이상지질혈증 치료의 최신 Update

이 준 형
인제대학교 일산백병원 가정의학과

RISK

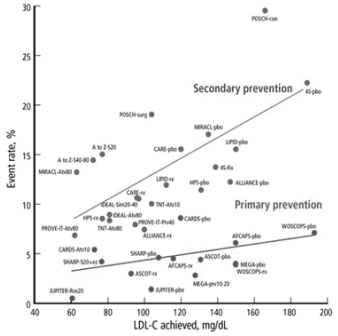
sTATIN

TARGET ?

SAFETY!

Lower is batter !!

LDL-C levels vs rates of Coronary events



Statin

- Statins for the primary prevention of cardiovascular disease(2013, Cochrane Database Syst Rev)
  - 18 randomized control trials (19 trial arms; 56,934

THE COCHRANE COLLABORATION®

Comparison 1. Mortality and Morbidity

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total Mortality	13	48060	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.79, 0.94]
2 Total Number of CHD Events	14	48049	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.67, 0.80]
3 Number of Fatal CHD Events	10	46094	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.70, 0.96]
4 Number of Non-fatal CHD Events	11	40977	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.59, 0.76]
5 Total Number of CVD Events	9	23805	Risk Ratio (M-H, Fixed, 95% CI)	0.75 [0.70, 0.81]
6 Number of Fatal CVD Events	5	34012	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.72, 0.96]
7 Number of Non-fatal CVD Events	2	8696	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.62, 0.96]
8 Total Number of Stroke Events	10	40295	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.68, 0.89]
9 Number of Fatal Stroke Events	3	27238	Risk Ratio (M-H, Random, 95% CI)	0.63 [0.18, 2.23]
10 Number of Non-fatal Stroke Events	5	28097	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.58, 0.83]
11 Total Number of Fatal and Non-fatal CHD, CVD and Stroke Events	4	35254	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.58, 0.73]
12 Number of Study Participants who underwent Revascularisation	7	42403	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.54, 0.72]

Statin – DM

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials

Naveed Sattar, David Preiss, Heather M Murray, Paul Welsh, Brendan M Buckley, Anton J M de Craen, Sreenivasa Rao Kondapally Seshasai, John J McMurray, Ian Ford, Peter W Macfarlane, Chris J Packard, David J Stott, Rudi G Westendorp, James Shepherd, Barry R Davis, Sara L Pressel, Roberto Marchioli, Rosa Maria Marfisi, Aldo P Maggioni, Luigi Tavazzi, Gianni Tognoni, John Kjekshus, Terje R Pedersen, Thomas J Cook, Antonio M Gotto, Michael B Clearfield, John H Downs, Haruo Nakamura, Yasuo Ohashi, Kyoichi Mizuno, Kausik K Ray, Ian Ford

Summary

Background **Trials of statin therapy have had conflicting findings on the risk of development of diabetes mellitus in patients given statins. We aimed to establish by a meta-analysis of published and unpublished data whether any relation exists between statin use and development of diabetes.**

Methods **We searched Medline, Embase, and the Cochrane Central Register of Controlled Trials from 1994 to 2009.**

Lancet 2010; 375: 735–42
Published Online
February 12, 2010
DOI:10.1016/S0140-6736(09)61965-6

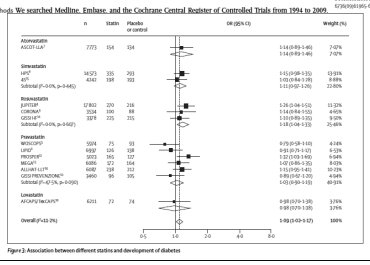
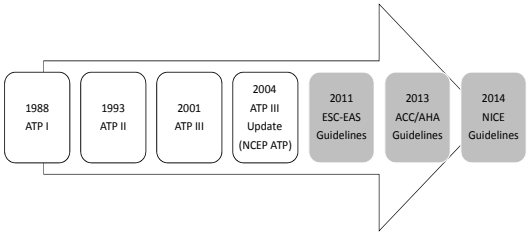


Figure 2: Association between different statins and development of diabetes

Dyslipidemia Guideline



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

ESC-EAS Guidelines(2011)

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

ESC/EAS GUIDELINES

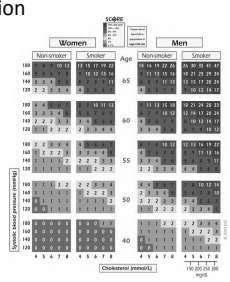
ESC/EAS Guidelines for the management of dyslipidaemias

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 Hyperlipidermia
  - 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

