Lipid Guidelines Comparison

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What do ACC/AHA guidelines say?

• Identify 4 major statin benefit groups for whom ASCVD risk reduction clearly outweighs the risk of adverse events based on a strong body of evidence
Guidelines identify four statin benefit groups

**Group 1**

Clinical ASCVD
- CHD, stroke, and peripheral arterial disease, all of presumed atherosclerotic origin

**Group 2**

LDL-C ≥190 mg/dL (~5 mmol/L)

**Group 3**

Diabetes mellitus
- + age of 40–75 years
- + LDL-C 70–189 mg/dL (~1.8–5 mmol/L)

**Group 4**

ASCVD risk ≥7.5%
- No diabetes
- + age of 40–75 years
- + LDL-C 70–189 mg/dL (~1.8–5 mmol/L)

ASCVD, atherosclerotic cardiovascular disease
CHD, coronary heart disease
LDL-C, low density lipoprotein cholesterol

ASCVD risk calculator

10-year risk (%) of ASCVD (non-fatal MI, CHD death, or fatal/non-fatal stroke) is calculated from simple parameters:

<table>
<thead>
<tr>
<th>Risk factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male or female)</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Race (African-American or White/other)</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
</tr>
<tr>
<td>Treatment for high BP (yes or no)</td>
</tr>
<tr>
<td>Diabetes (yes or no)</td>
</tr>
<tr>
<td>Smoker (yes or no)</td>
</tr>
</tbody>
</table>


BP, blood pressure
HDL-C, high density lipoprotein-cholesterol
SBP, Systolic blood pressure
Treatment decision flow for four statin benefit groups

ASCVD Statin Benefit Groups
In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-year ASCVD risk every 4–6 years in individuals aged 40–75 years without clinical ASCVD or diabetes and with LDL-C 70–189 mg/dL (~1.8–5 mmol/L)

Adults age >21 years and a candidate for statin therapy

Clinical ASCVD
Yes

Age ≤75 years
High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

No

Moderate-intensity statin
Age >75 years or if not candidate for high-intensity statin

LDL-C ≥190 mg/dL
Yes

High-intensity statin
(Moderate-intensity statin if not candidate for high-intensity statin)

No

Diabetes*
Yes

Moderate-intensity statin

No

Estimated 10-year ASCVD risk ≥7.5%

High-intensity statin

10-year ASCVD risk*
Yes

Moderate-to-high intensity statin

No

High-intensity statin
Expected to reduce LDL-C by ≥50%

Moderate-intensity statin
Expected to reduce LDL-C by 30% to <50%

ASCVD prevention benefit of statin therapy may be less clear in other groups
Consider additional factors influencing ASCVD risk and potential ASCVD risk benefits and adverse effects, drug–drug interactions, and patient preferences for statin treatment

* Aged 40–75 years

Diabetes

LDL-C ≥190 mg/dL

High-intensity statin

Moderate-intensity statin

Estimated 10-year ASCVD risk ≥7.5%
Guidelines specify statin doses

<table>
<thead>
<tr>
<th></th>
<th>High-intensity ↓ LDL-C by ≥50%</th>
<th>Moderate-intensity ↓ LDL-C by 30–50%</th>
<th>Low-intensity ↓ LDL-C by &lt;30%*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atorvastatin</strong></td>
<td>(40)–80 mg</td>
<td>10–20 mg</td>
<td>–</td>
</tr>
<tr>
<td><strong>Rosuvastatin</strong></td>
<td>20–40 mg</td>
<td>5–10 mg</td>
<td>–</td>
</tr>
<tr>
<td><strong>Simvastatin</strong></td>
<td>–</td>
<td>20–40 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td><strong>Pravastatin</strong></td>
<td>–</td>
<td>40–80 mg</td>
<td>10–20 mg</td>
</tr>
<tr>
<td><strong>Lovastatin</strong></td>
<td>–</td>
<td>40 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td><strong>Fluvastatin XL</strong></td>
<td>–</td>
<td>80 mg</td>
<td>–</td>
</tr>
<tr>
<td><strong>Fluvastatin</strong></td>
<td>–</td>
<td>40 mg bid</td>
<td>20–40 mg</td>
</tr>
<tr>
<td><strong>Pitavastatin</strong></td>
<td>–</td>
<td>2–4 mg</td>
<td>1 mg</td>
</tr>
</tbody>
</table>

