台灣血脂衛教協會
Taiwan Association of Lipid Educators

Insights & Implications from NHI Lipid Guideline Change

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Outline

- Lipid – One of the major player in Atherosclerosis
- Lipid Guideline Evolution
- Taiwan NHI Lipid Guideline Changes & Rationale
- AHA/ACC 2013 New Cholesterol Guideline
- Implication & Insights

Attributable Risks of Major Risk Factors for Stroke and CHD

Alison E et al. JACC 2010 (56): P.245

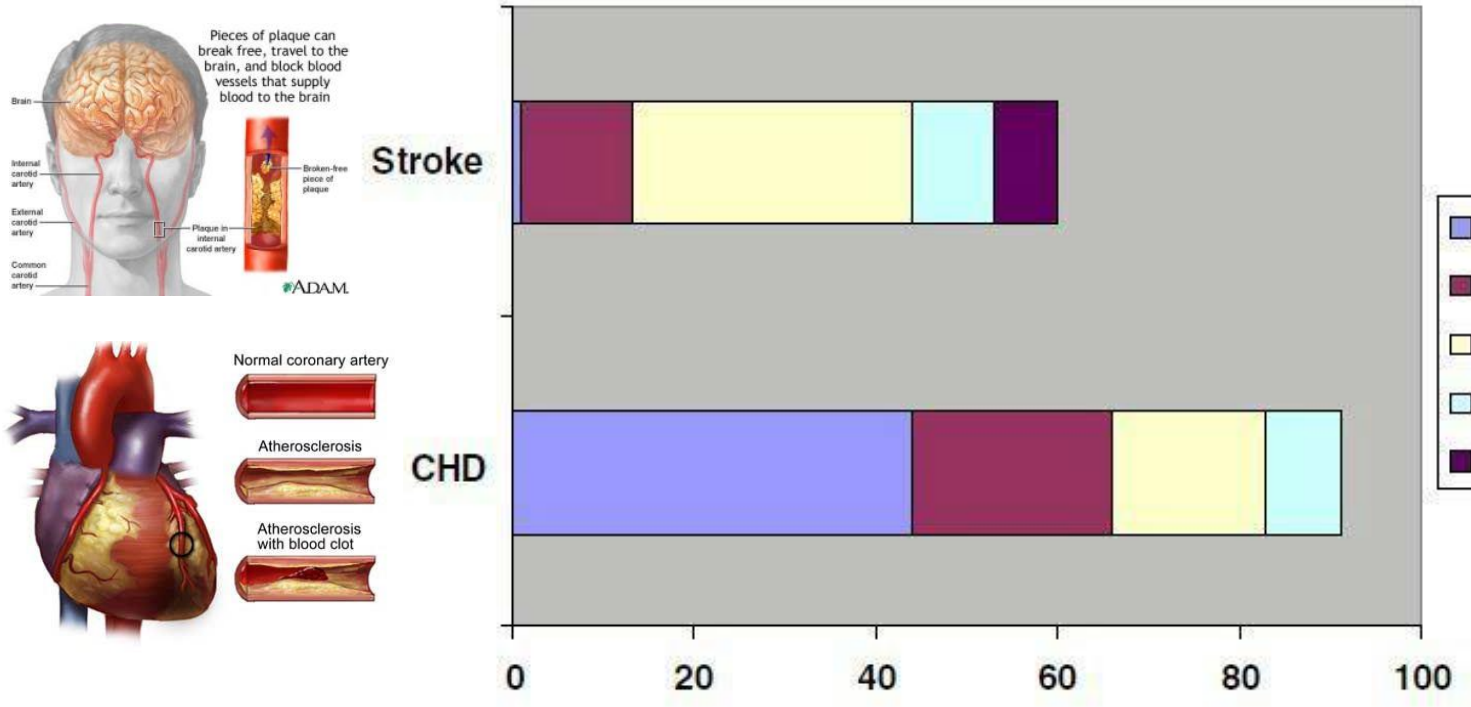


Figure 2 **Attributable Risks of Major Risk Factors for Stroke and CHD**

Vascular disorders, such as coronary heart disease (CHD) and stroke, share a number of risk factors in common. CHD also accounts for 1
attributable risk for stroke. Data were obtained from the INTERHEART (Effect of Potentially Modifiable Risk Factors Associat
study (11) using Northern American statistics and data from current guidelines for primary prevention of stroke (50).

Atherosclerosis is a Chronic, Dynamic, Inflammatory Disease of Deadly Consequence

I. Initiation

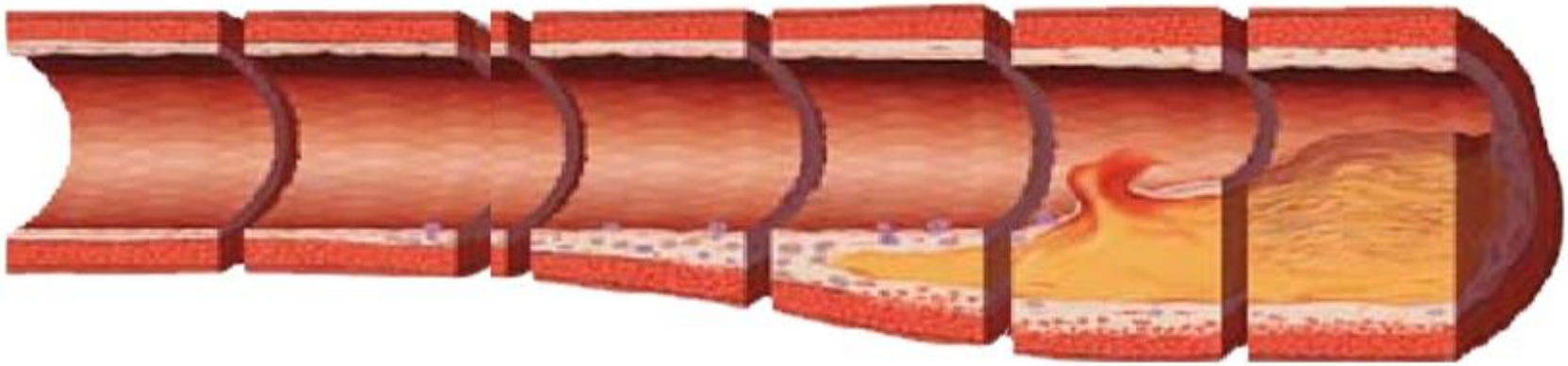
- Infiltration of LDL into artery wall
- Oxidation of LDL,
- Monocytes infiltration into vessel wall
- Decreased endothelial function

II. Evolution

- Continued LDL infiltration, oxidation and endothelial dysfunction
- Formation of foam cells
- SMC migration & fibrous production
- Vascular inflammation and formation of lipid core

III. Complication

- Increased inflammation and lipid core
- Fewer SMCs & fibrous material
- Unstable plaque formation (vulnerable plaque)
- Plaque rupture leads to spilling of plaque materials and acute thrombosis

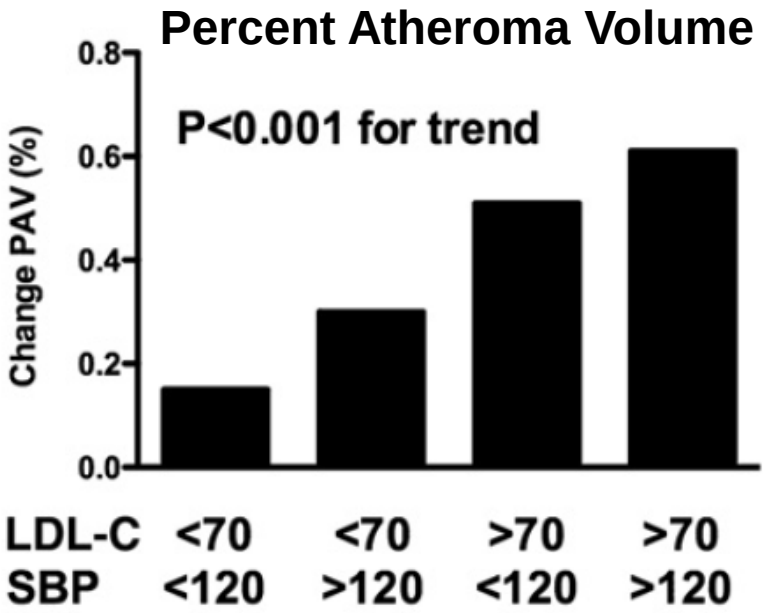


SMC: smooth muscle cell, LDL: low-density lipoprotein

Percent atheroma volume increases with the elevation of both LDL-C and SBP

- "Lower levels of LDL-C and SBP were associated with less progression of Percent Atheroma Volume (PAV)" *

Effects of LDL-C and SBP on Coronary Atherosclerosis

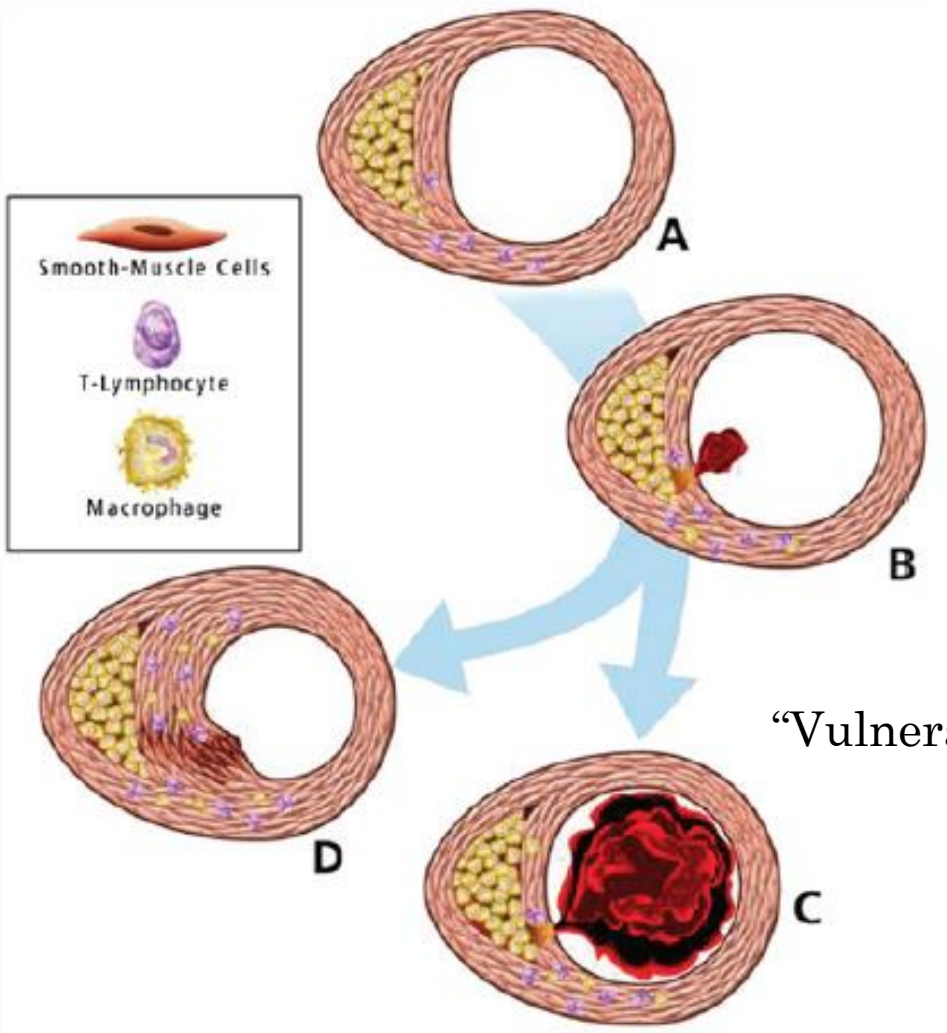


Changes in atheroma burden monitored by intravascular ultrasound were studied in 3,437 patients with coronary artery disease (CAD) who were stratied according to on-treatment LDLC and SBP.
Change in percent atheroma volume (PAV) stratied according to on-treatment low-density lipoprotein cholesterol and systolic blood pressure