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

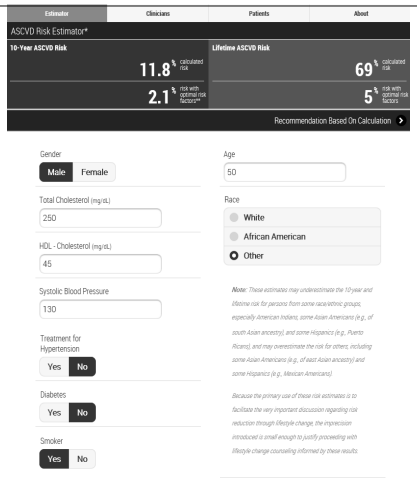
American Heart Association. | AMERICAN COLLEGE of CARDIOLOGY

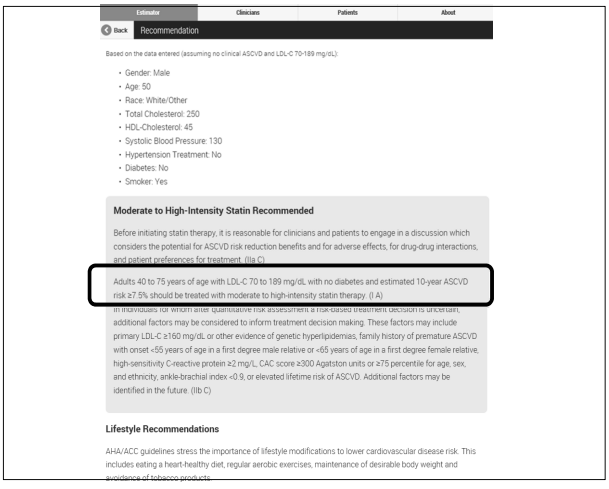
The American Heart Association and the American College of Cardiology are excited to provide a series of new cardiovascular prevention guidelines for the assessment of cardiovascular risk, lifestyle modifications that reduce risk, management of elevated blood cholesterol, and management of increased body weight in adults. To support the implementation of these guidelines, the new Pooled Cohort Equations 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

Available on the App Store | Google play | Download CV Risk Calculator | Launch Web Version





Statin Benefit Groups

Clinical ASCVD
acute coronary syndromes, history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease

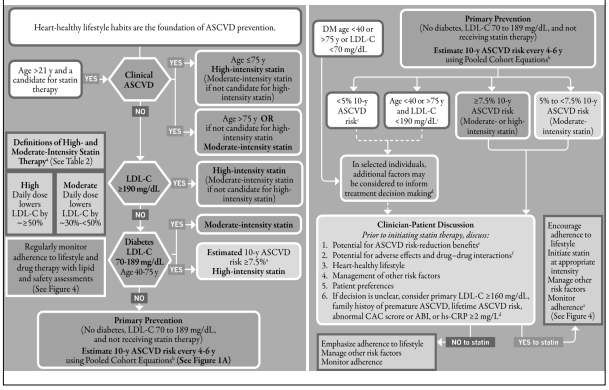
Primary LDL–C >190 mg/dL

4 Benefit Group

Diabetes
Age 40-75 years
LDL–C 70-189 mg/dL

No Diabetes
≥7.5% 10-year ASCVD risk
Age 40-75 years
LDL–C 70-189 mg/dL

Recommendations for 4 groups



Do not titrate to a specific LDL cholesterol target

- Evidence is inadequate to support treatment to specific LDL-C or non-HDL-C treatment goals
  - Unknown magnitude of additional ASCVD risk reduction with one target compared to another
  - Unknown rate of additional adverse effects from multidrug therapy used to achieve a specific goal

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**

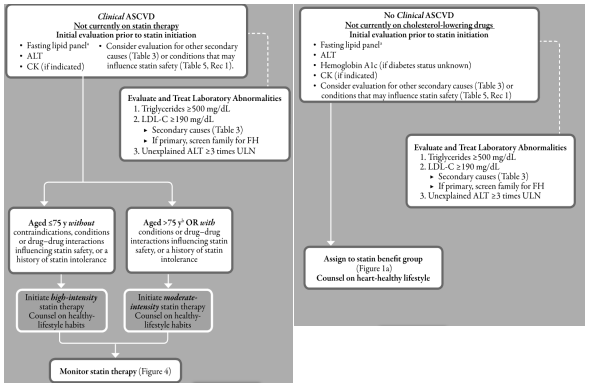
Relative LDL-lowering Efficacy(FDA)

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

Initiating Statin Therapy

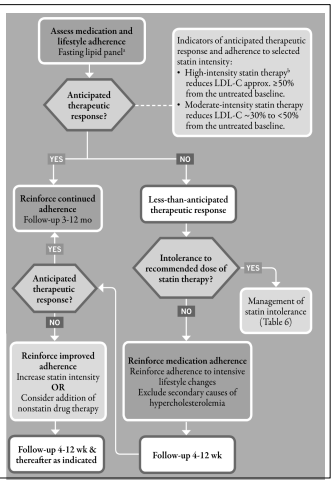


Statins Safety recommendations

- Predispoing factor of statin-associated Adverse Effects
  - Multiple or serious comorbidities, including impaired renal or hepatic function.
  - History of previous statin intolerance or muscle disorders.
  - Unexplained ALT elevations ≥3 times ULN.
  - Patient characteristics or concomitant use of drugs affecting statin metabolism.
  - Age >75 years.
  - History of hemorrhagic stroke.
  - Asian ancestry.

