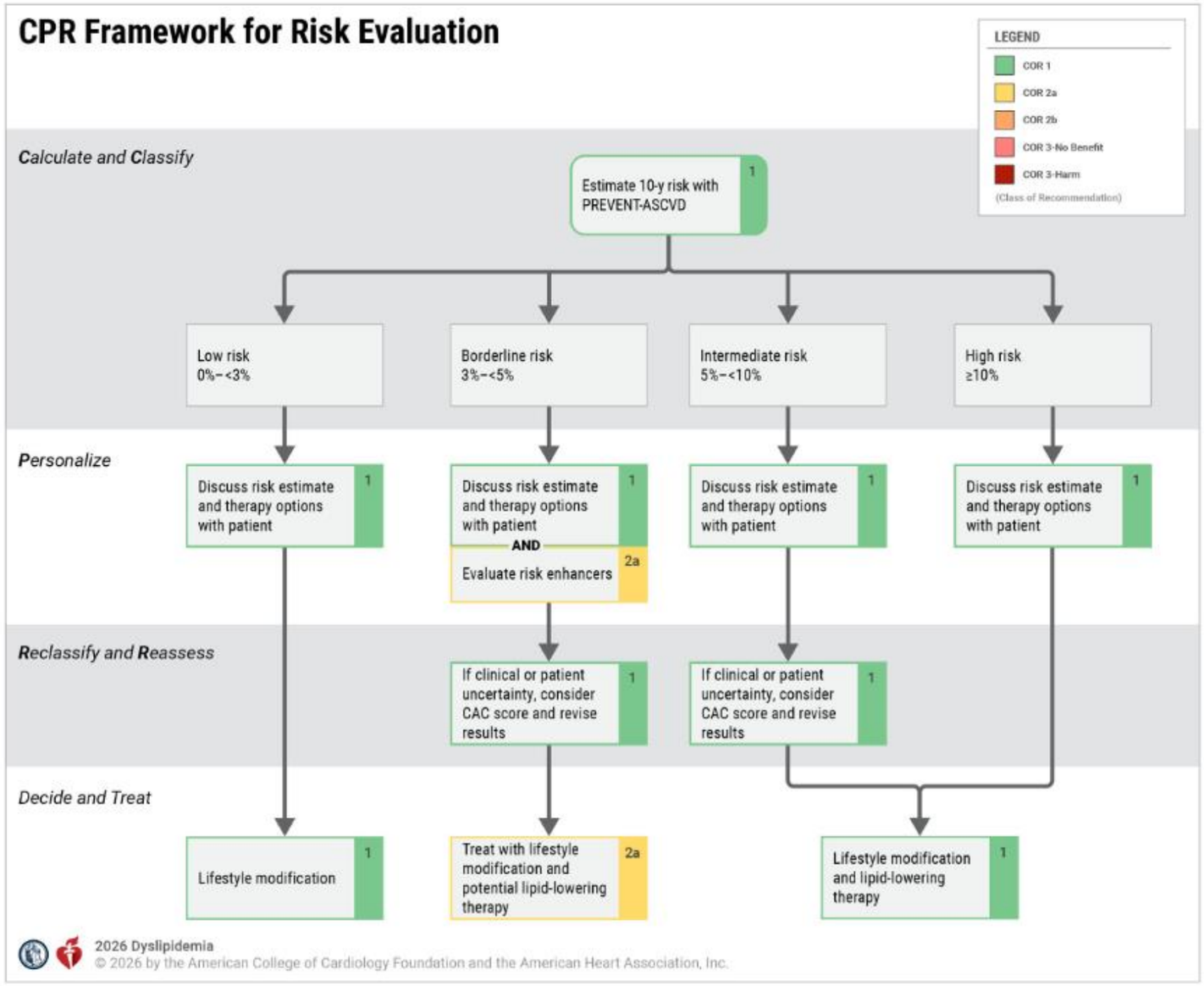
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### Ages >79 Years

Regular, tailored, high-frequency screening

Check Lp(a) at least once in adults

**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2




# Risk-Based Treatment Approach

Risk assessment guides treatment decisions based on cardiovascular risk stratification.

The approach balances aggressive risk reduction in high-risk individuals with judicious use of medications in lower-risk populations.

**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# LDL Cholesterol Goals: Primary Prevention

Target LDL-C levels vary based on individual cardiovascular risk assessment. Primary prevention focuses on preventing the first ASCVD event through risk stratification and appropriate lipid management.



## Low Risk (<3%)

LDL goal <100mg/dL

Lifestyle modifications emphasized. Statin therapy considered with risk-enhancing factors, if LDL at least 160, or 30-yr risk 10+%.



## Borderline Risk (3- <5%)

LDL-C goal <100 mg/dL.

Consider moderate-intensity statin if risk-enhancing factors are present.



## Intermediate Risk (5- <10%)

Reduce LDL by 30-49%

LDL-C goal: <100 mg/dL.

Moderate to high-intensity statin recommended. CAC scoring may be helpful for decision-making.



## High Risk (≥10%)

Reduce LDL by ≥50%

LDL-C goal: <70 mg/dL

High-intensity statin therapy indicated. Consider non-statin therapies if goal not achieved.

**Sources:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# Risk-Enhancing Factors

Risk-enhancing factors help refine treatment decisions, particularly for individuals at intermediate risk. These factors identify patients who may benefit from more intensive therapy.

## Family History

Premature ASCVD in first-degree relatives (men <55 years, women <65 years). Identifies genetic predisposition and elevated lifetime risk.

## Additional Risk Markers

Lp(a) ≥125 nmol/L or ≥50 mg/dL
hsCRP ≥2 mg/L on >1 occasion (if measured)
Triglycerides ≥175mg/dL non-fasting or ≥150mg/dL fasting

## Cardiovascular-Kidney-Metabolic (CKM) syndrome

Abdominal obesity (high BMI and/or large waist circ)
Insulin-resistant glucose metabolism (hyperinsulinemia IFG, IGT, T2D)
Dyslipidemia (high serum TG and low serum HDL
Increased BP
And sometimes microalbuminuria, proteinuria, or CKD

## Primary LDL-C, non-HDL, or apoB Elevation

LDL-C ≥160 mg/dL, non-HDL ≥190mg/dL, or apoB ≥120mg/dL

## Chronic Inflammatory Diseases

Psoriasis, rheumatoid arthritis, HIV (especially with protease inhibitors). Chronic inflammation accelerates atherosclerosis.

## Ancestral risk

Higher risk ancestry or high polygenic risk (if measured)



## Reproductive Risk Markers

Early (<45yo) or premature (<40yo) menopause, preeclampsia, gestational diabetes, gestational hypertension, preterm delivery, small for gestational age (<10$^{th}$ percentile), preterm delivery, recurrent spontaneous pregnancy loss, early menarche (<10yo), polyendocrine metabolic ovarian syndrome + irregular menses