**Bold**: Statins and doses evaluated in RCTs

**Italics**: Statins and doses approved by US FDA but not tested in RCTs reviewed

*Should be used in patients unable to tolerate moderate-to high-intensity therapy

Asian ancestry may modify the statin dose prescribed


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Is there evidence to treat to specific LDL and non-HDL targets in primary prevention?

• There was NO DATA to treat to specific LDL targets
• There was NO DATA to treat to specific non-HDL targets
  – RCTs used **FIXED DOSE** statin therapy
For primary and secondary prevention, what is the impact on lipids levels, effectiveness, and safety of specific cholesterol modifying drugs?

- NO DATA to support routine use of non-statin drugs combined with statin therapy to further reduce ASCVD events
  - Review included statins, fibrates, niacin, bile acid sequestrants, ezetimibe, O-3 fatty acids
  - AIM-HIGH: adding NIACIN to achieve non-HDL targets did NOT reduce ASCVD risk

- NO DATA for ASCVD outcomes in statin intolerant patients
AHA/ACC Guidelines

ATP III
• RISK FACTOR COUNTING
• TREAT TO LDL GOAL
• ADDRESS NON-HDL TARGET

AHA/ACC
• THERE IS NO TARGET
• THE INTENSITY OF STATIN THERAPY IS THE FOCUS OF TREATMENT
Atherogenic Lipoproteins

- TG < 200 mg/dL
- TG 200-500 mg/dL
Meta-Analysis: Changes in Non-HDL-C Predict CHD Risk Reduction
What is the Advantage of Non-HDL-C over LDL-C in Assessing ASCVD Risk?

• Non-HDL-C is more predictive of ASCVD risk than LDL-C in observational studies. The same is true for on-treatment levels in clinical trials of statin therapy.

• When non-HDL-C and LDL-C are discordant, risk follows non-HDL-C.

• Non-HDL-C testing is universally available, requires no additional cost, and accurate values may be obtained in the non-fasting state.

IMPROVE-IT: 7-year ACS RCT (Maximal Simvastatin ± Ezetimibe)

Cardiovascular death, MI, documented unstable angina requiring rehospitalization, coronary revascularization (≥30 days), or stroke

HR 0.936 CI (0.887, 0.988)  
P=0.016

Simva — 34.7%
2742 events

EZ/Simva — 32.7%
2572 events

NNT = 50

LDL-C = 70 mg/dL

LDL-C = 53 mg/dL
IMPROVE-IT vs. CTT: Ezetimibe vs. Statin Benefit

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

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Criteria</th>
<th>Treatment Goal</th>
<th>Consider Drug Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Non-HDL-C mg/dL</td>
<td>LDL-C mg/dL</td>
</tr>
<tr>
<td>Low</td>
<td>0-1 major ASCVD risk factors&lt;br&gt;Consider other risk indicators, if known</td>
<td>&lt;130</td>
<td>≥190</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;100</td>
<td>≥160</td>
</tr>
<tr>
<td>Moderate</td>
<td>2 major ASCVD risk factors&lt;br&gt;Consider quantitative risk scoring&lt;br&gt;Consider other risk indicators</td>
<td>&lt;130</td>
<td>≥160</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;100</td>
<td>≥130</td>
</tr>
<tr>
<td>High</td>
<td>≥3 major ASCVD risk factors&lt;br&gt;Diabetes mellitus* (Type 1 or 2)&lt;br&gt;0-1 other major ASCVD risk factors, and&lt;br&gt;No evidence of end organ damage&lt;br&gt;Chronic kidney disease stage 3B or 4&lt;br&gt;LDL-C ≥190 mg/dL (severe hypercholesterolemia)&lt;br&gt;Quantitative risk score reaching the high-risk threshold</td>
<td>&lt;130</td>
<td>≥130</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;100</td>
<td>≥100</td>
</tr>
<tr>
<td>Very High</td>
<td>ASCVD*&lt;br&gt;Diabetes mellitus* (Type 1 or 2)&lt;br&gt;≥2 other major ASCVD risk factors or&lt;br&gt;Evidence of end organ damage</td>
<td>&lt;100</td>
<td>≥100</td>
</tr>
</tbody>
</table>