Monitoring

- Fasting lipid panel
- Creatinine Kinase (CK)
  - Routine monitoring of CK not recommended
  - at baseline(useful)
- Alanine Transaminase (ALT)
  - Baseline(recommended)
  - Routine hepatic monitoring not recommended



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/cg181

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, ≤ 84
    - 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

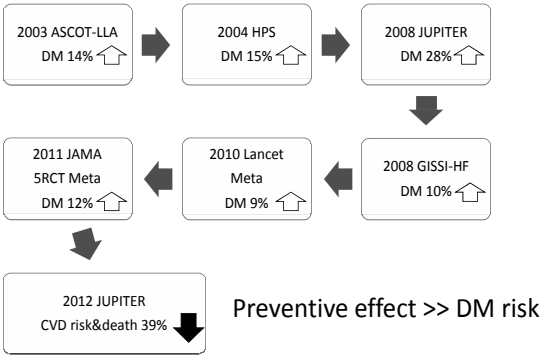
NICE Guideline(2014)

- Primary prevention
  - QRISK2 10-yr CVD risk ≥ 10%
    - atorvastatin 20 mg
  - Type I DM
    - Not assess CVD risk, atorvastatin 20 mg
  - Type II DM
    - UKPDS 10-yr CVD risk ≥ 10%
    - atorvastatin 80 mg -> If needed, decrease
  - CKD
    - Without CVD, QRISK2 10-yr CVD risk ≥ 10%: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

Recent Issues - DM



Preventive effect >> DM risk

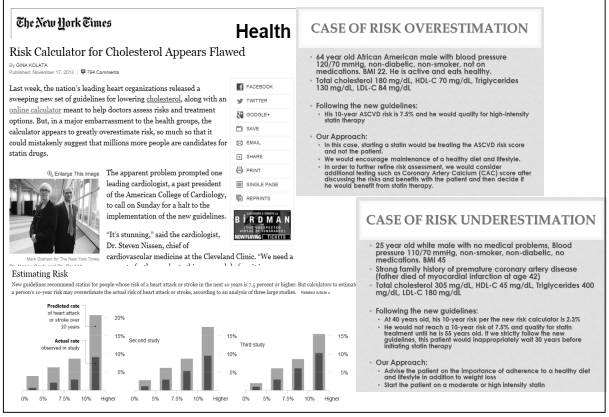
Recent Issues - DM

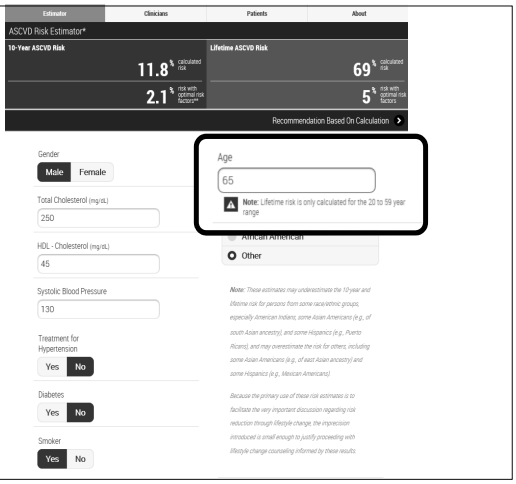
American Diabetes Association. Diabetes Care

Statins and the Risk of Diabetes: Evidence From a Large Population-Based Cohort Study

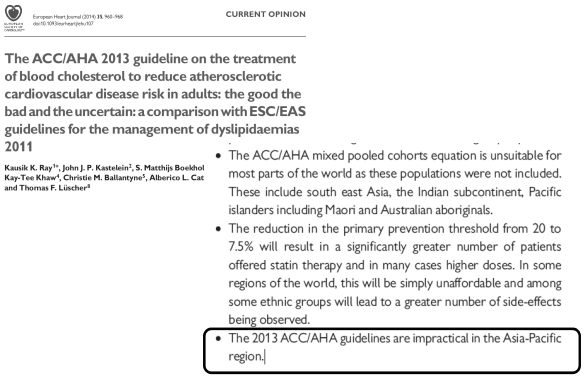
- In a real-world setting, the risk of new-onset diabetes rises as adherence with statin therapy increases.
- Benefits of statins in reducing cardiovascular events clearly overwhelm the diabetes risk.

Recent Issues – Risk calculation





Recent Issues – In Aisa?



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