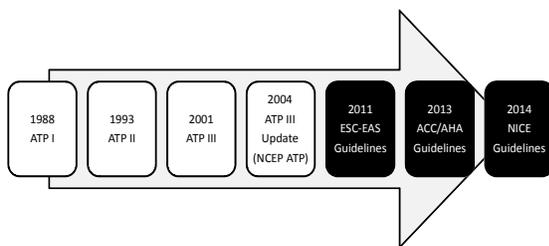


새로운 이상지질혈증 관리지침

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Dyslipidemia Guideline



ESC/EASD 2007, ADA/AHA/ACC 2007, JBS2 2005, CCS 2012, JAS 2012, IAS 2013, ADA 2014 권

ESC-EAS Guidelines(2011)



European Heart Journal (2011) 32, 1769–1818
doi:10.1093/eurheartj/ehr158

ESC/EAS GUIDELINES

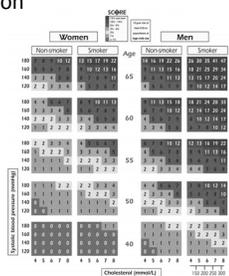
ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Developed with the special contribution of: European Association for Cardiovascular Prevention & Rehabilitation[†]

ESC-EAS Guidelines(2011)

- Total cardiovascular risk estimation
 - Risk group
 - SCORE system
- Risk levels & treatment goals
 - Very high risk
 - High risk
 - Moderate risk
 - Low risk
- Treatment targets
 - 1st: LDL-C
 - Alternative: apo B, non-HDL-C
 - do not provide targets: HDL-C, TG



ESC-EAS Guidelines(2011)

- Lifestyle modifications
- Drugs for Hyperlipidemia
 - Statins: treatment of first choice
 - Other drug combinations
- Drugs for hyperTG
 - Fibrates, Nicotinic acid, n-3 fatty acids
 - Statins and combinations
- Drugs for Low HDL-C
 - Nicotinic acid
 - no clear direct evidence that raising HDL-C really results in CVD prevention
- Different clinical settings
 - DM, Metabolic syndrome, Renal disease, Stroke?
- improve adherence to lifestyle changes and compliance with drug therapy

AHA/ACC Guidelines(2013)

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION



2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines
Neil J. Stone, Jennifer G. Robinson, Alice H. Lichtenstein, C. Noel Bairey Merz, Conrad B. Blum, Robert H. Eckel, Anne C. Goldberg, David Gordon, Daniel Levy, Donald M. Lloyd-Jones, Patrick McBride, J. Sanford Schwartz, Susan T. Shero, Sidney C. Smith, Jr, Karol Watson and Peter W. F. Wilson

AHA/ACC Guidelines(2013)

- Goal
 - Treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults
- Estimated 10-year ASCVD risk
- 4 Statin Benefit Groups
- Intensity of Statin Therapy in primary and secondary prevention
- Do not titrate to a specific LDL cholesterol target
- Statins Safety recommendations

New 10 year ASCVD risk assessment

- Age, Gender, Race
- total Cholesterol, HDL-C, Systolic blood pressure
- Tx of HTN, DM, Smoking
- <http://my.americanheart.org/cvriskcalculator>
- <http://www.cardiosource.org/en/Science-And-Quality/Practice-Guidelines-and-Quality-Standards/2013-Prevention-Guideline-Tools.aspx>



The American Heart Association and the American College of Cardiology are excited to provide a series of new cardiovascular prevention guidelines for the assessment of cardiovascular risk, lifestyle modifications that reduce risk, management of elevated blood cholesterol, and management of increased body weight in adults. To support the implementation of these guidelines, the new Pool of Outcomes CV Risk Calculator and additional Prevention Guideline Tools are available below. Others may be developed and available in the near future.

2013 Prevention Guidelines Tools
CV RISK CALCULATOR



Gender: Male Female

Age: 50

Total Cholesterol (mg/dL): 250

HDL - Cholesterol (mg/dL): 45

Systolic Blood Pressure: 130

Treatment for Hypertension: Yes No

Diabetes: Yes No

Smoker: Yes No

Race: White African American Other

Note: These estimates may underestimate the 10-year and lifetime risk for persons from some racial/ethnic groups, especially American Indians, some Asian Americans (e.g., of south Asian ancestry) and some Hispanics (e.g., Puerto Ricans), and may overestimate the risk for others, including some Asian Americans (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans). Because the primary use of these risk estimates is to facilitate the very important discussion regarding risk reduction through lifestyle change, the impression presented is small enough to justify proceeding with lifestyle change counseling informed by these results.

