



ACC/AHA & ESC Cholesterol Management Guidelines: Similarities and Differences

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How are the Guidelines Similar?

- Both emphasize lifestyle as the foundation in risk reduction
- Both highlight the role of LDL-C in atherosclerotic cardiovascular risk despite how it is measured (LDL-C, non-HDL-C, apo B)
- Both match the intensity of treatment to the risk of atherosclerotic cardiovascular events
- Both identify statins as the mainstay of treatment in risk reduction

How are they Different?

- Development of the guidelines
- At risk populations
- Risk score used
- Targets for therapy

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Guideline Background: ACC/AHA

1. What is the evidence for LDL-C and non-HDL-C Goals in secondary prevention of ASCVD?
2. What is the evidence for LDL-C and non-HDL-C goals in primary prevention of ASCVD?
3. What are the effectiveness and safety of lipid-modifying drugs in the primary and secondary prevention of ASCVD?

Guideline Background: ESC

- Use all available evidence in comprehensive literature review
- Goal to assist health professionals to select best management strategy for an individual patient with a given condition

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4 Statin Benefit Groups

- Clinical ASCVD
- LDL-C ≥ 190 mg/dL (Age ≥ 21 years)
- Diabetes: Age 40-75 years, LDL-C 70-189 mg/dL
- No Diabetes: Age 40-75 years, LDL-C 70-189 mg/dL and estimated 10-year ASCVD risk $\geq 7.5\%$

ESC 2016

- Persons with documented CVD
 - Includes evidence of subclinical disease
- Type 1 or Type 2 diabetes
- Very high levels of individual risk factors
- Chronic kidney disease
- For all others risk estimation recommended

Eur Heart J. 2016;37(39):2999-3058.

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10-year ASCVD Pooled Cohort Risk Calculator

- Risk of first nonfatal myocardial infarction, coronary heart disease death, nonfatal or fatal stroke
- Pooled data from 4 cohorts

ASCVD Risk Calculator

Pooled Cohort Equations

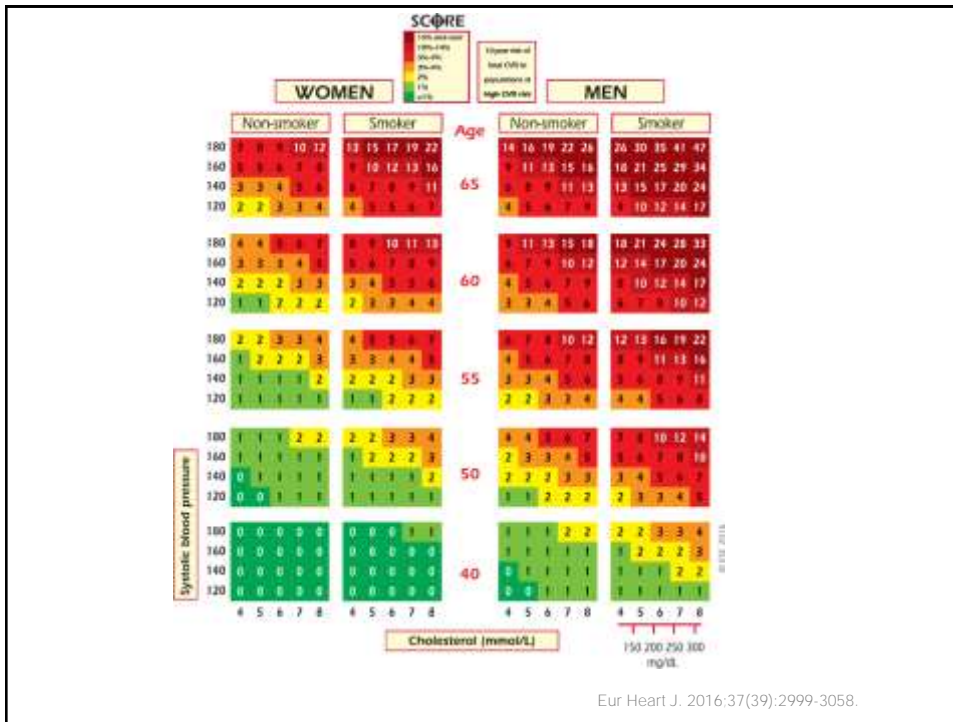
Risk Factor	Units	 Value	Acceptable range of values	Optimal values
Sex	M or F	F	M or F	
Age	years	55	20-79	
Race	AA or WH	AA	AA or WH	
Total Cholesterol	mg/dL	210	130-320	170
HDL-Cholesterol	mg/dL	56	20-100	50
Systolic Blood Pressure	mm Hg	145	90-200	110
Treatment for High Blood Pressure	Y or N	Y	Y or N	N
Diabetes	Y or N	N	Y or N	N
Smoker	Y or N	N	Y or N	N