**Sources:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# Low Risk: Selective Statin Use

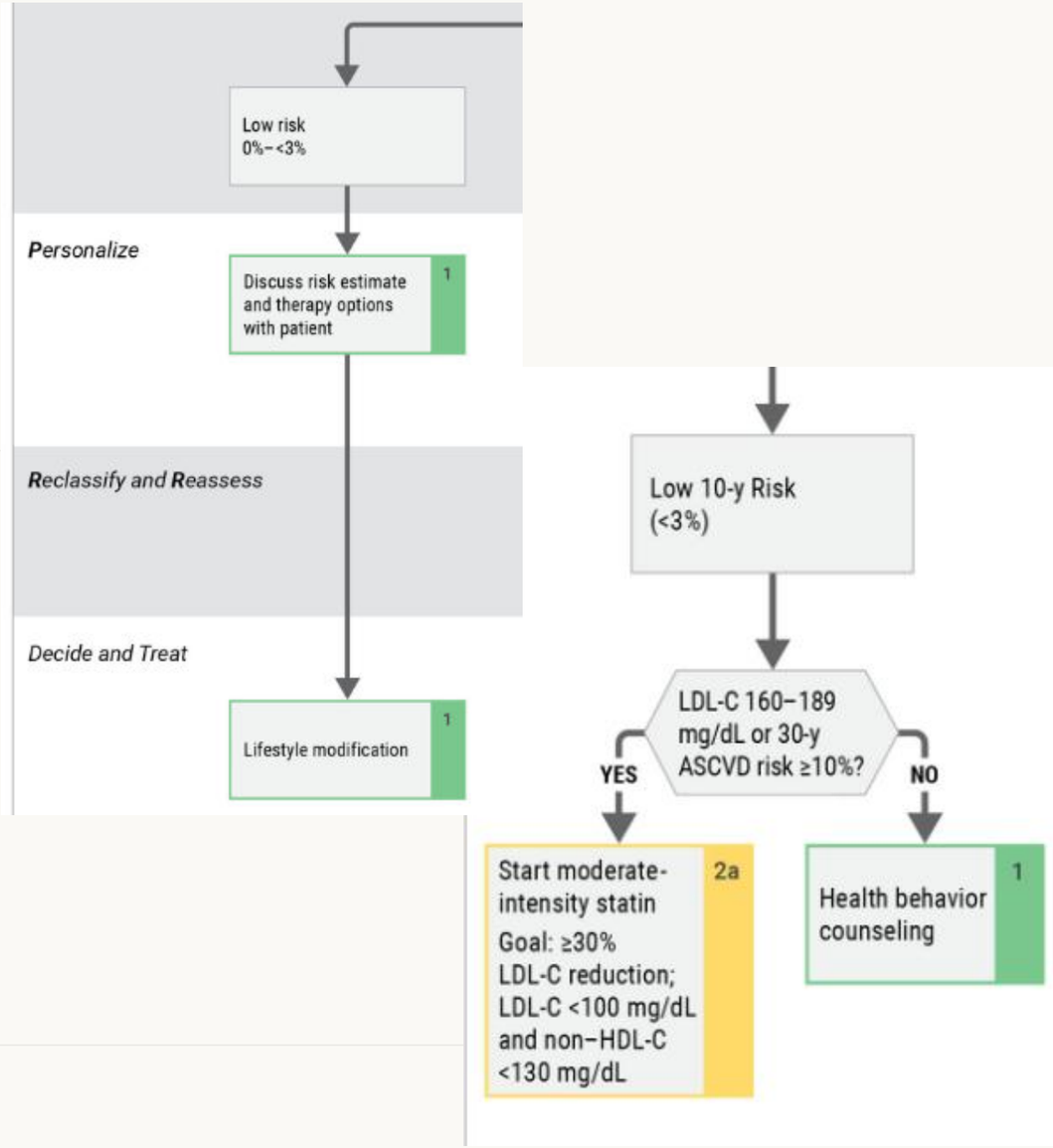
For individuals with 10-year ASCVD risk <3%, the focus is on lifestyle modification. Statin therapy may be considered in select cases with risk-enhancing factors.

## Low Risk (<3%)

LDL goal <100mg/dL and lower by ≥ 30%

Lifestyle modifications emphasized.

- Statin therapy considered if
  - LDL ≥ 160 or
  - 30-year risk ≥ 10% or
  - Risk-enhancers present




**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

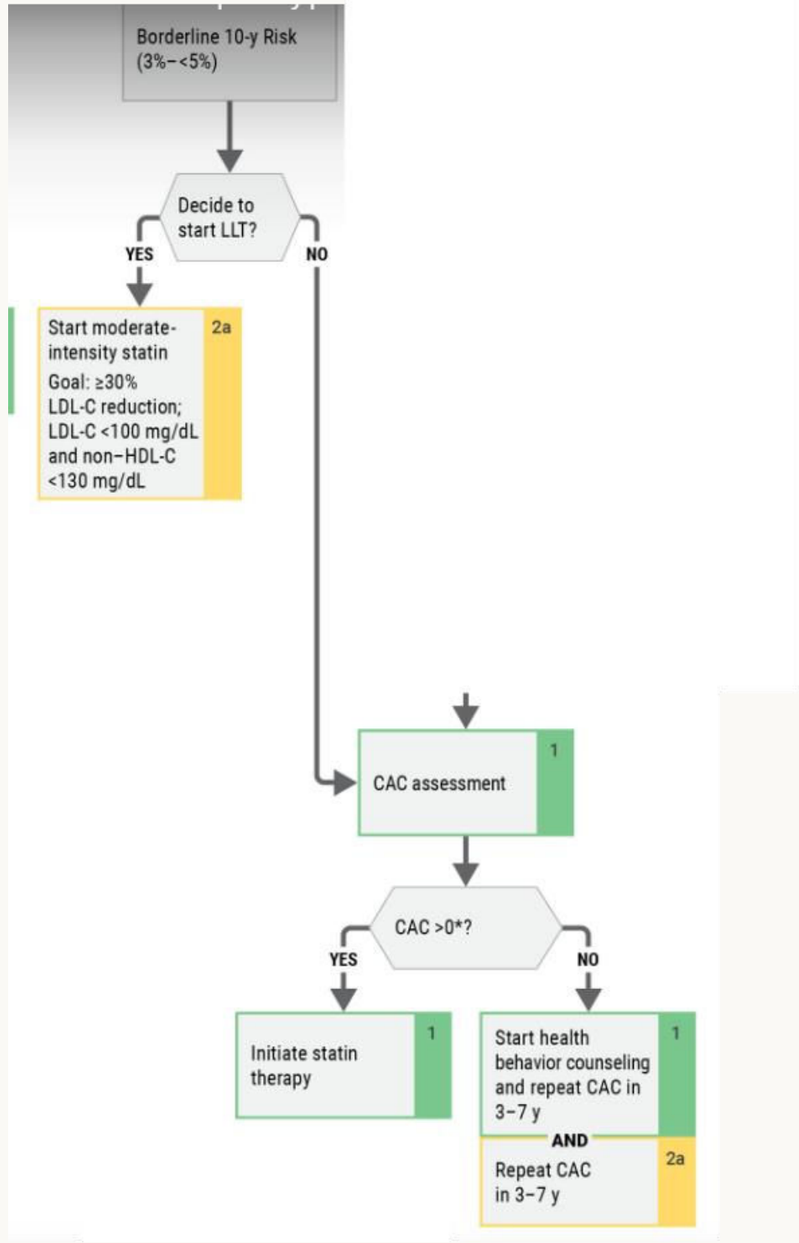
# Borderline Risk: Risk Discussion Essential

Individuals with 3% to <5% 10-year ASCVD risk benefit from thorough risk assessment and discussion. The presence of risk-enhancing factors often tips the balance toward statin initiation. Coronary Artery Calcium (CAC) score can be considered to aide in the risks vs benefits discussion.

## Borderline Risk (3- <5%)

LDL-C goal: <100 mg/dL and lower by ≥30%

Consider moderate-intensity statin if
- Risk-enhancing factors are present or
- CAC >0




Available generic statins are cost-effective in this risk range. The challenge is identifying those who will benefit while avoiding overtreatment.