Recommendation

Based on the data entered (assuming no clinical ASCVD and LDL-C 70-189 mg/dL)

- Gender: Male
- Age: 50
- Race: White/Other
- Total Cholesterol: 250
- HDL-Cholesterol: 45
- Systolic Blood Pressure: 130
- Hypertension Treatment: No
- Diabetes: No
- Smoker: Yes

Moderate to High-Intensity Statin Recommended

Before initiating statin therapy, it is reasonable for clinicians and patients to engage in a discussion which considers the potential for ASCVD risk reduction benefits and for adverse effects, for drug-drug interactions, and patient preferences for treatment. (III C)

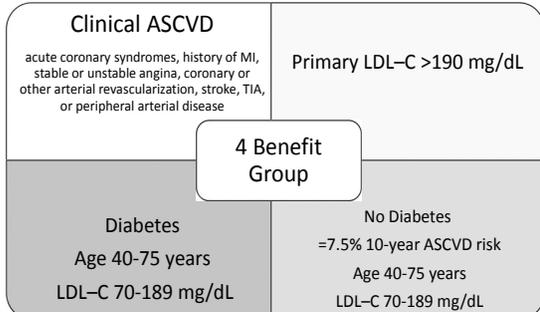
Adults 40 to 75 years of age with LDL-C 70 to 189 mg/dL, with no diabetes and estimated 10-year ASCVD risk $\geq 7.5\%$ should be treated with moderate to high-intensity statin therapy. (I A)

In individuals for whom either quantitative risk assessors or a standard treatment decision is uncertain, additional factors may be considered to inform treatment decision making. These factors may include primary LDL-C ≥ 160 mg/dL or other evidence of genetic hyperlipidemia, family history of premature ASCVD with onset ≤ 55 years of age in a first degree male relative or < 65 years of age in a first degree female relative, high-sensitivity C-reactive protein ≥ 2 mg/L, CAC score ≥ 300 Agatston units or ≥ 75 percentile for age, sex, and ethnicity, ankle-brachial index < 0.9 , or elevated lifetime risk of ASCVD. Additional factors may be identified in the future. (III C)

Lifestyle Recommendations

AHA/ACC guidelines stress the importance of lifestyle modifications to lower cardiovascular disease risk. This includes eating a heart-healthy diet, regular aerobic exercise, maintenance of desirable body weight and avoidance of tobacco products.

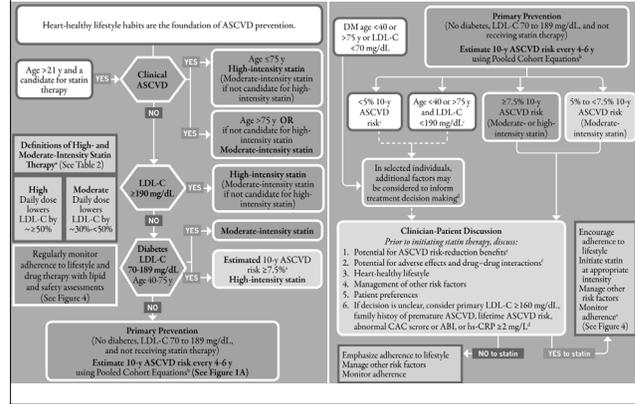
Statin Benefit Groups



Intensity of Statin Therapy

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

Recommendations for 4 groups



EAS/ESC vs AHA/ACC

	EAS/ESC	AHA/ACC
Secondary prevention	Target LDL-C < 70 mg/dL, or at least 50% reduction. If target cannot be reached with statin, drug combination may be considered.	High-intensity statin. If 50% reduction is not reached drug combination may be considered.
Statin intolerance in secondary prevention	Reduce statin dose, consider combination therapy.	Moderate or low dose statin, consider combination therapy.
Primary prevention LDL > 190 mg/dL	Target LDL-C < 100 mg/dL. If target cannot be reached maximal reduction of LDL-C, using appropriate drug combinations in tolerated doses.	High-intensity statin therapy, aimed at achieving at least 50% reduction of LDL-C. If 50% reduction cannot be achieved, consider additional therapy.
Primary prevention in diabetes	Diabetes with other risk factors or organ damage: Target 70 mg/dL, or at least 50% reduction. Uncomplicated diabetes: Target LDL < 100 mg/dL.	Diabetes with high risk: High-intensity statin therapy. Diabetes with low risk: Moderate-intensity statin therapy.
Primary prevention High risk	SCORE = 5% risk of fatal CVD: Target < 100 mg/dL.	Total risk for CVD event >7.5%: Moderate- to high-intensity statin therapy. Risk 5-7.5% risk of CVD event: moderate-intensity statin therapy.