The screenshot displays the ASCVD Risk Estimator interface. At the top, there are tabs for 'Estimate', 'Clinical', 'Facts', and 'Reset'. The main display area is divided into two columns. The left column, titled '10-Year ASCVD Risk', shows a calculated risk of 7.7% (with a note 'Calculated for 10 years') and a 1.8% risk 'With additional risk factors'. The right column, titled 'Lifetime ASCVD Risk', shows a calculated risk of 39% (with a note 'Calculated for 30 years') and an 8% risk 'With additional risk factors'. Below the risk calculations, there is a 'Recommendation Based On Calculation' button. The input fields are as follows:

- Gender: Male Female
- Race: White African American Other
- Systolic Blood Pressure: [input field]
- Age: 50
- Total Cholesterol (mg/dL): 210
- HDL - Cholesterol (mg/dL): 50

SCORE Risk Score

- Can be recalibrated for CVD mortality and risk factor prevalences in populations
- Estimates the 10-year cumulative risk of a first fatal atherosclerotic event
- Can modify to estimate fatal and nonfatal atherosclerotic events



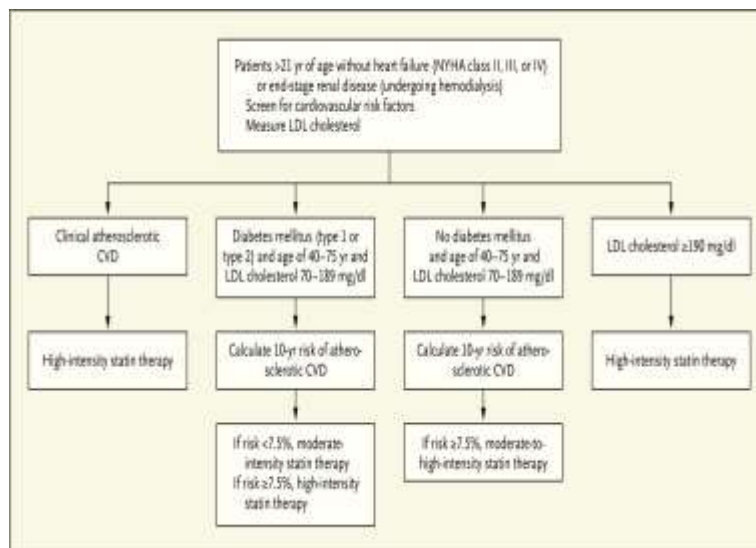
Risk Categories ESC

Very high-risk	<p>Subjects with any of the following:</p> <ul style="list-style-type: none"> • Documented cardiovascular disease (CVD), clinical or unequivocal on imaging. Documented CVD includes previous myocardial infarction (MI), acute coronary syndrome (ACS), coronary revascularization (percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG)) and other arterial revascularization procedures, stroke and transient ischaemic attack (TIA) and peripheral arterial disease (PAD). Unequivocally documented CVD on imaging is what has been shown to be strongly predisposed to clinical events, such as significant plaque on coronary angiography or carotid ultrasound. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking, hypertension or dyslipidaemia. • Severe CKD (GFR <30 mL/min/1.73 m²). • A calculated SCORE >10% for 10-year risk of fatal CVD.
High-risk	<p>Subjects with:</p> <ul style="list-style-type: none"> • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolemia) or BP >180/110 mmHg. • Most other people with DM (some young people with type 1 diabetes may be at low or moderate risk). • Moderate CKD (GFR 30-59 mL/min/1.73 m²). • A calculated SCORE >5% and <10% for 10-year risk of fatal CVD.
Moderate-risk	SCORE >1% and <5% for 10-year risk of fatal CVD.
Low-risk	SCORE <1% for 10-year risk of fatal CVD.

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2013 ACC/AHA Guideline for Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults



Kearney JF Jr et al. N Engl J Med 2013. DOI: 10.1056/NEJmms1314569

ACC/AHA 2013 Guidelines

- Anticipated therapeutic response:
 - High intensity \geq 50% reduction from baseline