**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# Intermediate Risk

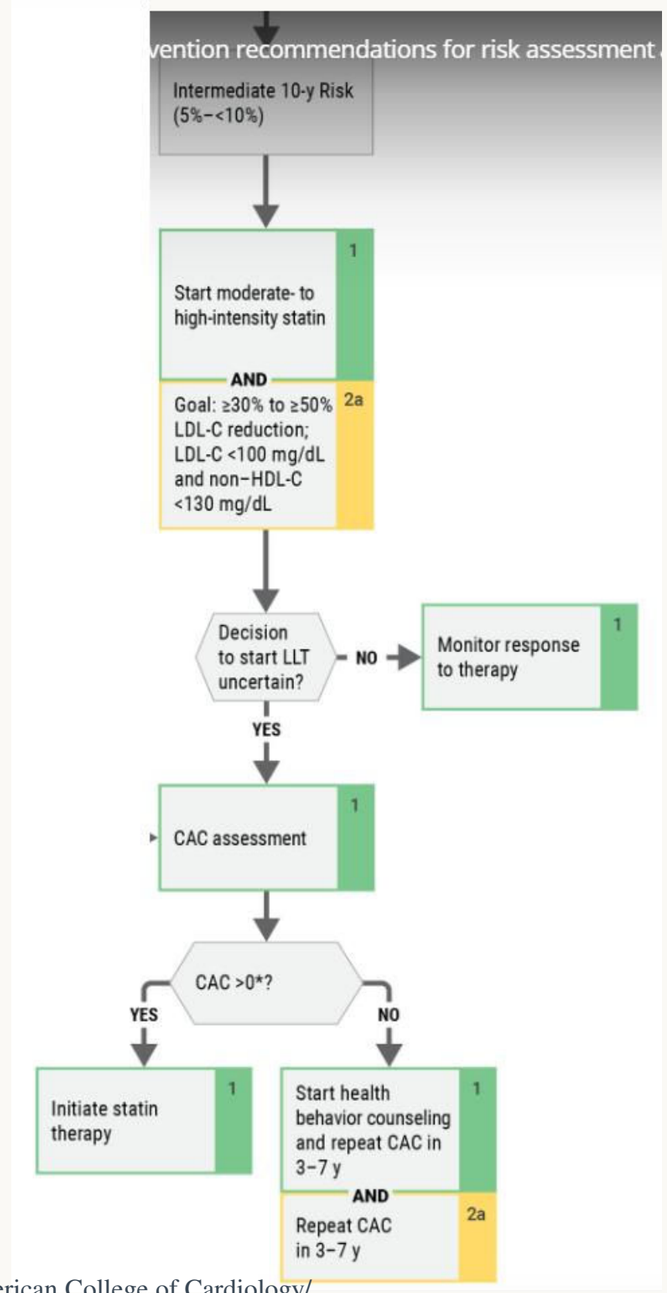
Individuals with 5% to <10% 10-year ASCVD risk benefit from moderate- to high-intensity statin. If the decision is uncertain, Coronary Artery Calcium (CAC) score can be considered to aide in the risks vs benefits discussion.

## Intermediate Risk (5- <10%)

LDL-C goal: <100 mg/dL and lower by ≥30% to ≥50%

Start moderate- to high-intensity statin

If decision is uncertain, start statin if
- Risk-enhancing factors are present or
- CAC >0




**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# Role of CAC Scoring

For adults at borderline or intermediate risk, CAC scoring can aide treatment decisions.

**Important:** CAC of zero does not rule out risk from non-calcified plaque in persistent smokers, patients with diabetes, or those with chronic inflammatory conditions.

1 **CAC = 0**

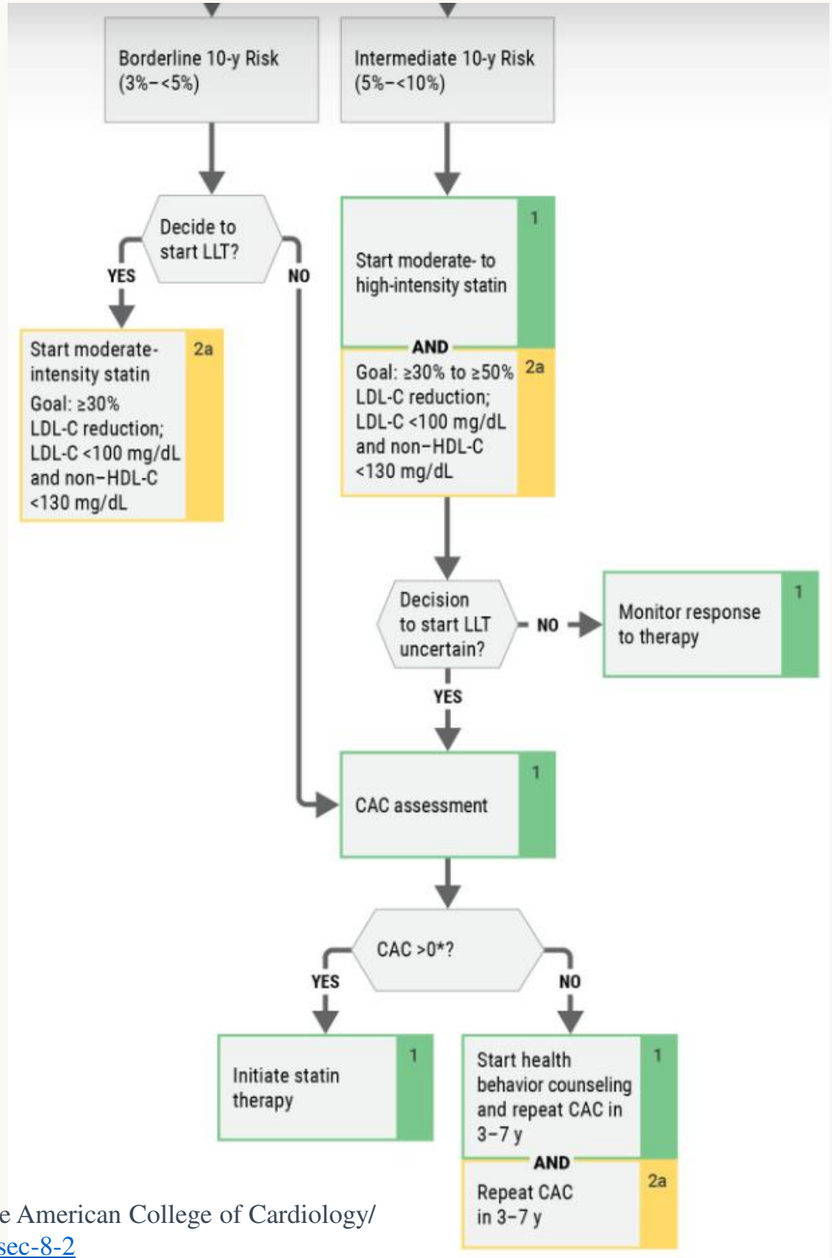
Ten-year event rates in lower range. Statin therapy may be of limited value. Consider withholding statin unless risk-enhancing factors present (diabetes, smoking, family history, inflammatory conditions).

2 **CAC 1-99**

Ten-year ASCVD event rates: 3.8% (ages 45-54), 6.5% (ages 55-64), 8.3% (ages 65-74). Repeat risk discussion. If untreated, consider repeat CAC in 5 years.

3 **CAC ≥100 or ≥75th Percentile**

ASCVD event rates support statin initiation. These individuals benefit from moderate to high-intensity statin therapy.





**Source:**

1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
2. Lloyd-Jones, D, Morris, P. et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2022 Oct, 80 (14) 1366–1418. https://doi.org/10.1016/j.jacc.2022.07.006
3. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 - 1207

# High Risk: Aggressive Intervention

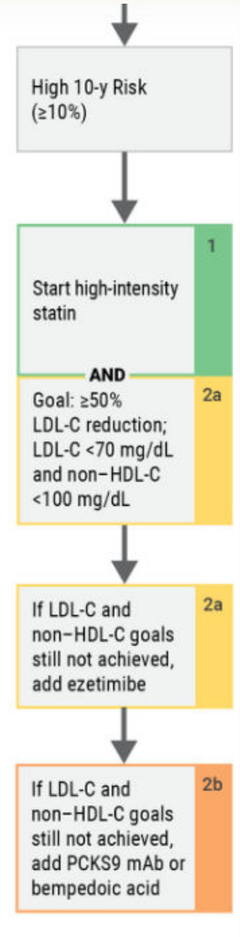
## High Risk (≥10%)

LDL-C goal <70 mg/dL and lower by ≥50%

High-intensity statin therapy indicated.

Consider non-statin therapies if goal not achieved.