- **The greatest reduction of coronary plaque progression was observed in patients with very low LDL-C (<70 mg/dL) and normal SBP (<120 mmHg) in combination.***

* *Adapted /changed from. JACC.* 2009; 53: 1110-15.

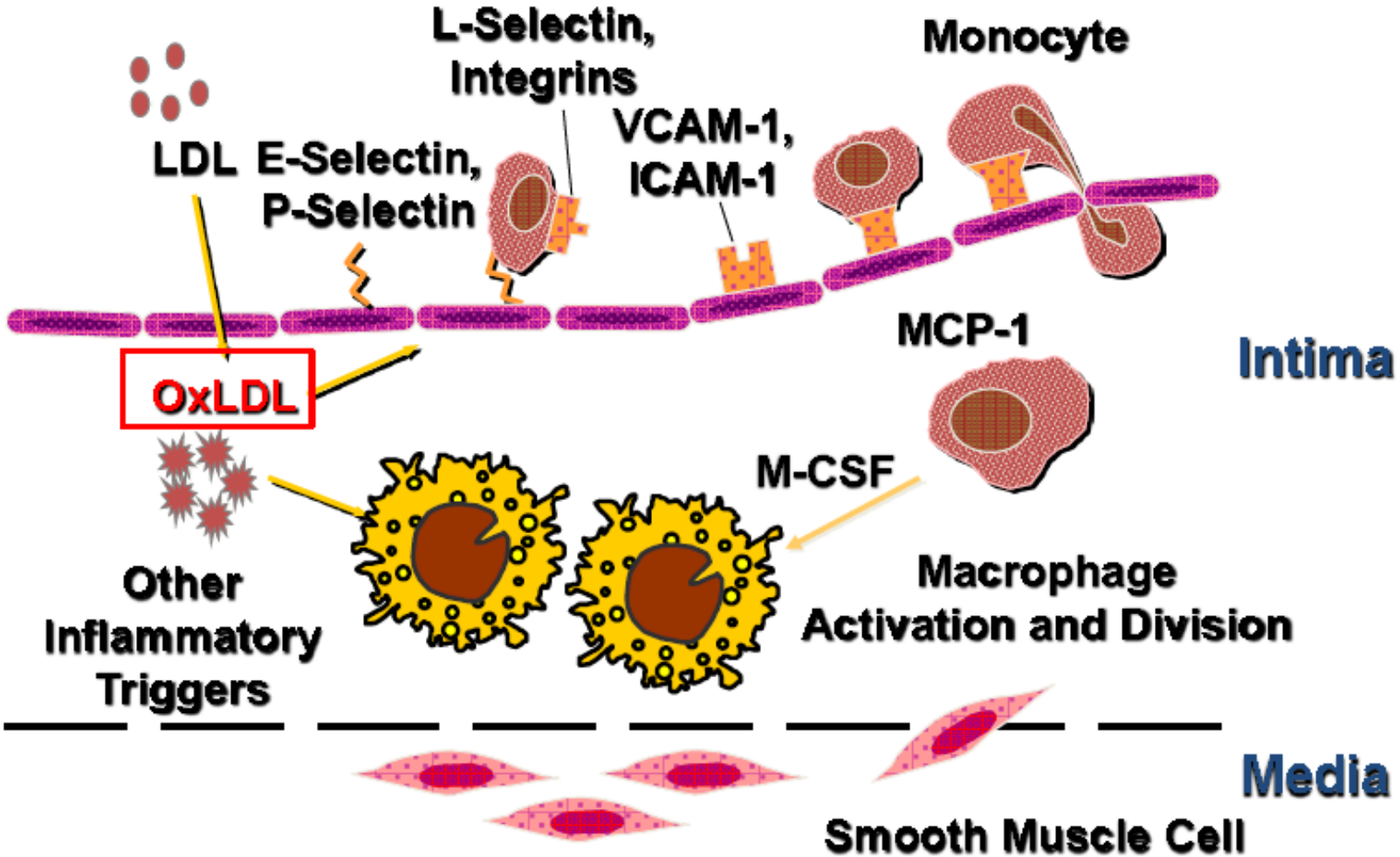
Atheroma Complications



"Vulnerable" plaque

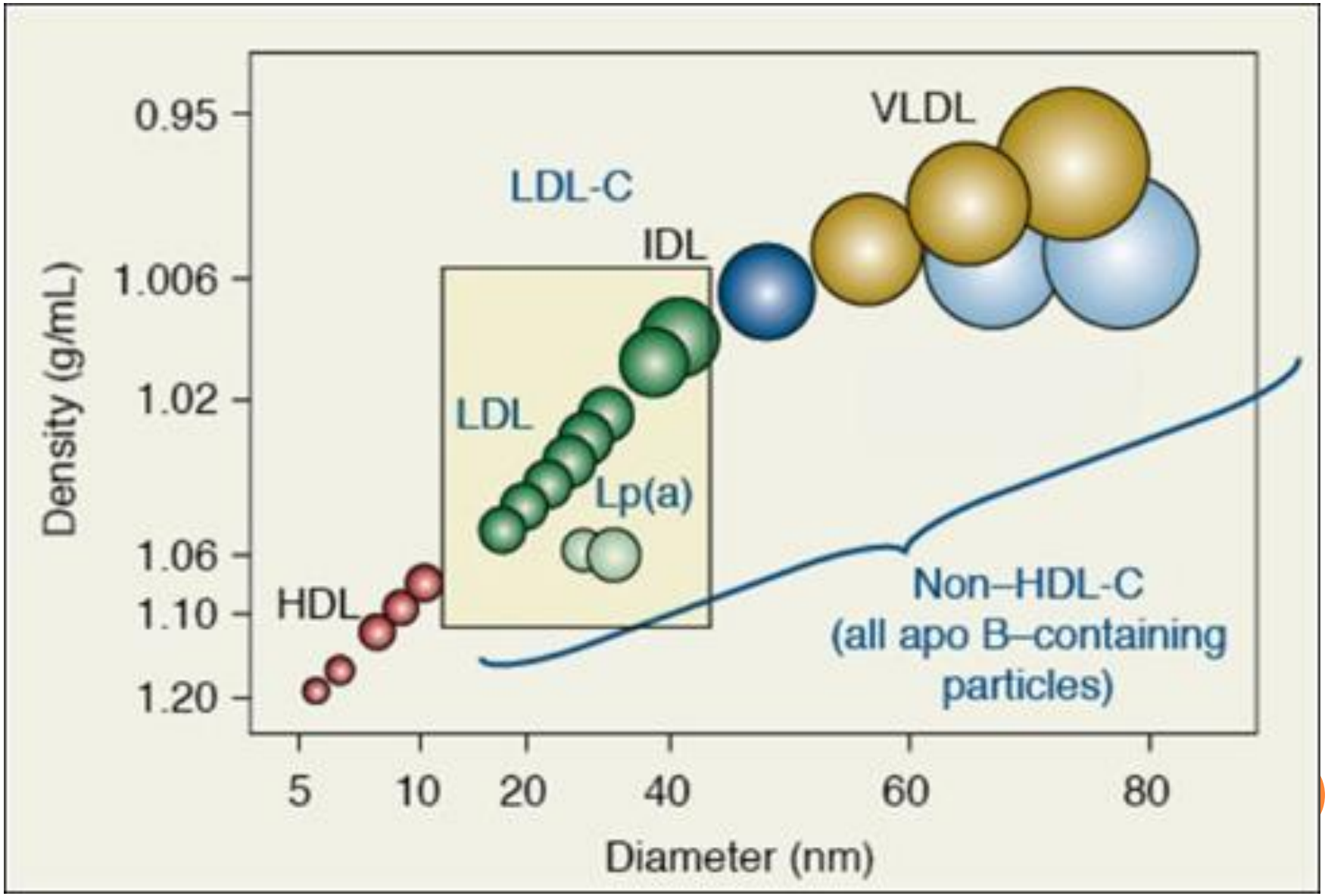
Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Atherosclerosis Is an Inflammatory Disease