 - Moderate intensity statin 30-50% reduction
- If do not achieve anticipated response
 - Evaluate for statin intolerance
 - Reinforce adherence
 - Consider addition of non-statin therapy

Treatment targets: ESC

Lipids LDL-C is the primary target^f	Very high-risk: LDL-C <1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline ^b is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL).
	High-risk: LDL-C <2.6 mmol/L (100 mg/dL) or a reduction of at least 50% if the baseline ^b is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL).
	Low to moderate risk: LDL-C <3.0 mmol/L (115 mg/dL).
	Non-HDL-C secondary targets are <2.6, 3.4 and 3.8 mmol/L (100, 130 and 145 mg/dL) for very high-, high- and moderate-risk subjects, respectively.
	HDL-C: no target, but >1.0 mmol/L (40 mg/dL) in men and >1.2 mmol/L (48 mg/dL) in women indicates lower risk.
	TG: no target but <1.7 mmol/L (150 mg/dL) indicates lower risk and higher levels indicate a need to look for other risk factors.

Comparisons

	ACC/AHA 2013	ESC 2016
Recommended lipoprotein for risk assessment	Fasting lipid panel to screen for more severe forms of dyslipidemia and secondary causes of dyslipidemia	<ul style="list-style-type: none"> Fasting lipid panel with calculation of non-HDL-C (esp with high triglycerides), HDL. Apo B alternative (high TG's)
Recommended lipoprotein target of therapy	None 4 categories of patients who benefit from high- or moderate-dose statin therapy	<ul style="list-style-type: none"> Primary target: LDL-C Secondary targets: non-HDL-C or apoB in patients with cardiometabolic risk (TG's)
Risk Assessment Tool	Pooled Cohort Equations	SCORE Risk Assessment Tool

	ACC/AHA 2013	ESC 2016
Goals for High Risk or ASCVD	High intensity Statin ($\geq 50\%$ reduction in LDL-C)	<ul style="list-style-type: none"> Very high-risk: LDL-C < 1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) High-risk: LDL-C < 2.6 mmol/L (100 mg/dL) or a reduction of at least 50% if the baseline is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL).
Goals for Prevention in Diabetics	<ul style="list-style-type: none"> 30-50% LDL-C reduction if risk $< 7.5\%$ $\geq 50\%$ if risk $> 7.5\%$ 	<ul style="list-style-type: none"> Type 1 diabetes (and evidence of renal dysfunction) LDL-C lowering at least 50% regardless of LDL-C Type 2 diabetes (+CVD or CKD), and those without CVD (> 40 years of age) with one or more other CVD risk factors or target organ damage, LDL-C < 1.8 mmol/L (< 70 mg/dL) and the secondary goal for non-HDL-C is < 2.6 mmol/L (< 100 mg/dL) and for apoB is < 80 mg/dL. Type 2 diabetes and no additional risk factors and/or evidence of target organ damage, LDL-C < 2.6 mmol/L (< 100 mg/dL) is the primary goal. Non-HDL-C < 3.4 mmol/L (< 130 mg/dL) and apoB < 100 mg/dL are the secondary goals.