- First, ezetimibe
- Next, PCSK9 inhibitor or bempedoic acid




**Source:**

1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
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# Special Populations

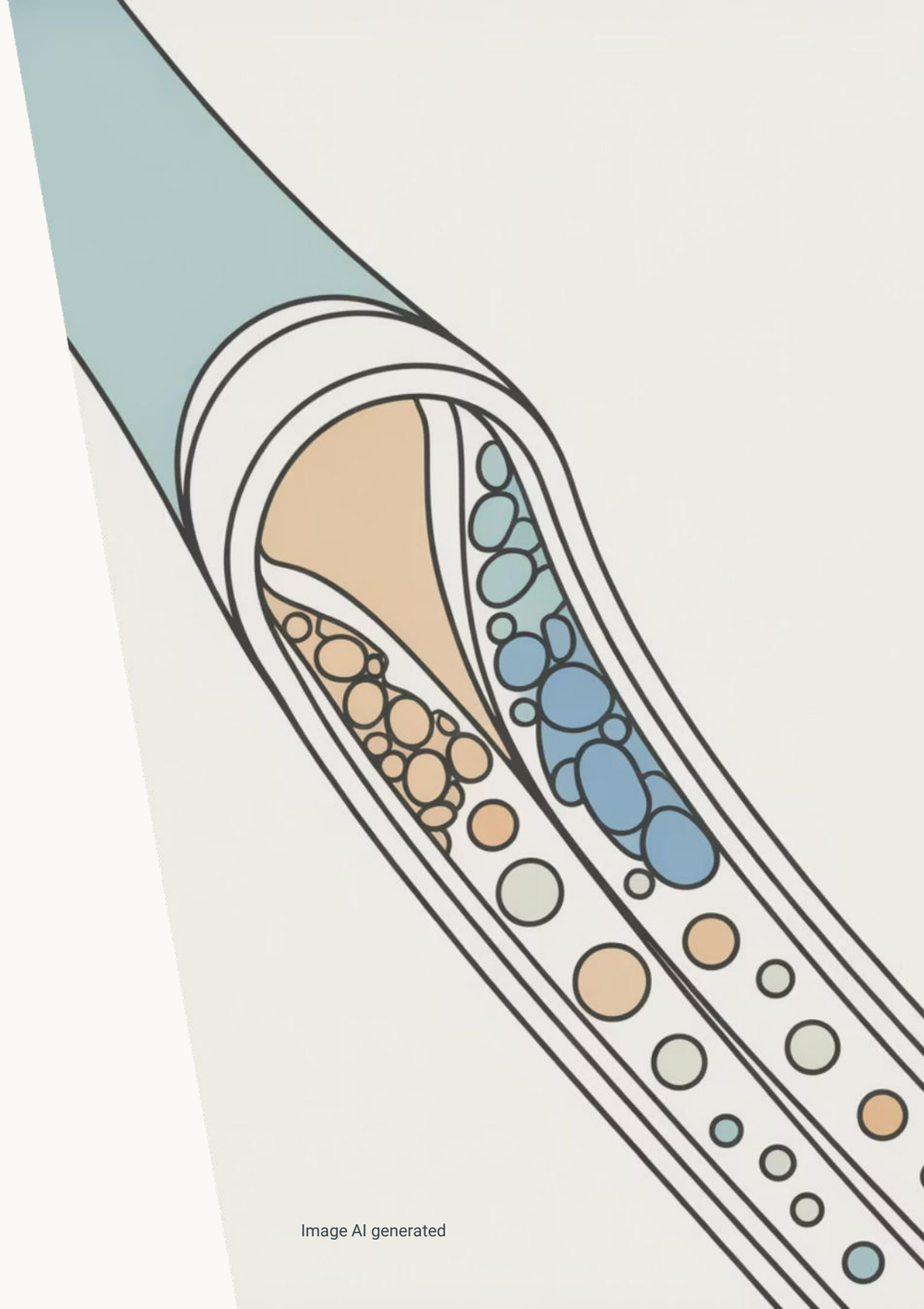


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# Statins in Diabetes: Strong Evidence

Patients aged 40-75 years with diabetes are typically at intermediate or high ASCVD risk. Statin therapy provides significant benefit in this population.

## Evidence-Based

Three of four double-blinded primary-prevention RCTs of moderate statin therapy in large cohorts with diabetes showed significant ASCVD event reductions. Meta-analysis found 25% risk reduction, similar to people without diabetes.

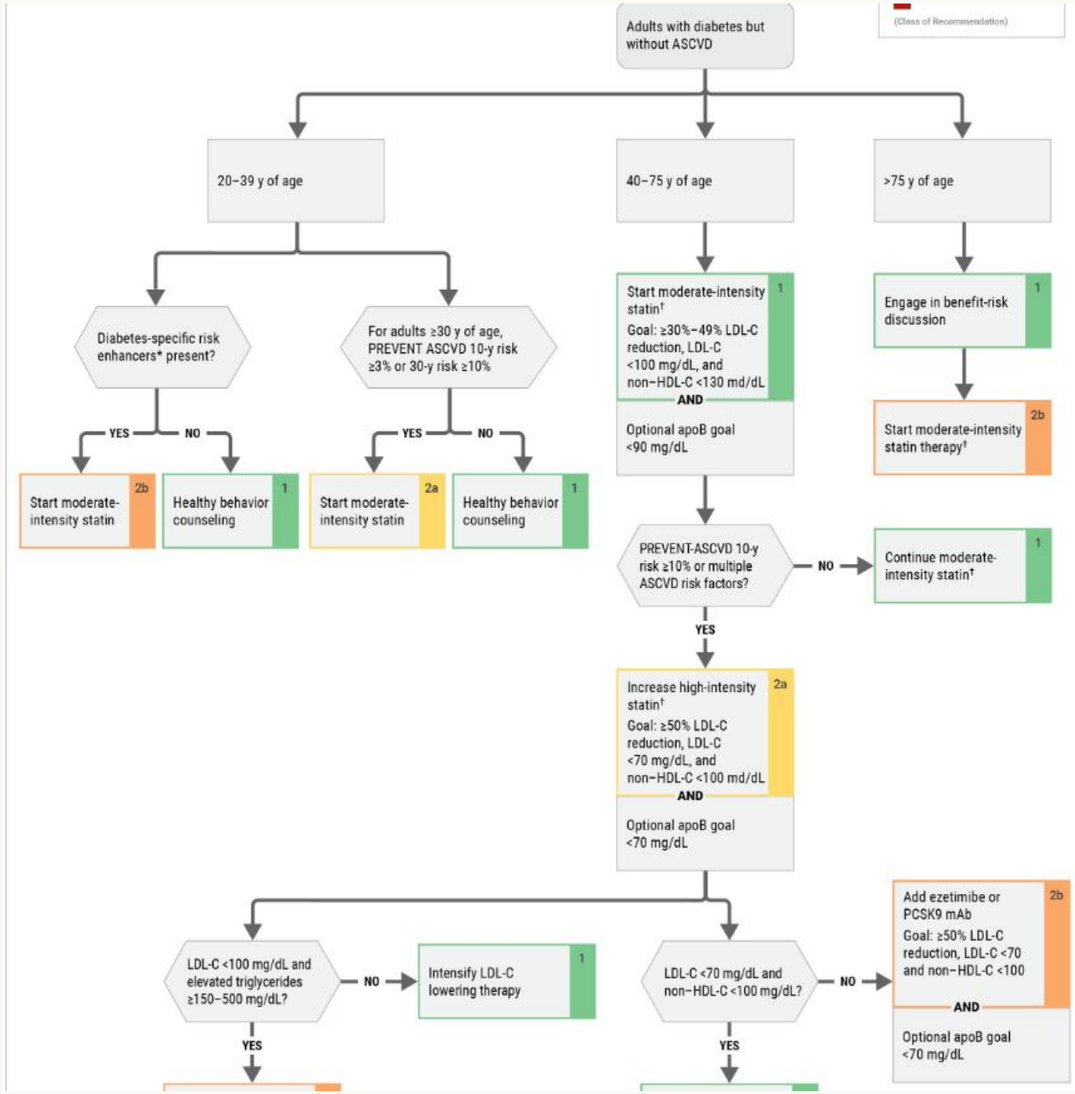
No apparent difference in benefit between T1D and T2D.

***Moderate-intensity statin:*** Indicated for all patients 40-75 years with diabetes for primary prevention.

- Goal LDL <100mg/dL and lower LDL by ≥30%

***High-intensity statin:*** Preferred as patients develop risk modifiers including duration of diabetes ≥10 years, albuminuria, eGFR <60, retinopathy, neuropathy, or ankle-brachial index <0.9.

- Goal LDL <70mg/dL and lower LDL by ≥50%
- If goal not reached, add ezetimibe or PCSK9 inhibitor





**Source:**

1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
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3. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 - 1207

# Severe Hypercholesterolemia: LDL ≥190 mg/dL

Patients with primary severe hypercholesterolemia have high ASCVD risk and risk of premature and recurrent coronary events. Maximally tolerated statin therapy is essential.

## High Lifetime Risk

LDL-C ≥190 mg/dL indicates likely genetic hypercholesterolemia. These patients accumulate cholesterol burden from birth, dramatically increasing lifetime ASCVD risk, including familial hypercholesterolemia (FH).