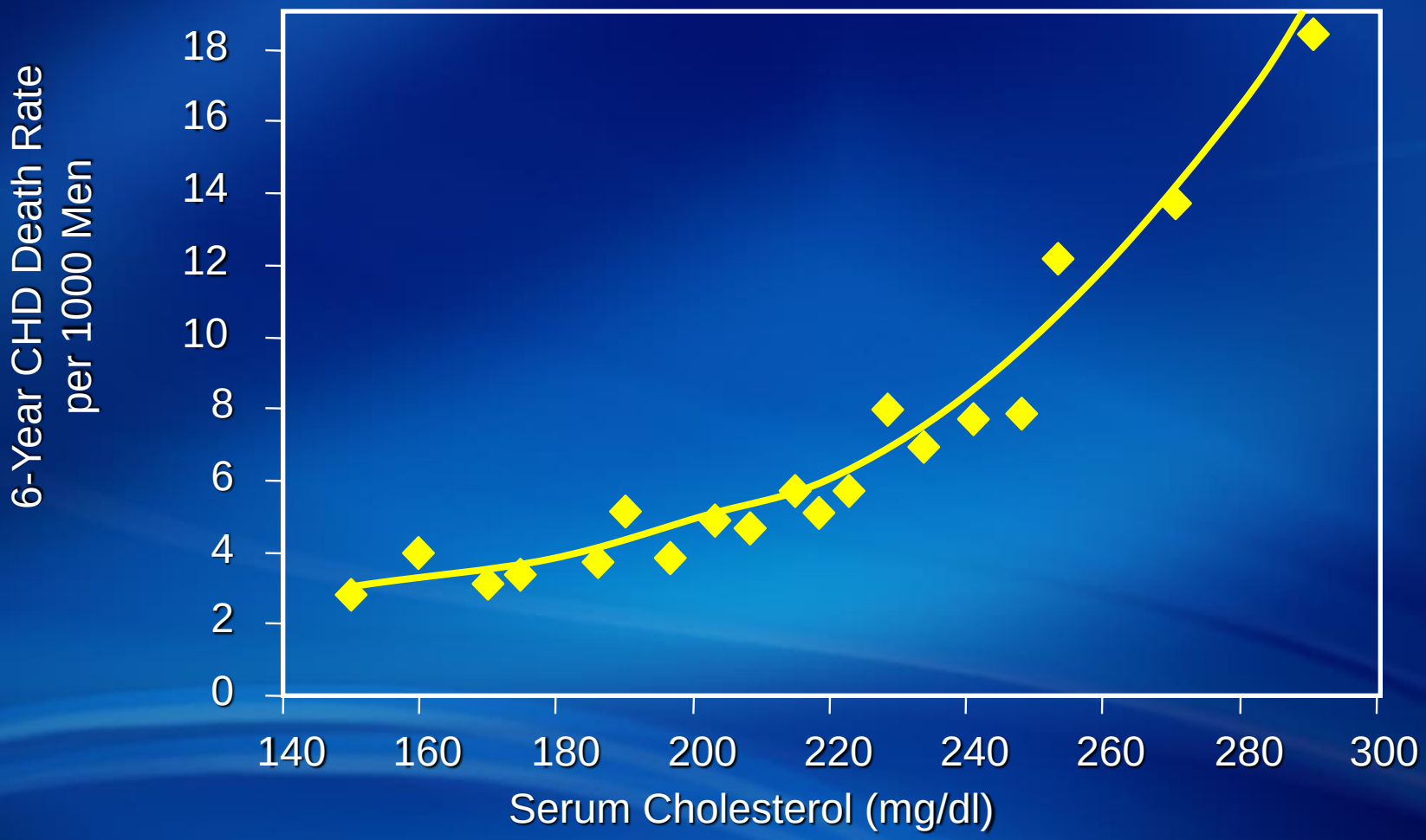


Libby et al. *Circulation*. 2002;105:1135-1143;
Newby et al. *Cardiovasc Res*. 1999;41:345-360.

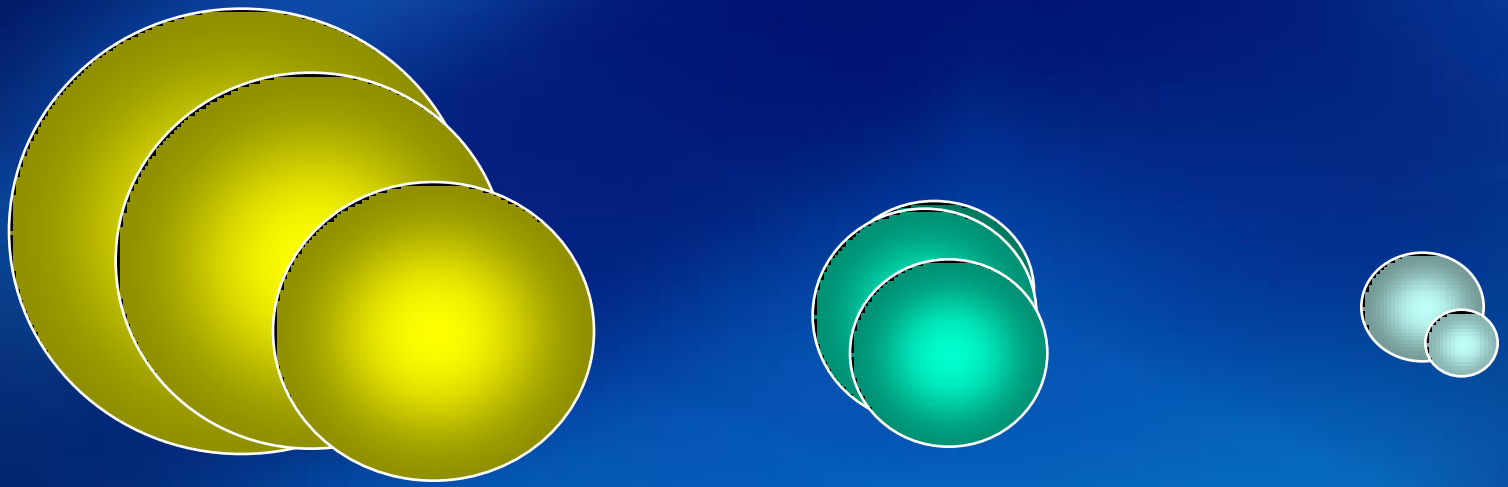
Classification of Lipoproteins



Serum Cholesterol and CHD in 361,662 US Men: MRFIT



Lipoprotein classes and atherosclerosis



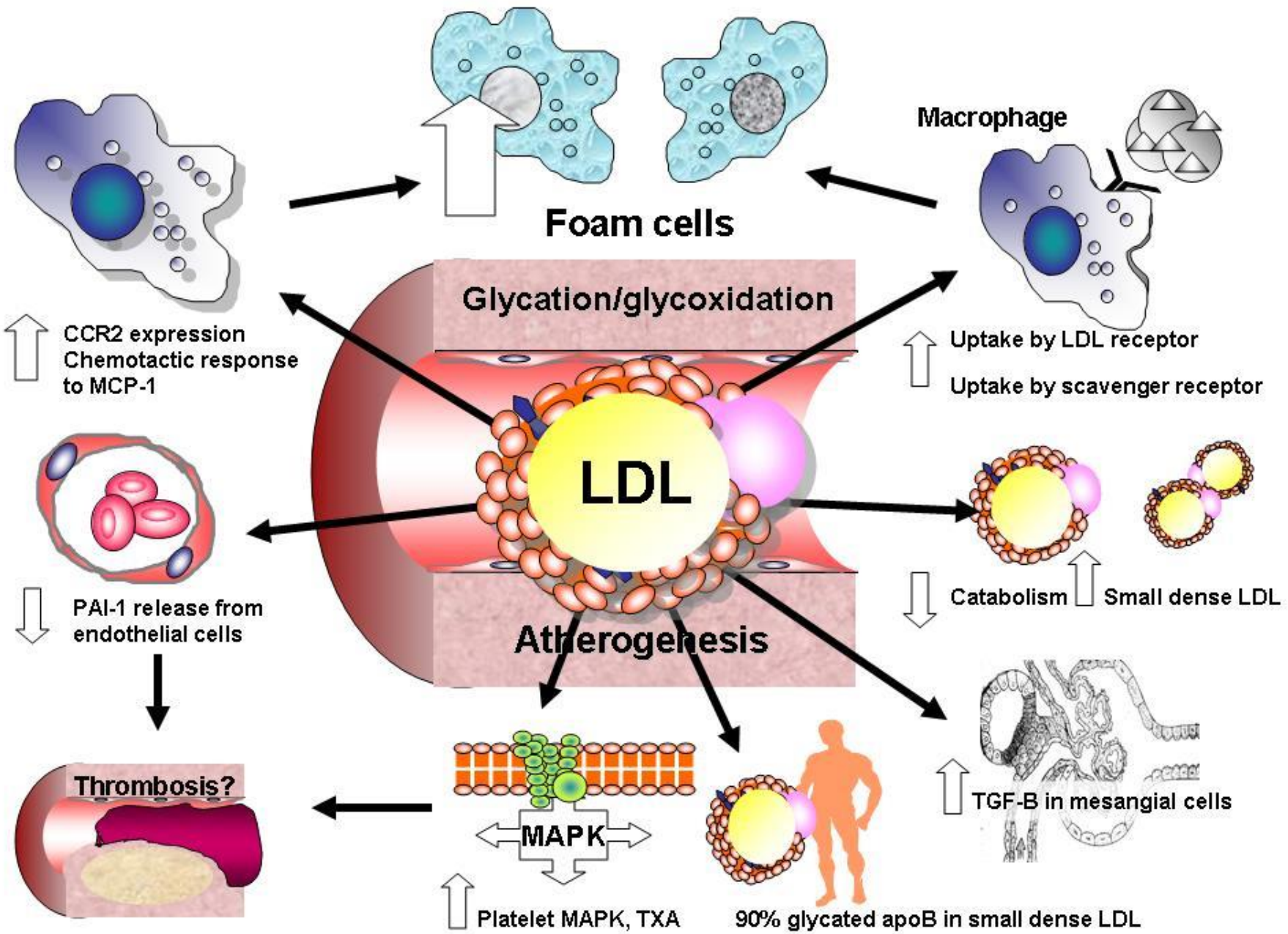
Chylomicrons, VLDL, and their catabolic remnants