Comparisons

	ACC/AHA 2013	ESC 2016
Lipid Lowering for Primary Prevention without diabetes	<ul style="list-style-type: none"> • LDL-C 70-189 mg/dL: <ul style="list-style-type: none"> ○ 10 year risk \geq 7.5% after discussion w patient ○ 10 year risk < 7.5 % after discussion with patient and consideration of other factors 	<ul style="list-style-type: none"> • In patients at HIGH CV risk, an LDL-C goal of <2.6 mmol/L (100 mg/dL), or a reduction of at least 50% if the baseline LDL-C is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL) is recommended. • In subjects at LOW or MODERATE risk an LDL-C goal of <3.0 mmol/L (<115 mg/dL) should be considered

Conclusions

- Treatment according to risk
- Statins are the mainstay of treatment
- Risk assessment useful to identify at risk individuals
- ESC guidelines support the continuum of risk with LDL-C cholesterol and variation in response to treatment, and therefore target LDL-C levels based upon risk

Table 1 | Recommendations for treatment goals for low-density lipoprotein-cholesterol

Recommendations	Class ^a	Level ^b	Ref ^c
In patients at VERY HIGH CV risk ^d , an LDL-C goal of <1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline LDL-C is between 1.8 and 2.3 mmol/L (70 and 105 mg/dL) is recommended.	I	B	41, 42, 45, 48, 49, 128
In patients at HIGH CV risk ^d , an LDL-C goal of <2.6 mmol/L (100 mg/dL) or a reduction of at least 50% if the baseline LDL-C is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL) is recommended.	I	B	45, 129
In subjects at LOW or MODERATE risk ^d an LDL-C goal of <3.0 mmol/L (<115 mg/dL) should be considered.	IIa	C	-

CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol.
^aClass of recommendation.
^bLevel of evidence.
^cReferences supporting recommendations.
^dFor definitions see section 2.3.
^eThe term "baseline LDL-C" refers to the level in a subject not taking any lipid lowering medications.

Table 3 | Intervention strategies as a function of total cardiovascular risk and low-density lipoprotein cholesterol level

Total CV risk (SCORE) %	LDL-C levels				
	<75 mg/dL, <1.8 mmol/L	75 to <100 mg/dL, 1.8 to <2.6 mmol/L	100 to <155 mg/dL, 2.6 to <4.8 mmol/L	155 to <190 mg/dL, 4.8 to <4.9 mmol/L	≥190 mg/dL, ≥4.8 mmol/L
<1	No lipid intervention	No lipid intervention	No lipid intervention	No lipid intervention	Lifestyle intervention, consider drug if unacceptable
Class ^a /Level ^b	IC	IC	IC	IC	IIa
1 to <5	No lipid intervention	No lipid intervention	Lifestyle intervention, consider drug if unacceptable	Lifestyle intervention, consider drug if unacceptable	Lifestyle intervention, consider drug if unacceptable
Class ^a /Level ^b	IC	IC	IIa	IIa	IIa
5 to >10, or high-risk	No lipid intervention	Lifestyle intervention, consider drug if unacceptable	Lifestyle intervention and conventional drug intervention	Lifestyle intervention and conventional drug intervention	Lifestyle intervention and conventional drug intervention
Class ^a /Level ^b	IIa	IIa	IIa	IIa	IIa
≥10 or very high-risk	Lifestyle intervention, consider drug	Lifestyle intervention and conventional drug intervention	Lifestyle intervention and conventional drug intervention	Lifestyle intervention and conventional drug intervention	Lifestyle intervention and conventional drug intervention
Class ^a /Level ^b	IIa	IIa	IIa	IIa	IIa

CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol; SCORE = Systematic Coronary Risk Estimator.
^aClass of recommendation.
^bLevel of evidence.
^cIn patients with recurrent MI/Stroke, statin therapy should be considered irrespective of total cholesterol levels.