*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.
Risk Calculators

**ACC/AHA**
- Use Pooled Cohort Risk calculator in non-Hispanic Whites and non-Hispanic African Americans age 40-79 without ASCVD and not on statin therapy; may be considered in other populations
- Assessment of lifetime risk may be considered in those aged 20-59 with no ASCVD and not at high short-term risk

**NLA**
- Count number of major risk factors and use other risk indicators for clinical decision-making
- Consider the use of either the 10-year FRS, ACC/AHA Pooled Cohort Risk calculator, or 30-year risk in those with 2 major ASCVD risk factors; re-classify to higher risk those with ≥10% 10-year FRS, ≥15% ACC/AHA risk, or ≥45% long-term risk
NLA Perspective on Statin Therapy

- Statin therapy is the most potent and evidence-based approach to lowering atherogenic lipoproteins (non-HDL-C and LDL-C) and reduces ASCVD events
- Statin intensity trials showed clear benefit for high-intensity versus moderate-intensity statins
- Broad-based evidence supports “lower is better” concept, and provides an opportunity for clinicians to address residual risk above that addressed by appropriately-dosed statin therapy
NLA Perspective on Non-Statin Lipid Drug Therapy

- If non-HDL-C and LDL-C goals are not achieved with statin therapy, the addition of evidence-based non-statin therapy should be considered to lower atherogenic cholesterol levels and to achieve goals
  - Ezetimibe is a safe, evidence-based non-statin therapy that may be considered in post MI patients and selected other patients with elevated non-HDL-C and/or LDL-C
  - Resins or niacin may be considered in selected patients
  - Meta-analyses of fibrate therapy in subgroups with atherogenic dyslipidemia suggest ASCVD risk reduction
Central Focus of Guidelines: Summary

- ACC/AHA: define statin benefit groups; risk/benefit discussion; use moderate- or high-intensity statin therapy with lifestyle change as background therapy; generally avoid non-statin drug therapy; no lipid goals
- NLA: identify ASCVD risk level; risk/benefit discussion; emphasize healthy lifestyle and use moderate- or high-intensity statin therapy, and under appropriate circumstances, adjunctive non-statin therapy, to lower atherogenic cholesterol; maintain lipid goals (non-HDL-C is favored lipoprotein lipid target)
The 10-year risk of a coronary event (high, intermediate, or low) should be determined by detailed assessment using one or more of the following tools:

- Framingham Risk Assessment Tool
- MESA 10-year ASCVD Risk with Coronary Artery Calcification Calculator
- Reynolds Risk Score, which includes hsCRP and family history of premature ASCVD
- UKPDS risk engine to calculate ASCVD risk in individuals with T2DM

When the HDL-C concentration is greater than 60 mg/dL, one risk factor should be subtracted from an individual’s overall risk profile.