NICE Guideline(2014)

- Update and replaces NICE guideline on lipid modification 2006

NICE National Institute for Health and Care Excellence

Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease

Issued: July 2014 last modified: September 2014

NICE clinical guideline 181
guidance.nice.org.uk/ig181

NICE Guideline(2014)

- Identifying and assessing CVD risk
 - Full formal risk assessment 10-yr risk of CVD 10%
 - QRISK2 risk assessment tool [new 2014]
 - Primary prevention,
 - Type 2 DM
 - Do not use type 1 DM
 - eGFR = 60ml/min/1.73 m2 and not albuminuria
 - 1933-2010, GB
 - Age, Sex, Total-C, HDL-C, systolic BP, DM, Smoking, race, FHx. Of early CVD, CKD, Af, RA, BMI, Socioeconomic state

NICE Guideline(2014)

- Primary prevention
 - QRISK2 10-yr CVD risk
 - atorvastatin 20 mg
 - Type I DM
 - Not assess CVD risk, atorvastatin 20 mg
 - Type II DM
 - UKPDS 10-yr CVD risk
 - atorvastatin 80 mg → If needed, decrease
 - CKD
 - Without CVD, QRISK2 10-yr CVD risk :atorvastatin 20 mg
 - With CVD: atorvastatin 20 mg start → 40% reduction in non-HDL-C → increase statin(if eGFR> 30 mL/min/1.73 m2)
- Secondary prevention
 - atorvastatin 80 mg start
 - Do not delay treatment to manage modifiable risk factors

NICE Guideline(2014)

- Follow-up
 - 40% reduction in non-HDL-C
 - 3mo: Total cholesterol, HDL-C, non-HDL-C check
 - medicines adherence and lifestyle modification
 - monitoring for adverse effects
 - Other drugs, foods, supplements
 - unexplained muscle pain (+) -> CK
- Fibrates for preventing CVD
 - Do not routinely offer
 - Also Nicotinic acid, Bile Acid, Omega-3 fatty acid

이상지질혈증 치료지침(2015)

- 선별검사
 - 20세 이상의 성인
 - 4~6년 간격
 - 공복 후 지질 검사
 - Total C, HDL-C, TG, LDL(Friedewald 공식 계산 값 가능)
- 위험인자
 - 흡연
 - 고혈압(SBP =140 or DBP =90 or HTN Mx. 중)
 - 저 HDL 콜레스테롤(<40mg/dL)
 - 고 HDL(=60mg/dL)은 위험인자 하나 제거
 - 연령(남 =45, 여=55)
 - 관상동맥질환 조기 발병 가족력
 - 부모, 형제자매 중 남=55, 여= 65

이상지질혈증 치료지침(2015)

- 치료 기준

위험도	LDL-콜레스테롤 농도(mg/dL)				
	70-99	100-129	130-159	160-189	≥190
초고위험군* 관상동맥질환 허혈성 뇌졸중 일과성 뇌허혈발작 말초혈관질환	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작
고위험군 경동맥질환† 복부동맥류 당뇨병	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작
중등도 위험군 주요 위험인자 2개 이상	생활습관 개선	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작
저위험군 주요 위험인자 1개 이하	생활습관 개선	생활습관 개선	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작	생활습관 개선 및 투약시작

이상지질혈증 치료지침(2015)

- 목표치

위험도	LDL-콜레스테롤 목표(mg/dL)	non-HDL-콜레스테롤 목표(mg/dL)
초고위험군* 관상동맥질환 허혈성 뇌졸중 일과성 뇌허혈발작 말초혈관질환	<70	<100
고위험군 경동맥질환 복부동맥류 당뇨병	<100	<130
중등도 위험군 주요 위험인자 2개 이상	<130	<160
저위험군 주요 위험인자 1개 이하	<160	<190

*50%가 넘는 경동맥 협착이 확인된 경우

이상지질혈증 치료지침(2015)