## Maximally Tolerated Statin

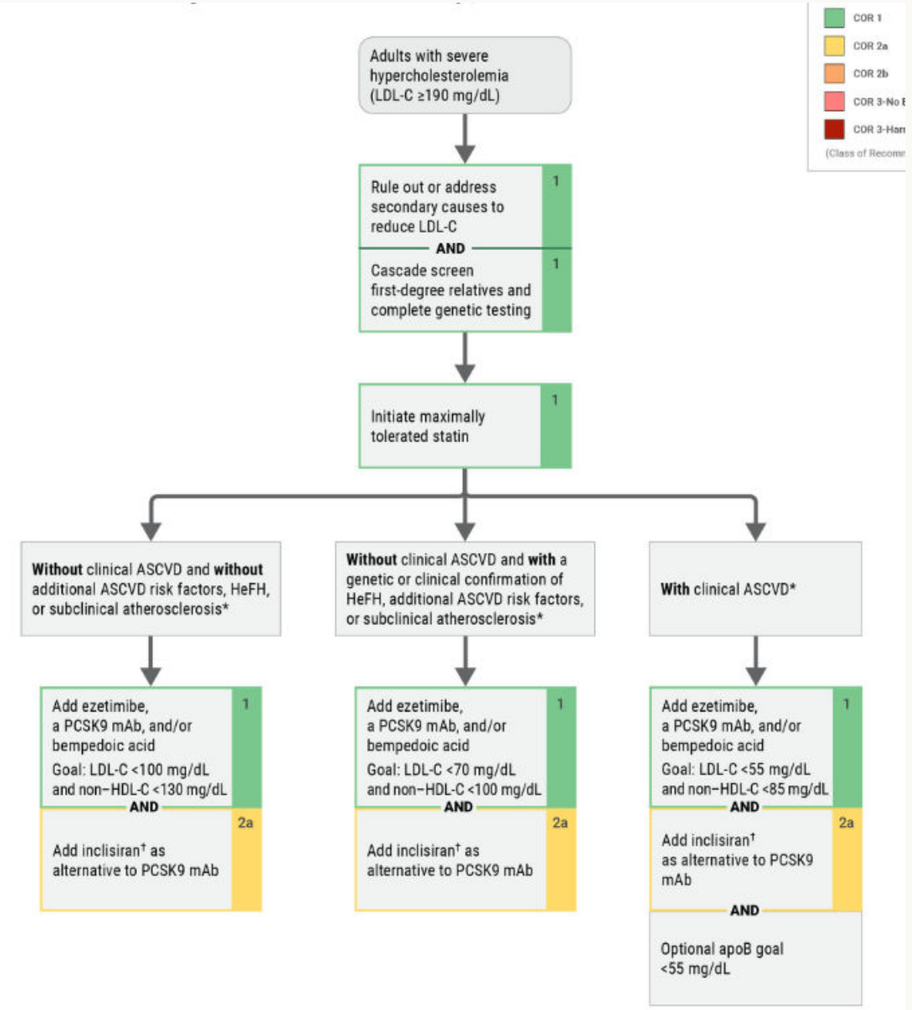
Start high-intensity statin therapy.

No clinical/subclinical ASCVD, FH, or additional risk factors for ASCVD?
Goal LDL reduction ≥ 50% and LDL <100mg/dL

No clinical ASCVD **but *with* FH**, positive CAC, or additional risk factors?
Goal LDL reduction ≥ 50% and LDL <70mg/dL

## Non-Statin Therapies Often Needed

Most patients require combination therapy to achieve adequate LDL-C goal.
Add ezetimibe, PCSK9, and/or bempedoic acid if additional LDL reduction is needed
Alternative: Inclisiran




**Source:**
1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
2. Lloyd-Jones, D, Morris, P. et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2022 Oct, 80 (14) 1366–1418. https://doi.org/10.1016/j.jacc.2022.07.006
3. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 - 1207

# Statin Intensity and LDL-C Reduction

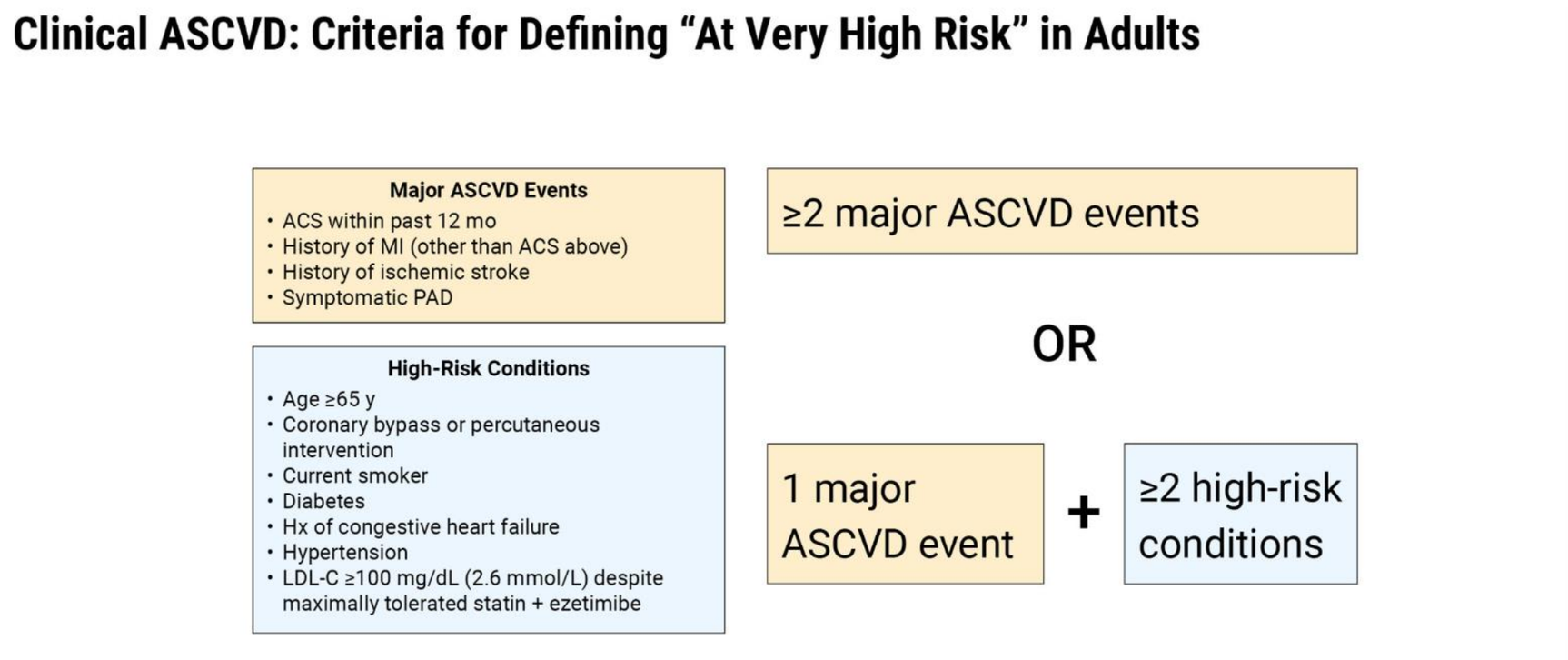
Statins are classified by their expected LDL-C lowering effect. Understanding these categories helps clinicians select appropriate therapy and set realistic expectations.

| Intensity | Expected LDL-C Reduction | Medications |
|---|---|---|
| High-Intensity | ≥50% | Atorvastatin 40-80 mg<br>Rosuvastatin 20-40 mg |
| Moderate-Intensity | 30-49% | Atorvastatin 10-20 mg<br>Rosuvastatin 5-10 mg<br>Simvastatin 20-40 mg<br>Pravastatin 40-80 mg<br>Lovastatin 40-80 mg<br>Fluvastatin 80 mg<br>Pitavastatin 1-4 mg |
| Low-Intensity | <30% | Simvastatin 10 mg<br>Pravastatin 10-20 mg<br>Lovastatin 20 mg<br>Fluvastatin 20-40 mg |

**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# LDL Cholesterol Goals: Secondary Prevention

Patients with established ASCVD require aggressive lipid lowering to prevent recurrent cardiovascular events. These individuals have the highest risk and benefit most from intensive therapy.