LDL

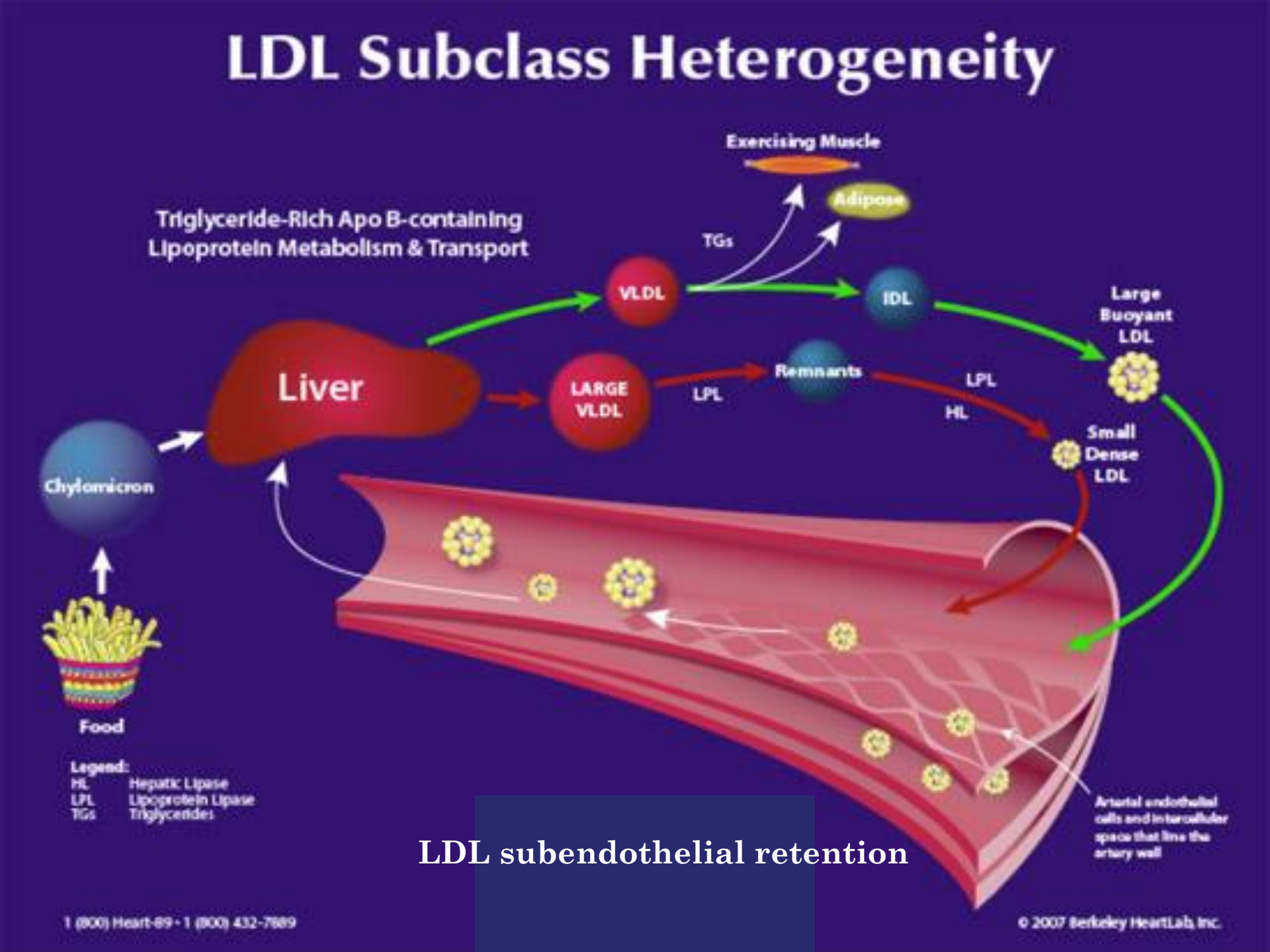
HDL

Pro-atherogenic

Anti-atherogenic

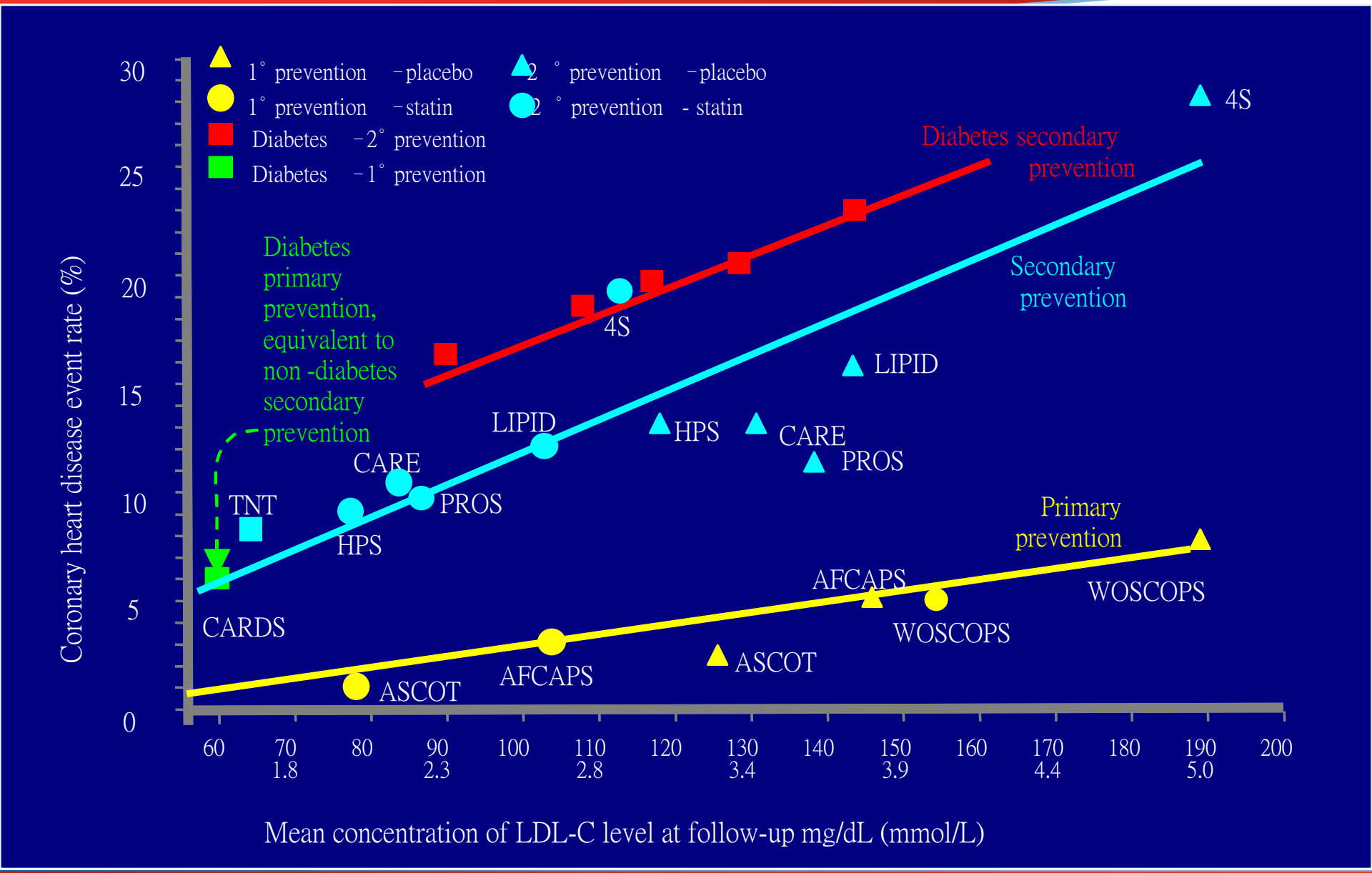


LDL Subclass Heterogeneity



LDL subendothelial retention

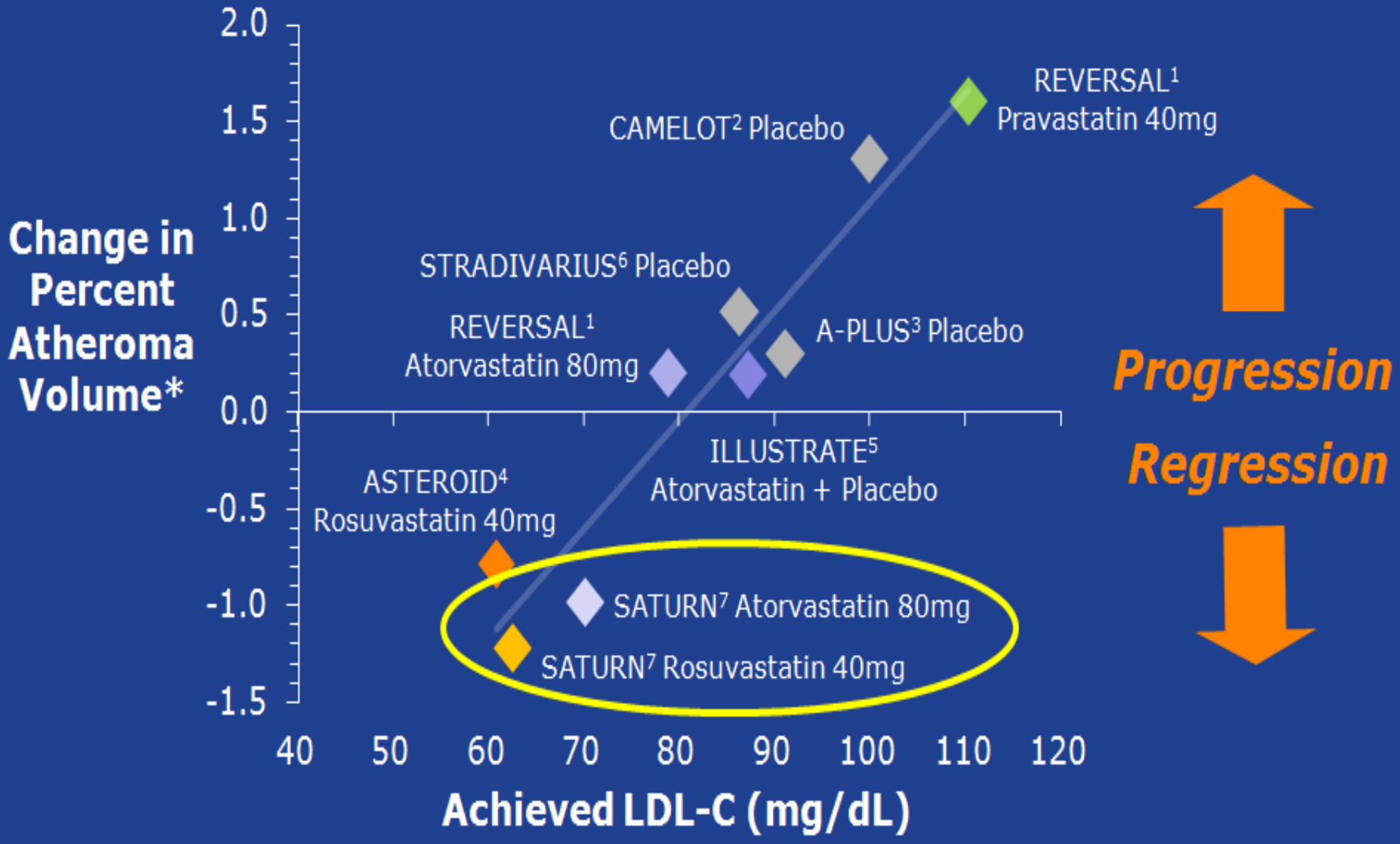
Effect of LDL-C Reduction on Coronary Heart Disease Event Rate