A classification of elevated TG should be incorporated into risk assessments to aid in treatment decisions.
Multi-Ethnic Study of Atherosclerosis

- **MESA investigated the correlates of subclinical CVD**¹
  - The study enrolled 6,814 patients between July 2000 and September 2002; at baseline, all patients were free of clinical CVD²

- **10-year outcomes showed that CAC is an independent risk factor for CVD**³
  - CAC predicts CVD risk in patients with or without traditional risk factors and in patients with family history of premature CHD⁴⁻⁵
  - CAC was the strongest predictor of CVD in low-risk patients⁶

- **The MESA risk score uses traditional risk factors and CAC to predict 10-year CHD risk**⁷
  - The incorporation of CAC into this risk score has improved risk prediction⁷

Abbreviations: CAC, CHD, coronary heart disease; CVD, cardiovascular disease; MESA, Multi-Ethnic Study of Atherosclerosis.

ASCVD Risk Categories

• **Low risk:**
  – No risk factors

• **Moderate risk:**
  – 2 or fewer risk factors and a calculated 10-year risk of less than 10%

• **High risk:**
  – An ASCVD equivalent including diabetes or stage 3 or 4 CKD with no other risk factors, or individuals with 2 or more risk factors and a 10-year risk of 10%-20%

• **Very high risk:**
  – Established or recent hospitalization for ACS; coronary, carotid or peripheral vascular disease; diabetes or stage 3 or 4 CKD with 1 or more risk factors; a calculated 10-year risk greater than 20%; or HeFH

• **Extreme risk:**
  – Progressive ASCVD, including unstable angina that persists after achieving an LDL-C less than 70 mg/dL, or established clinical ASCVD with diabetes, stage 3 or 4 CKD, and/or HeFH, or in those with a history of premature ASCVD (<55 years of age for males or <65 years of age for females)
  – This category was added in this CPG based on clinical trial evidence and supported by meta-analyses that further lowering of LDL-C produces better outcomes in individuals with ACS. IMPROVE-IT demonstrated lower rates of cardiovascular events in those with ACS when LDL-C levels were lowered to 53 mg/dL combining ezetimibe with statins.
For patients with diabetes, what risk categories does AACE recommend?

Based on epidemiologic studies, individuals with T2DM should be considered as high, very high, or extreme risk for ACSVD.

Based on epidemiologic and prospective cohort studies, individuals with T1DM and duration more than 15 years or with ≥2 major CV risk factors (e.g., albuminuria, stage 3 or 4 CKD, initiation of intensive control >5 years after diagnosis), poorly controlled hemoglobin A1C, or insulin resistance with metabolic syndrome should be considered to have risk-equivalence to individuals with T2DM.

- T1DM is associated with increased ASCVD risk
- Individuals with T1DM should be screened annually for dyslipidemia
- Individuals with T1DM should be treated aggressively for dyslipidemia according to risk level recommendations

Abbreviations: A1C, glycated hemoglobin; AACE, American Association of Clinical Endocrinologists; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cerebrovascular; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

# Lipid Goals for Individuals at Risk for ASCVD

<table>
<thead>
<tr>
<th>Lipid parameter</th>
<th>Goal (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td>&lt;200</td>
</tr>
<tr>
<td>LDL-C</td>
<td>&lt;130 (low risk)</td>
</tr>
<tr>
<td></td>
<td>&lt;100 (moderate risk)</td>
</tr>
<tr>
<td></td>
<td>&lt;100 (high risk)</td>
</tr>
<tr>
<td></td>
<td>&lt;70 (very high risk)</td>
</tr>
<tr>
<td></td>
<td>&lt;55 (extreme risk)</td>
</tr>
<tr>
<td>Non-HDL-C</td>
<td>30 above LDL-C goal; 25 above LDL-C goal (extreme risk individuals)</td>
</tr>
<tr>
<td>TG</td>
<td>&lt;150</td>
</tr>
<tr>
<td>Apo B</td>
<td>&lt;90 (individuals at high risk of ASCVD, including those with diabetes)</td>
</tr>
<tr>
<td></td>
<td>&lt;80 (individuals at very high risk with established ASCVD or diabetes plus</td>
</tr>
<tr>
<td></td>
<td>≥1 additional risk factor)</td>
</tr>
<tr>
<td></td>
<td>&lt;70 (individuals at extreme risk)</td>
</tr>
</tbody>
</table>

Abbreviations: apo, apolipoprotein; ASCVD, atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.
What treatments are available for dyslipidemia?