**Source:**
1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
2. Lloyd-Jones, D, Morris, P. et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2022 Oct, 80 (14) 1366–1418. https://doi.org/10.1016/j.jacc.2022.07.006
3. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 - 1207

# LDL Cholesterol Goals: Secondary Prevention

## Established ASCVD Not at Very High Risk

*LDL-C goal: <70 mg/dL and reduce by ≥50%*

*Optional LDL-C goal: <55 mg/dL*

High-intensity statin recommended as foundation.

Next, add ezetimibe, PCSK9 inhibitor or bempedoic acid

Decision based on:

- Amount of LDL reduction needed
- Pt preference

Alternative: Inclisiran

## Established ASCVD at Very High Risk

*LDL-C goal: <55 mg/dL and reduce by ≥50%*

High-intensity statin plus non-statin therapy often required.

Next, add ezetimibe or PCSK9 inhibitor

Alternative: Inclisiran

Then add bempedoic acid if needed.

**Source:**

1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
2. Lloyd-Jones, D, Morris, P. et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2022 Oct, 80 (14) 1366–1418. https://doi.org/10.1016/j.jacc.2022.07.006
3. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 - 1207

# Non-Statin Therapy: When to Add

Nonstatins in combination with low- or moderate-intensity statin therapy can produce ≥50% LDL-C reductions. Nonstatins remain underutilized[12–14] due to clinical inertia, misconceptions that only statin therapy reduces ASCVD risk, medication access barriers for brand-name products, concerns about potential side effects, and perceived lack of need by clinicians and patients.[15–17]

AHA/ACC 2026

Additional non-statin therapies may be needed based on patient risk category and LDL-C response to statin therapy.

Non-statin agents should be added when LDL remains elevated despite maximally tolerated statin therapy.

**Source:** 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

# 1. Ezetimibe: First-Line Non-Statin Therapy

Effective, well-tolerated, and generic

Preferred first non-statin agent to add when LDL-C remains above goal despite maximally tolerated statin therapy.

## Mechanism and Efficacy

Inhibits cholesterol absorption in the small intestine

***LDL-C Reduction:*** Approximately 15-20% additional reduction when added to statin therapy.

## Evidence-Based

***IMPROVE-IT Trial:*** Demonstrated effectiveness for secondary prevention of ASCVD.
Relative risk reduction for MACE ~12% for initial and subsequent events

***EWTOPIA 75 Trial:*** Primary Prevention in patients ≥75 years old.

Relative risk reduction for MACE 20%

## Side Effects

Generally well-tolerated. Possible side effects include diarrhea, upper respiratory tract infection, fatigue, myalgia, elevated liver enzymes.

## Contraindications

Moderate to severe hepatic impairment

Active liver disease or unexplained persistent elevations in serum transaminases (combination tx)

**Sources:**

1. IMPROVE-IT Trial. https://www.nejm.org/doi/full/10.1056/NEJMoa1410489; Primary Prevention Study. https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.039415;

2. Ouchi Y, Sasaki J, Arai H, Yokote K, Harada K, Katayama Y, Urabe T, Uchida Y, Hayashi M, Yokota N, Nishida H, Otonari T, Arai T, Sakuma I, Sakabe K, Yamamoto M, Kobayashi T, Oikawa S, Yamashita S, Rakugi H, Imai T, Tanaka S, Ohashi Y, Kuwabara M, Ito H. Ezetimibe Lipid-Lowering Trial on Prevention of Atherosclerotic Cardiovascular Disease in 75 or Older (EWTOPIA 75): A Randomized, Controlled Trial. Circulation. 2019 Sep 17;140(12):992-1003. doi: 10.1161/CIRCULATIONAHA.118.039415. Epub 2019 Aug 22. PMID: 31434507.

3. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2

4. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 - 1207

# 2. PCSK9 Inhibitors: Novel Mechanism

Injectable monoclonal antibodies dosed every 2 weeks or monthly.

## Evolocumab

***Indications:*** Secondary prevention and familial hypercholesterolemia

***FOURIER Trial:*** 20% relative risk reduction in MACE for secondary prevention

## Alirocumab

***Indications:*** Secondary prevention and familial hypercholesterolemia

***ODYSSEY Trial:*** 15% relative risk reduction in MACE for secondary prevention

**NEW: VESALIUS-CV Trial (November 2025)**

25% relative risk reduction for composite MACE in patients at high CV risk WITHOUT prior MI or stroke. Not yet in label—cite trial in prior authorizations for primary prevention.

**LDL-C Reduction:** ~60% additional reduction when added to statin therapy. Among the most potent LDL lowering agents available.

**Mechanism of Action:** Inhibit PCSK9*, which normally degrades LDL receptors. Blocking PCSK9 increases LDL receptor availability, dramatically lowering circulating LDL.

**Adverse Reactions:** injection site reactions, diarrhea, myalgia, cold/flu-like symptoms

**Contraindications:** hypersensitivity to class

**Considerations:** Injectable administration may affect compliance. Cost perceived as barrier - use aggressive, evidence-based prior auths with templates.

*proprotein convertase subtilis/kexin type 9


**Sources:**

1. Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, Kuder JF, Wang H, Liu T, Wasserman SM, Sever PS, Pedersen TR; FOURIER Steering Committee and Investigators. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. N Engl J Med. 2017 May 4;376(18):1713-1722. doi: 10.1056/NEJMoa1615664. Epub 2017 Mar 17. PMID: 28304224.
2. Schwartz GG, Steg PG, Szarek M, Bhatt DL, Bittner VA, Diaz R, Edelberg JM, Goodman SG, Hanotin C, Harrington RA, Jukema JW, Lecorps G, Mahaffey KW, Moryusef A, Pordy R, Quintero K, Roe MT, Sasiela WJ, Tamby JF, Tricoci P, White HD, Zeiher AM; ODYSSEY OUTCOMES Committees and Investigators. Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome. N Engl J Med. 2018 Nov 29;379(22):2097-2107. doi: 10.1056/NEJMoa1801174. Epub 2018 Nov 7. PMID: 30403574.
3. Bohula, Erin A, et al. Evolocumab in Patients without a Previous Myocardial Infarction or Stroke. New England Journal of Medicine. doi: 10.1056/NEJMoa2514428
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5. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 - 1207

# 3. Inclisiran: Long-Acting PCSK9 Inhibitor

Novel approach to PCSK9 inhibition using small interfering RNA (siRNA) technology

1

**Initial Dose**

First injection administered by healthcare provider

2

**3 Months**

Second injection

3

**Every 6 Months**

Maintenance dosing thereafter

### Mechanism

Prevents formation of PCSK9 protein through RNA interference, allowing more LDL-C receptors to remain on liver cells and remove circulating LDL-C.

### Efficacy

LDL-C Reduction: 52% reduction. Sustained effect due to long duration of action.

### Cardiovascular Outcomes

*Important Note:* No cardiovascular outcome reduction data available yet. Trials ongoing to assess MACE reduction.

**Contraindications:** hypersensitivity to drug class

**Adverse effects:** injection site reactions, arthralgias, URI-like symptoms

**Advantage:** Twice-yearly dosing by healthcare provider may improve adherence compared to self-administered biweekly injections.

**Source:**
1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
2. Lloyd-Jones, D, Morris, P. et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2022 Oct, 80 (14) 1366–1418. https://doi.org/10.1016/j.jacc.2022.07.006
3. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 - 1207

# 4. Bempedoic Acid: Oral Non-Statin Option

Bempedoic acid offers an oral alternative for patients who cannot tolerate statins or need additional LDL-C lowering. It works upstream of statins in the cholesterol synthesis pathway.

## Mechanism and Efficacy

*Mechanism:* Inhibits ATP citrate lyase, reducing cholesterol biosynthesis in the liver two steps upstream of statins.

Activated only in the liver, not in skeletal muscle, potentially reducing myalgia risk.

*LDL-C Reduction:* 38% reduction

## **Cardiovascular Outcomes:** CLEAR Trial

*Primary Prevention:* 30% relative risk reduction in MACE

*Secondary Prevention:* 15% relative risk reduction in MACE

*Formulations:* Available alone or in fixed-dose combination with ezetimibe for enhanced LDL-C lowering

## Advantages

Oral administration improves convenience. May be better tolerated than statins in patients with muscle symptoms.