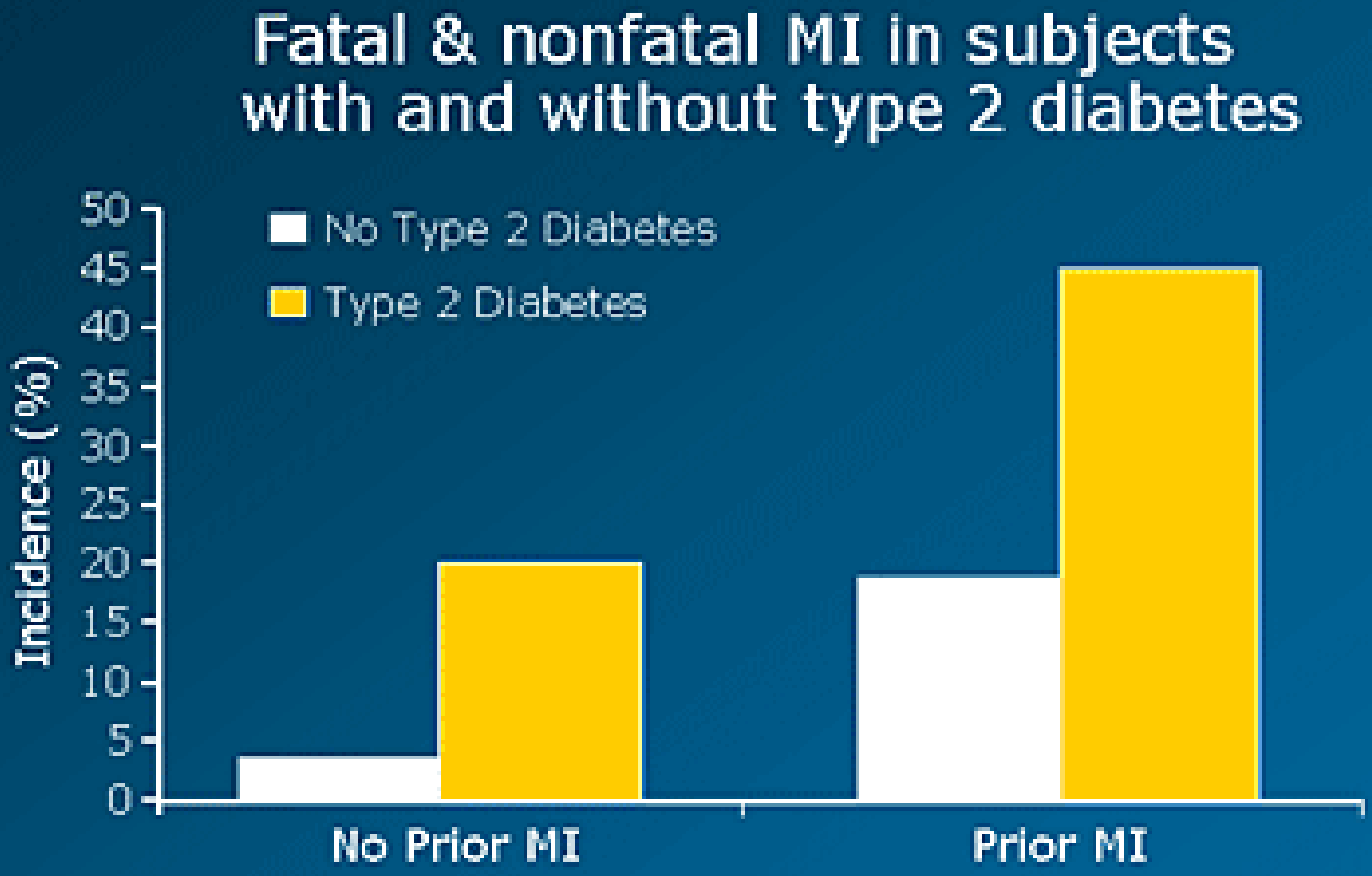
Adapted from Opie LH et al. The Lancet 2006; 367: 69-78. Boden WE et al. Am J Cardiol 2000; 85: 645-650.

Results

Relationship between achieved LDL-C and change in PAV



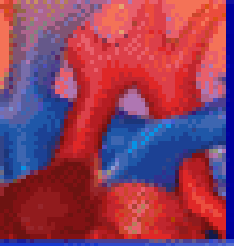
Is Type 2 Diabetes a Coronary Equivalent?



7-year incidence of fatal and nonfatal MI in 1373 nondiabetic and 1059 diabetic subjects ($P<.001$).

Haffner SM et al. *N Engl J Med*. 1998;339:229-234.

Complications of Diabetes Mellitus

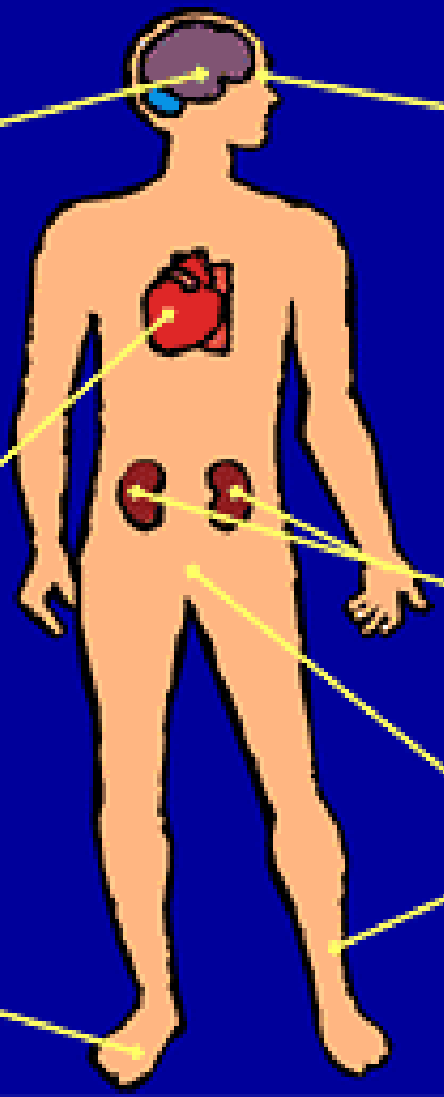


Macrovascular

Brain
TIA, CVA, Dementia

Heart
ACS
CHF

PVD



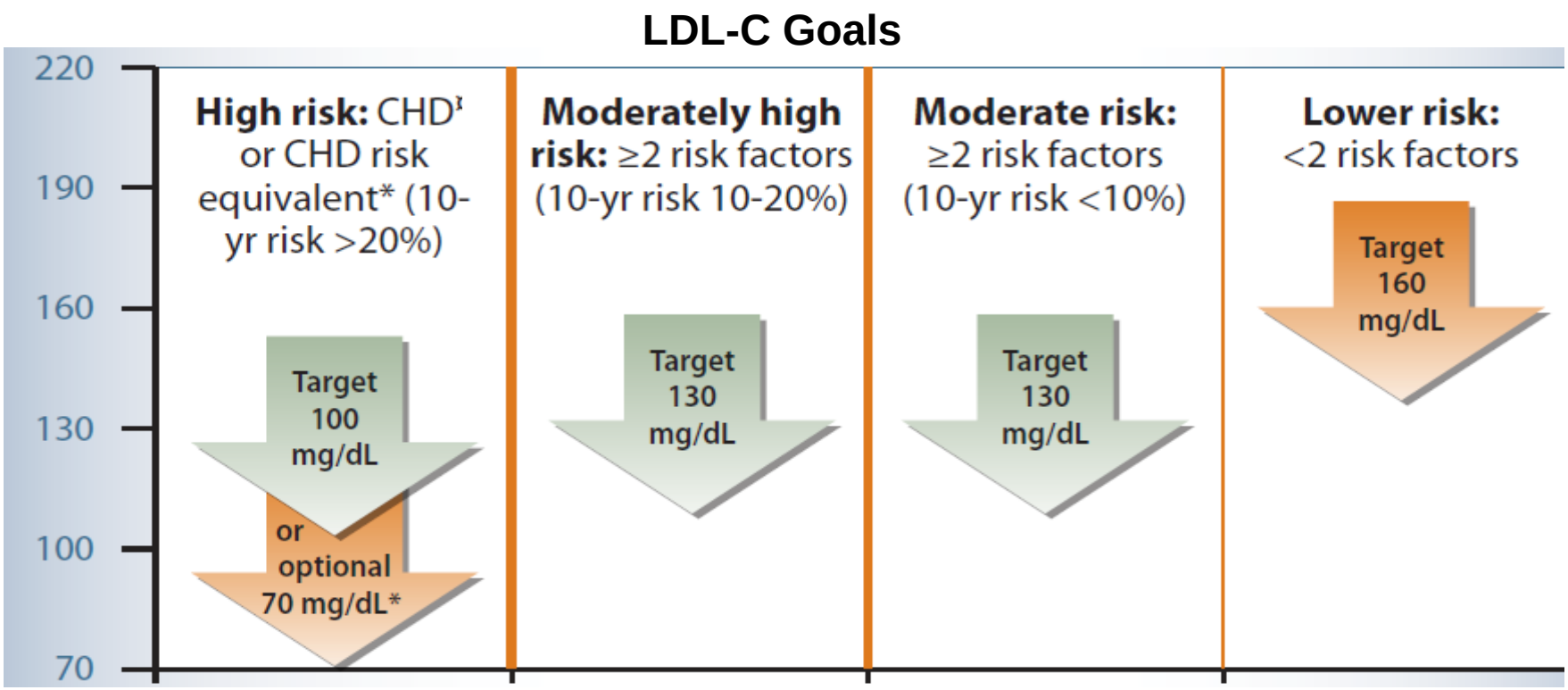
Microvascular

Eye
Retinopathy
Glaucoma
Cataracts

Renal
Microalbuminuria
Nephropathy
ESRD

Neuropathy
Peripheral
Autonomic

National Guidelines on Hypertension and Dyslipidemia - NCEP ATP III (2004 Updates)



* CHD risk equivalents include clinical manifestations of non-coronary forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and carotid artery disease [transient ischemic attacks or stroke of carotid origin or >50% obstruction of a carotid artery]), diabetes, and 2 or more risk factors with 10-year risk for hard CHD >20%.

Adapted/changed from *Circulation.* 2004; 110: 227-39.