- 고중성지방혈증
 - =500 mg/dL
 - 이차적인 원인 확인필요
 - 약물치료 권고
 - fibrate, nicotinic acid, omega-3 fatty acid
 - 200 ~ 500 mg/dL
 - Statin
 - 1st LDL chol
 - 2nd Non-HDL chol
 - fibrate, nicotinic acid, omega-3 fatty acid 추가: 중성지방 200 이상 지속될 경우 권고되나, 유용성에 대해서는 논란

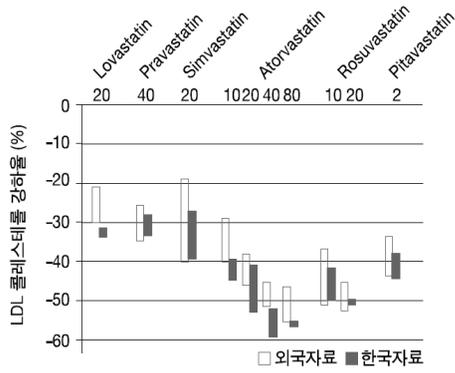
Relative LDL-lowering Efficacy(FDA)

Atorva	Fluva	Pitava	Lova	Prava	Rosuva	Vytorin	Simva	%? LDL-C
-----	40 mg	1 mg	20 mg	20 mg	-----	-----	10 mg	30%
10 mg	80 mg	2 mg	40 or 80 mg	40 mg	-----	-----	20 mg	38%
20 mg	-----	4 mg	80 mg	80 mg	5 mg	10/10 mg	40 mg	41%
40 mg	-----	-----	-----	-----	10 mg	10/20 mg	80 mg	47%
80 mg	-----	-----	-----	-----	20 mg	10/40 mg	-----	55%
-----	-----	-----	-----	40 mg	10/80 mg	-----	-----	63%

Atorva=Atorvastatin; Fluva=Fluvastatin; Pitava=Pitavastatin; Lova=Lovastatin; Prava=Pravastatin; Rosuva=Rosuvastatin; Simva=Simvastatin.

<http://www.fda.gov/Drugs/DrugSafety/ucm256581.htm>

Relative LDL-lowering data (KOREA)



Statin

- lovastatin: 20~80 mg/일, 저녁식사와 함께 복용
- pravastatin: 10~40 mg/일, 저녁 시간 투여가 더 효과적
- simvastatin: 20~40 mg/일, 저녁 시간 투여가 더 효과적
- fluvastatin: 20~80 mg/일, 저녁 시간 투여가 더 효과적
- atorvastatin: 10~80 mg/일, 복용시간에 영향(-)
- rosuvastatin: 5~20 mg/일, 복용시간에 영향(-)
- pitavastatin: 1~4 mg/일, 복용시간에 영향(-)

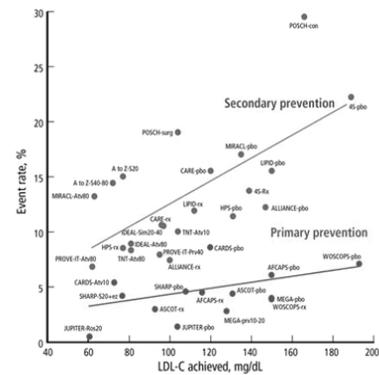
우리나라 보험급여기준 (2014.1.1 시행)

위험요인*에 따른 LDL-C 급여기준		*위험요인
위험요인*이 0~1개인 경우	LDL-C ≥ 160mg/dl	흡연, 고혈압(140/90mmHg 이상), 또는 항고혈압제 복용, 낮은 HDL-C*(40mg/dl) 관상동맥질환 조기발병의 가족력**, 나이(남자≥45세, 여자≥55세)
위험요인*이 2개 이상인 경우	LDL-C ≥ 130mg/dl	
관상동맥질환(CAD)이나 이에 준하는 위험인 경우(말초동맥질환, 복부대동맥류, 증상이 동반된 경동맥질환, 당뇨병)	LDL-C ≥ 100mg/dl	*HDL-C ≥ 60mg/dl은 보호인자로 간주하여 총 위험요인 수에서 하나를 감한다. **부모, 형제자매 중 55세 미만 남자, 65세 미만 여자에서 관상동맥질환이 발병한 경우
급성관동맥증후군(ACS)	LDL-C ≥ 70mg/dl	

순수 고중성지방혈증 1) 위험요인 (없음) : TG > 500mg/dl
2) 위험요인 (있음) or 당뇨 : TG > 200mg/dl

보건복지부 고시 제 2013-210호

Lower is better !!



LDL-C levels vs rates of Coronary events

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