Available in combination tablet with ezetimibe—may lower pill fatigue.

## Considerations

*Contraindications:* hypersensitivity to drug class

*Adverse reactions:* tendon rupture (rare but serious), increased uric acid levels, URI/flu-like symptoms, diarrhea, arthralgia, sinusitis, pain in extremity, and fatigue.

**Source:**
1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
2. Lloyd-Jones, D, Morris, P. et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2022 Oct, 80 (14) 1366–1418. https://doi.org/10.1016/j.jacc.2022.07.006
3. Jackson, Elizabeth J. et al. LDL cholesterol management simplified in adults—lower for longer is better: Guidance from the National Lipid Association. Journal of Clinical Lipidology, Volume 19, Issue 5, 1200 – 1207
4. Sayed, Ahmed; Brophy, James M. Effect of bempedoic acid on mortality and cardiovascular events in primary and secondary prevention: A post-hoc analysis of the CLEAR-outcomes trial. International Journal of Cardiology. https://doi.org/10.1016/j.ijcard.2024.132074

# Non-Statin Therapies: Comparative Overview

| Medication | LDL-C Reduction | Secondary Prevention | RRR MACE (2°) | Primary Prevention | RRR MACE (1°) | In Guidelines |
|---|---|---|---|---|---|---|
| Ezetimibe | 15-20% | Yes | ~12% | Yes (≥75 yrs) | 20% | Yes |
| Evolocumab | 50-60% | Yes | 20% | Yes | 25%* | Yes (Secondary) |
| Alirocumab | 50-60% | Yes | 15% | No | N/A | Yes |
| Inclisiran | 52% | No | N/A | No | N/A | Yes |
| Bempedoic Acid | 38% | Yes | 13% | Yes | 39% | Yes |

***VESALIUS-CV Trial (November 2025):** Showed 25% RRR for composite MACE in high CV risk patients without prior MI/stroke. Not yet in ACC/AHA guidelines—cite trial and label in prior authorizations.

**RRR:** Relative Risk Reduction; **MACE:** Major Adverse Cardiovascular Events; **2°:** Secondary Prevention; **1°:** Primary Prevention

# Non-Statin Therapy: Primary Prevention

This decision tree outlines the recommended non-statin therapy options based on patient risk stratification and LDL-C levels for primary prevention, as per current guidelines.

1

## High Risk

- LDL >70 or NOT reduced by at least 50%
  - Consider ***ezetimibe***
  - Next, ***PCSK9*** or ***bempedoic acid***

2

## Diabetes

- LDL >70
  - Consider ***ezetimibe*** *or* ***PCSK9***

3

## Severe Hypercholesterolemia

- LDL >100 or NOT reduced by at least 50%
  - Consider ***ezetimibe*** and/or ***PCSK9 inhibitor*** (FH indication) and/or ***bempedoic acid*** (FH indication or primary prevention 75yo+)
    - Alternative: ***Inclisiran*** (FH indication)

**Source:**
1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/ American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
2. Lloyd-Jones, D, Morris, P. et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2022 Oct, 80 (14) 1366–1418. https://doi.org/10.1016/j.jacc.2022.07.006

# Non-Statin Therapy: Secondary Prevention

This decision tree outlines the recommended non-statin therapy options based on patient risk stratification and LDL-C levels for secondary prevention, as per current guidelines.

1

## Very High Risk

- LDL >55 OR NOT reduced at least 50%
  - Consider ***ezetimibe*** and/or ***PCSK9 inhibitor***
    - Alternative: ***Inclisiran***
    - Goals still not met? May consider ***bempedoic acid****

2

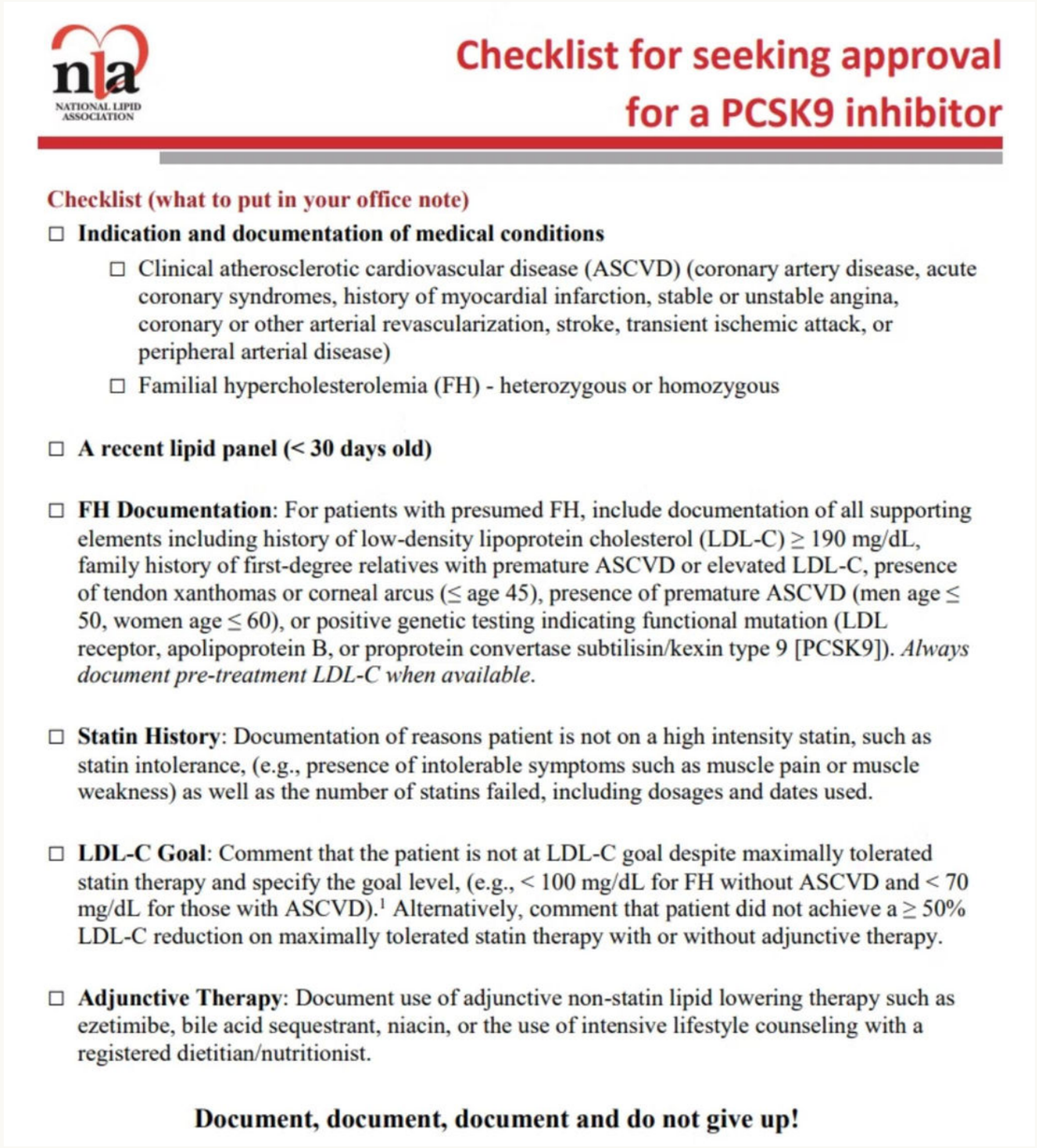
## Not at Very High Risk

- LDL >70 OR NOT reduced at least 50%
  - Consider ***ezetimibe*** and/or ***PCSK9 inhibitor*** and/or ***bempedoic acid***
    - Alternative: ***Inclisiran***

*AHA/ACC: “There are no CVOTs combining standard statin therapy and bempedoic acid, which is why bempedoic acid is given a Class 2a recommendation for patients with ASCVD.”