Caduet® amlodipine besylate/atorvastatin calcium

Past NHIA guideline (2008/7/1~2013/7/31)

血脂異常之起步治療準則		血脂濃度		≧2個危險因子(如附註二)	TC/HDL-C > 5 或 HDL-C< 40mg/dl	治療目標	處方規定
無心血管疾病患者（如附註一）	給予下列情況之一時，三至六個月非藥物治療，應	TC	≧200mg/dl	ˇ	×	< 200mg/dl	如非藥物治療未達治療目標，得使用降血脂藥物(請附三個月前及本次血脂檢查數據)，接受藥物治療後，應每三至六個月抽血檢查一次，同時請注意副作用產生，如肝功能異常或橫紋肌溶解症等，如已達治療目標得考慮減量至最低有效劑量，並持續衛教治療。(91/9/1、93/9/1、97/7/1)
			≧240mg/dl	×	×	< 240mg/dl	
		LDL-C	≧130mg/dl	ˇ	×	< 130mg/dl	
			≧160mg/dl	×	×	< 160mg/dl	
		TG ≧200mg/dl (需同時合併有TC/HDL-C>5或是HDL-C<40mg/dl)(91/9/1)		×	ˇ	< 200mg/dl (87/4/1)	
有心血管疾病患者或糖尿病	同時予以非藥物治療	TC ≧200mg/dl		×	×	< 160mg/dl (87/7/1)	接受藥物治療後，應每三至六個月抽血檢查一次，同時請注意副作用產生，如肝功能異常或橫紋肌溶解症等，如已達治療目標得考慮減量至最低有效劑量，並持續追蹤治療。(93/9/1、97/7/1)
		LDL-C ≧130mg/dl		×	×	≦100mg/dl (87/7/1)	
		TG ≧200mg/dl (需同時合併有TC/HDL-C>5或是HDL-C<40mg/dl) (91/9/1)		×	ˇ	< 150mg/dl (87/7/1)	

血中三酸甘油酯高於500mg/dl，具有罹患急性胰臟炎危險者，得使用降血脂藥物。(87/4/1、93/9/1)

(ˇ)需符合此項條件
(×)不需符合此項條件

附註一：心血管疾病：
(一)冠狀動脈粥狀硬化患者
有心導管檢查證實(附檢查報告、醫院名稱及日期)。
曾患心肌梗塞有心電圖(附心電圖)或住院證實(附檢查醫院名稱及日期)。
心絞痛病患，有缺氧性心電圖變化或運動試驗陽性反應者(附檢查報告)。
(二)腦血管病變患者
腦梗塞。
腦內出血(不含其他顱內出血)。
陣發性腦缺血患者(TIA)其頸動脈超音波證實有粥腫樣變化併有70%以上阻塞者。
(三)周邊血管粥狀硬化有缺血性症狀且經血管都卜勒超音波或血管攝影證實者。
附註二：危險因子：
1.高血壓2.糖尿病3.男性≧45歲4.有早發性冠心病家族史5.女性≧55歲或停經沒有雌激素療法者
6.吸菸(因吸菸而符合起步治療準則之個案，如要求藥物治療，應以自費治療)。

Source: Taiwan NHIA

New NHIA guideline (2013/8/1~)
心血管疾病或糖尿病患者的起始治療值由 LDL-C ≧130 降至100 mg/dL

附件一	非藥物治療	起始藥物治療血脂值	血脂目標值	處方規定
心血管疾病或 患者				6個月抽 二年
2個危險				個 同
1個危險				達 黃
0個危險				

心血管
(一) 冠
(二) 缺
1. 腦梗
2. 暫時
3. 有症

危險因
1. 高血壓
2. 男性≧4
3. 有早發性冠心病家族史(男性≦55歲，女性≦65歲)
4. HDL-C<40mg/dL
5. 吸菸(因吸菸而符合起步治療準則之個案，若未戒菸而要求藥物治療，應以自費治療)。

最主要的改變：

1. **心血管疾病或糖尿病患者，起始治療LDL-C由≧130mg/dl降為100mg/dl，目標＜100mg/dl**
2. **刪除達到治療目標需“減量至最低有效劑量”**

Source: Taiwan NHIA

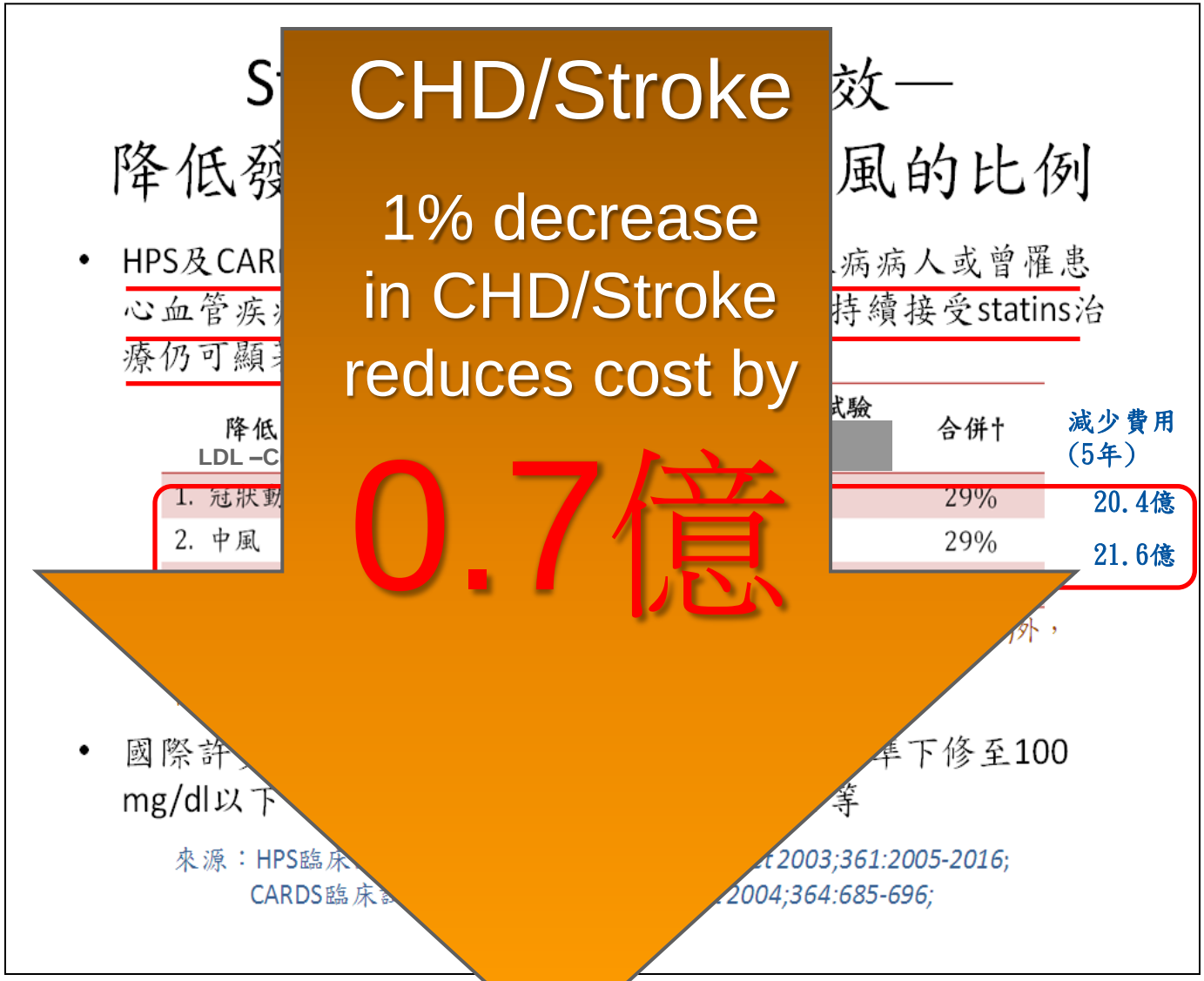
Rationale for NHIA guideline change

本項給付規定修訂推估可減少未來5年整體醫療資源耗用約14.5億元

- 本項給付規定修訂預估未來五年健保新增statins藥費總支出約27.5億。(增加費用)
- 用藥後，可降低5年內因冠狀動脈疾病罹病之費用約20.4億元，中風罹病之費用約21.6億元，合計42億元。(減少費用)
- 推估未來5年可減少因冠狀動脈疾病或中風之醫療資源耗用約14.5億元。

Source: Taiwan NHIA

Rationale for NHIA guideline change



Source: Taiwan NHIA

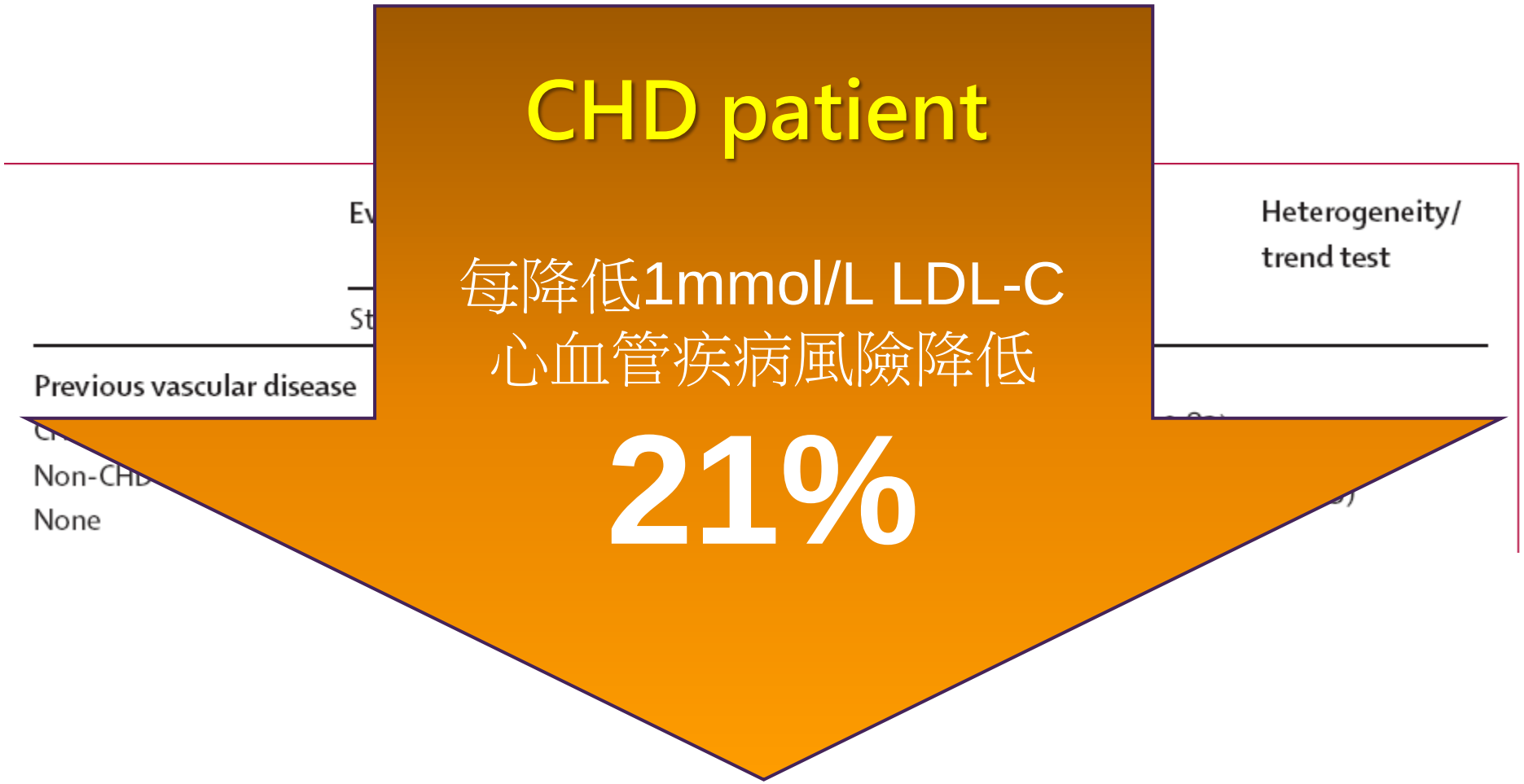
All statin clinical outcome trials: Effects of baseline LDL-C