Treatment categories for dyslipidemia:

– **Lifestyle changes**
  - Physical activity
  - Medical nutrition therapy
  - Smoking cessation

– **Pharmacologic therapy**
  - Statins
  - Fibrates
  - Omega-3 fish oil
  - Niacin
  - Bile acid sequestrants
  - Cholesterol absorption inhibitors
  - PCSK9 inhibitors
  - MTP inhibitor
  - Antisense apo B oligonucleotide
  - Combination therapies

A comprehensive strategy to control lipid levels and address associated metabolic abnormalities and modifiable risk factors is recommended primarily using lifestyle changes and patient education with pharmacotherapy as needed to achieve evidence-based targets.

Recommendations associated with this question:


Abbreviations: apo, apolipoprotein; MTP, microsomal transfer protein; PCSK9, proprotein convertase subtilisin/kexin type 9.
## Recommendations for Statin Treatment in People with Diabetes

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk Factors</th>
<th>Statin Intensity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>ASCVD risk factor(s)</td>
<td>Moderate or high</td>
</tr>
<tr>
<td></td>
<td>ASCVD</td>
<td>High</td>
</tr>
<tr>
<td>40–75 years</td>
<td>None</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>ASCVD risk factors</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>ACS &amp; LDL ≥50 or in patients with history of ASCVD who can’t tolerate high dose statin</td>
<td>Moderate + ezetimibe</td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>None</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>ASCVD</td>
<td>Moderate or high</td>
</tr>
<tr>
<td></td>
<td>ACS &amp; LDL ≥50 or in patients with history of ASCVD who can’t tolerate high dose statin</td>
<td>Moderate + ezetimibe</td>
</tr>
</tbody>
</table>

ACCORD-LIPID: Primary Outcomes of the Prespecified Subgroups: High TG (≥204 mg/dL) and Low HDL-C (≤34 mg/dL) vs. All Others in Full Cohort

The benefit associated with fenofibrate treatment was confined to the high TG/low HDL-C subgroup, comprising <18% of ACCORD-LIPID trial population.
• In clinical practice, providers may need to adjust intensity of statin therapy based on individual patient response to medication (e.g., side effects, tolerability, LDL cholesterol levels).

• Ezetimibe + moderate intensity statin therapy provides add’l CV benefit over moderate intensity statin therapy alone; consider for patients with a recent acute coronary syndrome w/ LDL ≥ 50mg/dL or in patients with a history of ASCVD who can’t tolerate high-intensity statin therapy.
ADA Lipid Management Guidelines

- Combination therapy (statin/fibrate) doesn’t improve ASCVD outcomes and is generally not recommended. Consider therapy with statin and fenofibrate for men with both trigs \( \geq 204 \text{ mg/dL (2.3 mmol/L)} \) and HDL \( \leq 34 \text{ mg/dL (0.9 mmol/L)} \).

- Combination therapy (statin/niacin) hasn’t demonstrated additional CV benefit over statins alone, may raise risk of stroke & is not generally recommended.

- Statin therapy is contraindicated in pregnancy.
### High- and Moderate-Intensity Statin Therapy

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lowers LDL by ≥50%</strong></td>
<td><strong>Lowers LDL by 30 - &lt;50%</strong></td>
</tr>
<tr>
<td>Atorvastatin 40-80 mg</td>
<td>Atorvastatin 10-20 mg</td>
</tr>
<tr>
<td>Rosuvastatin 20-40 mg</td>
<td>Rosuvastatin 5-10 mg</td>
</tr>
<tr>
<td>Simvastatin 20-40 mg</td>
<td>Simvastatin 20-40 mg</td>
</tr>
<tr>
<td>Pravastatin 40-80 mg</td>
<td>Pravastatin 40-80 mg</td>
</tr>
<tr>
<td>Lovastatin 40 mg</td>
<td>Lovastatin 40 mg</td>
</tr>
<tr>
<td>Fluvastatin XL 80 mg</td>
<td>Fluvastatin XL 80 mg</td>
</tr>
<tr>
<td>Pitavastatin 2-4 mg</td>
<td>Pitavastatin 2-4 mg</td>
</tr>
</tbody>
</table>