- ***Clinical pearls:***
  - Approval of bempedoic acid may be facilitated by citing *CLEAR trial* and medication’s primary (75+)/secondary indications
  - Patient struggling with taking pills daily or injections biweekly/monthly?
    - Consider inclisiran every 6 months

**Source:**
1. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guideline. https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423#sec-8-2
2. Lloyd-Jones, D, Morris, P. et al. 2022 ACC Expert Consensus Decision Pathway on the Role of Nonstatin Therapies for LDL-Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk: A Report of the American College of Cardiology Solution Set Oversight Committee. JACC. 2022 Oct, 80 (14) 1366–1418. https://doi.org/10.1016/j.jacc.2022.07.006



## Checklist for seeking approval for a PCSK9 inhibitor

**Checklist (what to put in your office note)**

- ☐ **Indication and documentation of medical conditions**
  - ☐ Clinical atherosclerotic cardiovascular disease (ASCVD) (coronary artery disease, acute coronary syndromes, history of myocardial infarction, stable or unstable angina, coronary or other arterial revascularization, stroke, transient ischemic attack, or peripheral arterial disease)
  - ☐ Familial hypercholesterolemia (FH) - heterozygous or homozygous
- ☐ **A recent lipid panel (< 30 days old)**
- ☐ **FH Documentation**: For patients with presumed FH, include documentation of all supporting elements including history of low-density lipoprotein cholesterol (LDL-C) ≥ 190 mg/dL, family history of first-degree relatives with premature ASCVD or elevated LDL-C, presence of tendon xanthomas or corneal arcus (≤ age 45), presence of premature ASCVD (men age ≤ 50, women age ≤ 60), or positive genetic testing indicating functional mutation (LDL receptor, apolipoprotein B, or proprotein convertase subtilisin/kexin type 9 [PCSK9]). *Always document pre-treatment LDL-C when available.*
- ☐ **Statin History**: Documentation of reasons patient is not on a high intensity statin, such as statin intolerance, (e.g., presence of intolerable symptoms such as muscle pain or muscle weakness) as well as the number of statins failed, including dosages and dates used.
- ☐ **LDL-C Goal**: Comment that the patient is not at LDL-C goal despite maximally tolerated statin therapy and specify the goal level, (e.g., < 100 mg/dL for FH without ASCVD and < 70 mg/dL for those with ASCVD).[1] Alternatively, comment that patient did not achieve a ≥ 50% LDL-C reduction on maximally tolerated statin therapy with or without adjunctive therapy.
- ☐ **Adjunctive Therapy**: Document use of adjunctive non-statin lipid lowering therapy such as ezetimibe, bile acid sequestrant, niacin, or the use of intensive lifestyle counseling with a registered dietitian/nutritionist.

**Document, document, document and do not give up!**

# Getting PCSK9 Inhibitors Approved: Documentation Checklist

Insurance approval for PCSK9 inhibitors requires thorough documentation.

The National Lipid Association provides a comprehensive checklist to improve approval success rates.

**Source:** National Lipid Association. Available at: https://www.lipid.org/sites/default/files/files/NLA%20Checklist%20Handout%20ACC%20Sympo.pdf

# *Case Study 1: Primary Prevention*

A 58-year-old male with hypertension, prediabetes, and family history of premature CAD. Non-smoker, BMI 29. Lipid panel: LDL-C 145 mg/dL, HDL-C 38 mg/dL, triglycerides 210 mg/dL.

## Risk Stratification

PREVENT calculator: 8% 10-year ASCVD risk (intermediate).

Risk-enhancing factors: family history, low HDL-C, elevated triglycerides, metabolic syndrome.

CAC score 80 (favors statins).

## Initial Treatment

Lifestyle: Mediterranean diet, 150 min/week moderate exercise, weight loss goal 10%.

Pharmacologic: Atorvastatin 20 mg daily (moderate-intensity statin).

## Follow-Up at 8 Weeks

LDL-C 95 mg/dL (34% reduction). Good adherence to lifestyle changes.

Continue current therapy, reinforce lifestyle modifications.

## Treatment Escalation

If LDL-C remained >100 mg/dL: Increase to atorvastatin 40 mg (high-intensity).

If still elevated:

Increase to atorvastatin 80mg daily OR
Add ezetimibe 10 mg daily.

# *Case Study 2: Secondary Prevention*

A 62-year-old female, 6 months post-MI with stent placement. Type 2 diabetes for 8 years, hypertension. Current medications include aspirin, metoprolol, lisinopril, metformin. Lipid panel: LDL-C 110 mg/dL, HDL-C 45 mg/dL, triglycerides 165 mg/dL.

## Risk Stratification

Very high risk: Recent MI with stent, diabetes, hypertension. Target LDL-C <55 mg/dL for very high-risk secondary prevention.

## Initial Treatment

High-intensity statin: Atorvastatin 80 mg daily.
Lifestyle: Cardiac rehabilitation, Mediterranean diet, diabetes management optimization. Smoking cessation counseling (if applicable).

## Follow-Up at 6 Weeks

LDL-C 72mg/dL (35% reduction). Above target of <55 mg/dL and 50% reduction. Taking med consistently. Needs 24% more reduction.

***2 treatment options:***

- *Add ezetimibe 10 mg daily* (15-20% reduction) but will likely need a 3rd agent
- *Add PCSK9* (50-60% reduction)

  Submit prior authorization emphasizing very high-risk status, recent MI, diabetes, and inadequate response to maximally tolerated statin. Include guidelines and trial references.

## Final Regimen

Atorvastatin 80 mg and evolocumab 140 mg subcutaneous every 2 weeks.
Achieved LDL-C 28 mg/dL.
Continue intensive lifestyle modifications and optimize other risk factors.

# Key Takeaways: Comprehensive Lipid Management

## Risk Stratification is Foundation

Use PREVENT calculator and assess for risk-enhancing factors.

Consider CAC scoring in intermediate-risk patients.

Individualize treatment based on comprehensive risk assessment.

## Lifestyle First, Always

Physical activity prescription using FITT-VP framework.

Evidence-based nutrition counseling with TAF method.

Lifestyle modifications reduce risk and enhance medication effectiveness.

## Statins Remain Cornerstone

Strong evidence for ASCVD risk reduction in primary and secondary prevention.

Choose intensity based on risk level and LDL-C reduction needed.

Monitor adherence and response.

## Non-Statins When Needed

Add ezetimibe first if LDL-C suboptimal on maximally tolerated statin.

If DM: consider PCSK9 inhibitors
If severe hyperlipidemia: consider PCSK9 or bempedoic acid

Secondary prevention: ezetimibe or PCSK9 (alternative inclisiran)
Not at very high risk? Consider bempedoic acid

Focus on therapies with proven cardiovascular outcome data.




# Implementing Evidence-Based Care

## Clinical Practice Points

- Screen appropriately based on age and risk factors
- Calculate 10-year and 30-year ASCVD risk using PREVENT
- Engage in shared decision-making with patients
- Consider CAC where appropriate
- Prescribe specific, actionable lifestyle interventions
- Choose statin intensity based on risk and goals
- Follow up to assess consistency and response
- Escalate therapy systematically when needed
- Address cost barriers proactively with evidence-based and guideline-directed prior authorizations

## Overcoming Barriers

**Patient Education:** Explain risk reduction and benefits in understandable terms. Address concerns about side effects with fair and balanced evidence.

**Medication Access:** Use generic medications when appropriate. Prepare thorough prior authorizations templates for branded therapies citing evidence, guidelines, and patient-specific factors.

**Adherence:** Simplify regimens, address side effects promptly, and provide ongoing support and education.

# Call to Action: Advancing Lipid Management

Comprehensive lipid management requires integration of lifestyle interventions, risk stratification, and evidence-based pharmacotherapy. The expanding arsenal of non-statin therapies provides powerful tools to achieve aggressive LDL-C goals in high-risk patients.

## Foundation

Lifestyle modifications remain essential for all patients regardless of medication use.

Move beyond “eat better and move more”

## Stratification

Accurate risk assessment guides appropriate therapy intensity and targets.

Consider each medication’s % reduction in LDL

## Optimization

Systematic escalation of therapy ensures patients achieve evidence-based goals.

## Outcomes

Focus on therapies proven to reduce cardiovascular events, not just lipid numbers.



By implementing these evidence-based strategies in primary care practice, we can significantly reduce the burden of atherosclerotic cardiovascular disease in our patient populations.



# Questions?

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