無論baseline LDL-C多少，只要降低LDL-C都有好處

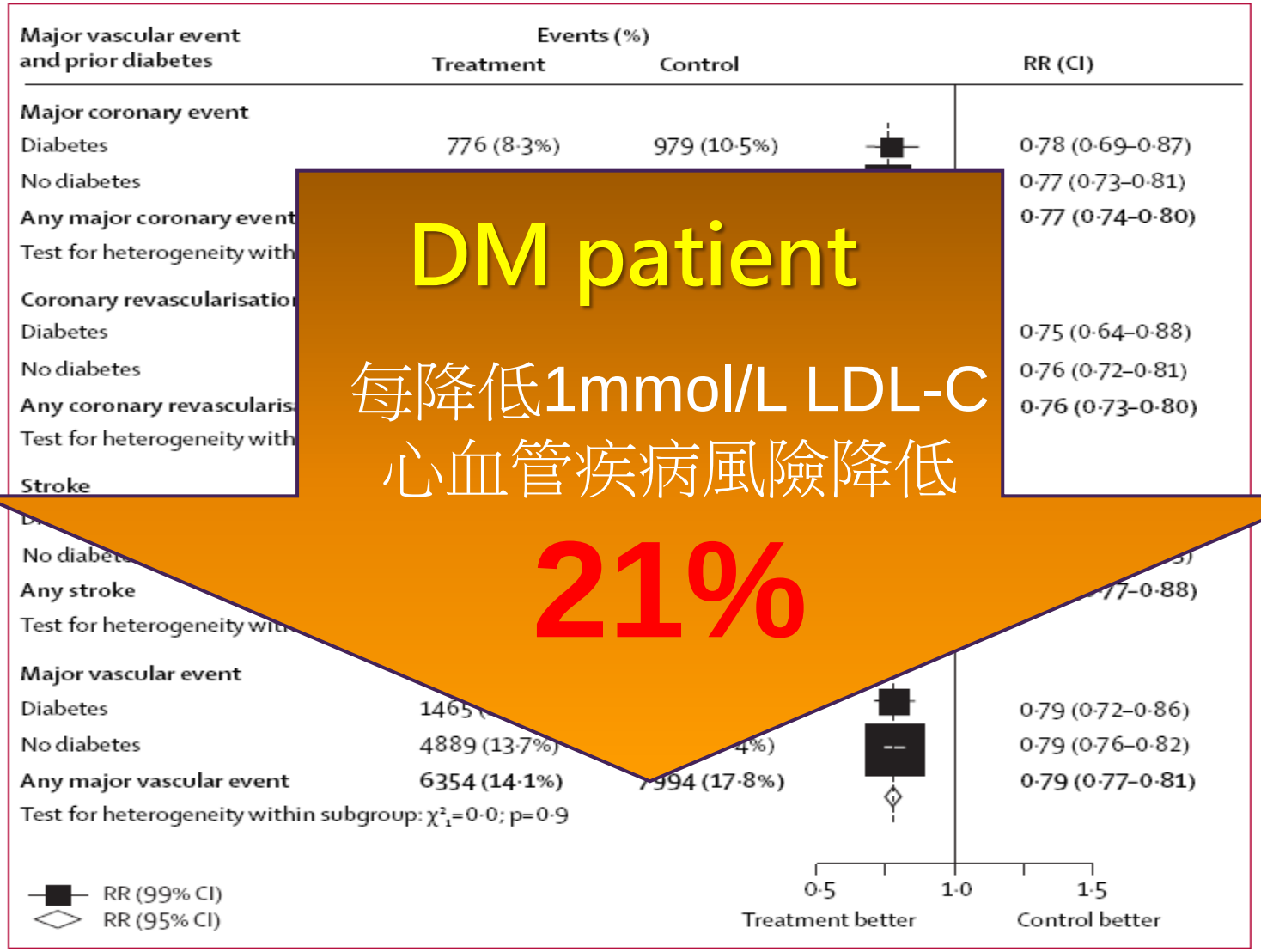
Baseli			
< 80 mg/dL	910	1012	0.78 (0.61-0.99)
80-100 mg/dL	1528	1729	0.77 (0.67-0.89)
100-120 mg/dL	1866	2225	0.77 (0.70-0.85)
120-150 mg/dL	2007	2454	0.76 (0.70-0.82)
> 150 mg/dL	4508	5736	0.80 (0.76-0.83)

CTT Collaborators. Lancet. 2010; 376:1670-1681.

Benefits for patients with CHD



Benefits for patients with DM



DM patient

每降低1mmol/L LDL-C
心血管疾病風險降低

21%

CTT Collaborators. Lancet. 2010; 376:1670-1681.

NCEP ATP III Guidelines 2004

Patient group	LDL-C treatment goal
CHD or CHD risk equivalents (10-year risk >20%) • very high risk*	<100 mg/dL <70 mg/dL
Multiple (2+) risk	
0–1 risk factor	

Very high risk

Established CVD +DM/metabolic syndrome/ACS

LDL-C <70 mg/dL

*For patients cons tegy'.

†Risk factors = cig HDL-C (<40 mg/dL), family hist gree relative <65 years), and age (r

- ***Very high risk***

  Established CVD *plus:*

  - Multiple major risk factors **(especially diabetes)**
  - Severe and poorly controlled risk factors
  - Multiple risk factors of the metabolic syndrome
  - Acute coronary syndromes

Grundy SM et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *Circulation.* 2004;110:227-239.

Updated European Guidelines: Task Force for the Management of Dyslipidaemias of the ESC and the EAS

Patient group	LDL-C treatment goal
Very high CV risk • **Established CVD**, **type 2 diabetes, type 1 diabetes** with target organ damage, moderate-to-severe CKD or a SCORE level of ≥10%	<1.8 mmol/L **(~<70 mg/dL)** and/or ≥50% reduction when target level cannot be reached
High CV risk • Markedly (<10%	mg/dL)
Moderate CV ri • SCORE le	mg/dL)

SCORE = Systemat

Very high risk

Established CVD /DM/CKD

LDL-C <70 mg/dL

European Association for Cardiovascular Prevention & Rehabilitation. 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). *Eur Heart J*. 2011;32(14):1769-1818.

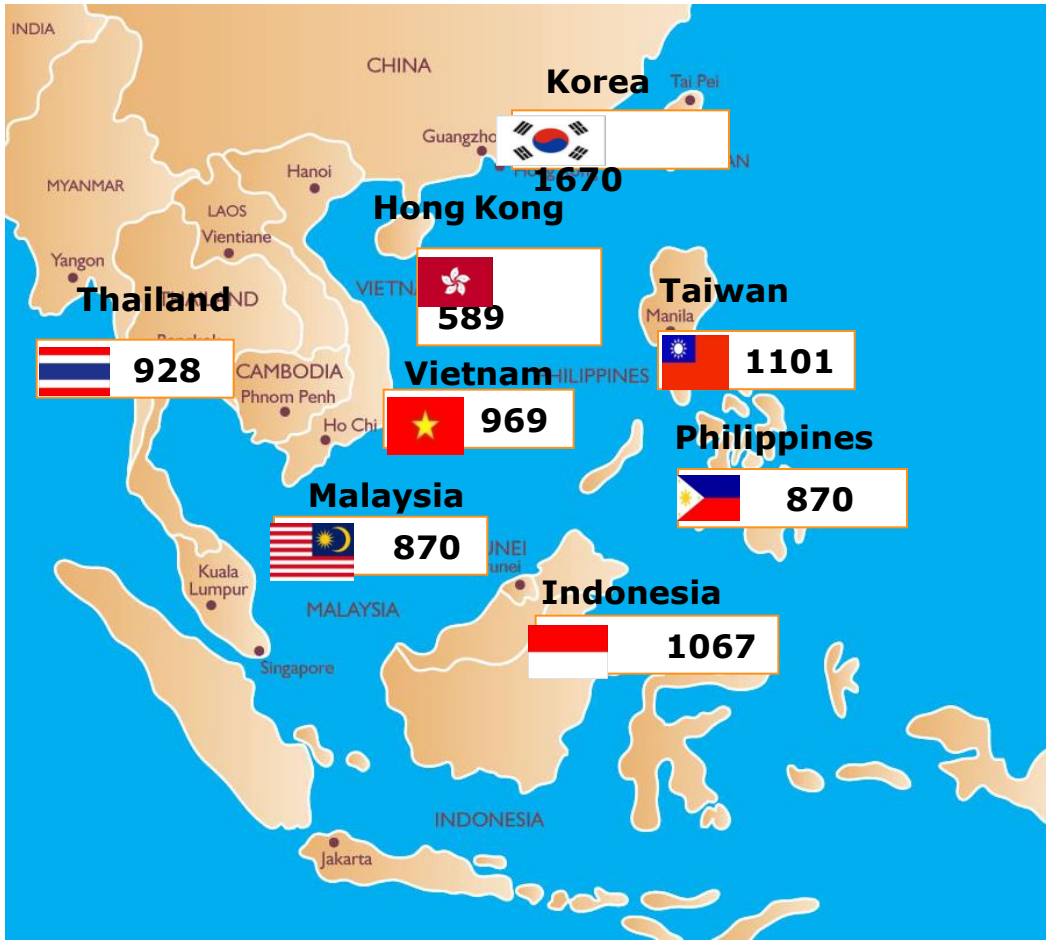
Summary

- High-risk patients need LDL<70 mg/dL (<1.8 mmol/L)
- 健保署於2013/8/1起實施新的血脂藥品給付規定， 最主要的改變包括：
  - 針對心血管疾病或糖尿病患者起始藥物治療血脂值由≧130mg/dl降為≧100mg/dl，血脂目標值＜100mg/dl
  - 刪除達到治療目標需 ”減量至最低有效劑量” 之規定

台灣目前的治療現況?