FOURIER Trial

27,564 high-risk, stable patients with established CV disease (prior MI, prior stroke, or symptomatic PAD)

Screening, Lipid Stabilization, and Placebo Run-in
High or moderate intensity statin therapy (± ezetimibe)

LDL-C ≥70 mg/dL or non-HDL-C ≥100 mg/dL

RANDOMIZED DOUBLE BLIND

Evolocumab SC 140 mg Q2W or 420 mg QM

Follow-up Q 12 weeks

Placebo SC Q2W or QM
FOURIER (Evolocumab): Primary Endpoint

Primary endpoint: CV death, MI, stroke, unstable angina, coronary revascularization

15% Reduction
NNT = 74
MACE: CHD death, non-fatal MI, ischemic stroke, or unstable angina requiring hospitalization

Odyssey (Alirocumab): MACE

ARR* 1.6%

HR 0.85 (95% CI 0.78, 0.93); P=0.0003

Number at Risk
Placebo 9462 8805 8201 3471 629
Alirocumab 9462 8846 8345 3574 653
Odyssey (Alirocumab): All cause death

ARR† 0.6%
The More, the Better (Oxford)
(ACC/AHA)

The Lower, the Better

Boekholdt et al.
JACC 2014;
64:485-94.

Delta LDL-C (mg/dL)

% Change In Risk

Cholesterol Rx Trialists Lancet 2005

Fractional Risk
Secondary Prevention ("the more the better")

- Based on Oxford paradigm
- High-intensity statins
  - Atorvastatin 80 mg
  - Rosuvastatin 20 mg
- LDL-C goal: 50% reduction
  (80 mg/dL reduction)
Secondary Prevention: ("the Lower, the Better")

LDL-C Goal: <70 mg/dL

*Boekholdt et al. JACC 2014; 64:485-94
Future of Secondary Prevention

LDL-C (mg/dL)

-50%

Atorvastatin 80 mg
Rosuvastatin 20-40 mg
+ Ezetimibe
+ PCSK9 inhibitor

-20%

-50%

35

70

140
Primary Prevention: Cholesterol-Lowering Therapy

• The lower the better
  – Shown by 5-year clinical trials
    - 1% ↓LDL-C → 1%↓ASCVD

• The earlier the better
  – Shown by population and genetic epidemiology
    - 1% ↓LDL-C → >3%↓ASCVD
Consider Cholesterol-Lowering Drugs to Reduce Lifetime Risk*

Higher Risk Conditions
- Diabetes mellitus (29.1M) (CARDS)
- Metabolic syndrome (77-86M) (JUPITER/AFCAPS/MEGA)
- Chronic kidney disease (20M) (SHARP)

Major Risk Factors
- Hypertension (70M) (ASCOT)
- Hypercholesterolemia (31M) (WOSCOPS)
- Cigarette smoking (42) (Multiple RCTs)

*Lifetime risk for ASCVD 35-50%
Who to Treat with Cholesterol-lowering Drugs

• 10 year risk for ASCVD ≥ 7.5% (ACC/AHA)
• Higher Risk Conditions
• Subclinical atherosclerosis
Considerations for the future

- Secondary prevention
  - Treat cholesterol aggressively
  - The lower, the better
  - Consider combined drug therapy

- Primary prevention
  - The earlier the better
  - Treat all risk factors
  - Lifestyle therapy for all
  - Consider drugs depending on risk factors