Pan Asian CEPHEUS—The Largest Survey of Its Kind Conducted in Asia

Total
8064
patients

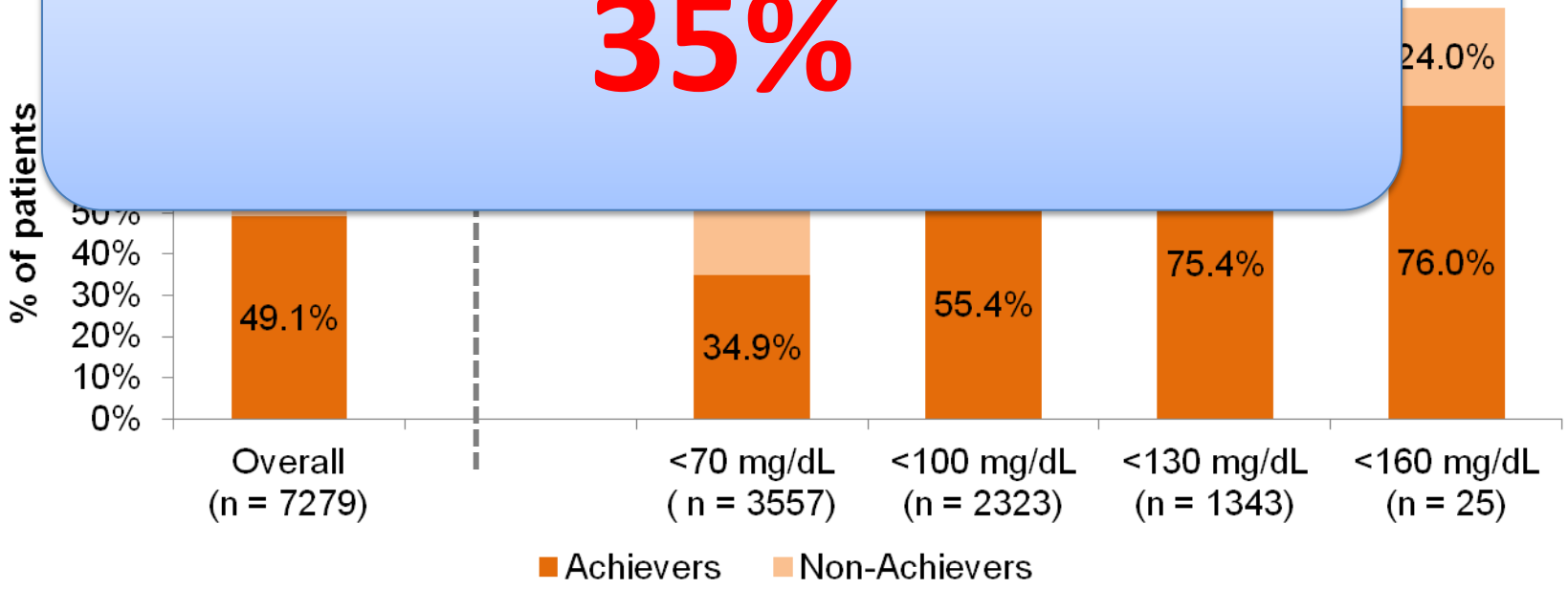


Park JE, Chiang CE, Munawar M, et al. Lipid-lowering treatment in hypercholesterolaemic patients: the CEPHEUS Pan-Asian survey. Eur J Prev Cardiol. 2012;19(4):781-794.

Proportion of Patients Attaining Their 2004 Updated NCEP ATP III-Recommended LDL-C Goals

Very high risk 病人達標率(LDL-C <70 mg/dL)只有

35%

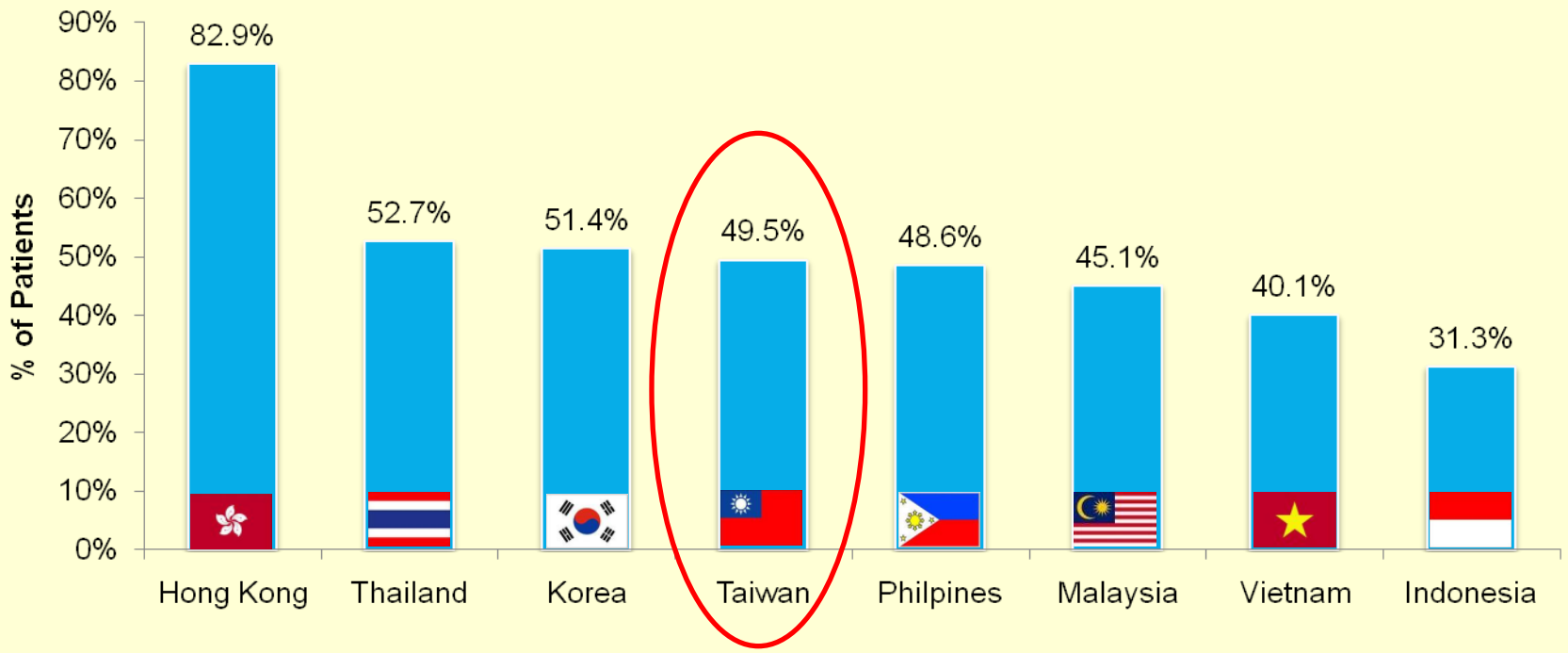


Overall 49.1% LDL-C goal attainment rate among all patients surveyed across Asia.
Proportion of patients attaining their respective LDL-C goal decreased with increasing cardiovascular risk.

Park JE, Chiang CE, Munawar M, et al. Lipid-lowering treatment in hypercholesterolaemic patients: the CEPHEUS Pan-Asian survey. Eur J Prev Cardiol. 2012;19(4):781-794.

Percentage of Patients at LDL-C goals recommended by the 2004 updated NCEP ATP III* guidelines

% of Patients at LDL-C goals recommended by 2004 updated NCEP ATP III* guidelines



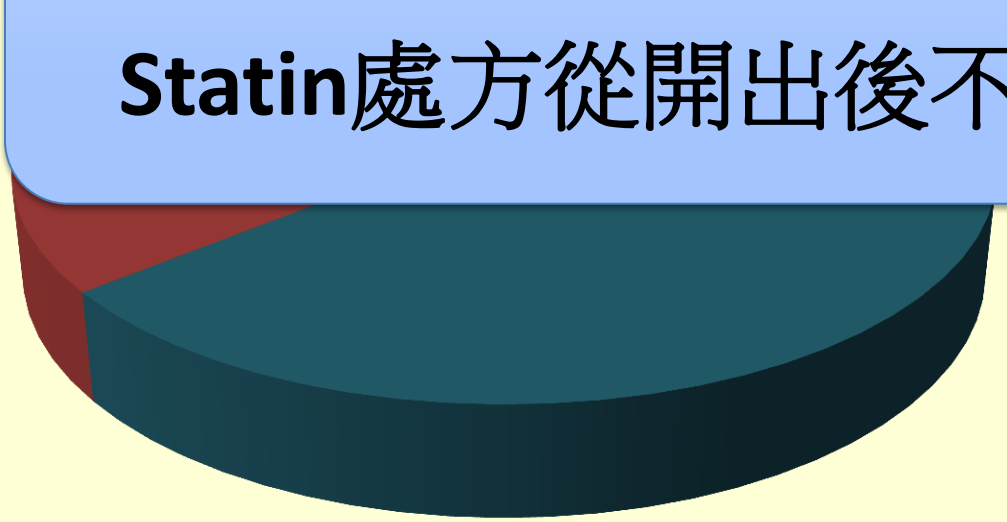
- **For patients in Hong Kong the treatment goal attainment rate was 82.9% while patients in other countries had very low LDL-C attainment rate (31.3 – 52.7%).**

Park JE, Chiang CE, Munawar M, et al. Lipid-lowering treatment in hypercholesterolaemic patients: the CEPHEUS Pan-Asian survey. Eur J Prev Cardiol. 2012;19(4):781-794.

Changes in the lipid-lowering drug since first prescribed a drug

65%

Statin處方從開出後不曾改變



Changed drug once or twice (n=1702)

Changed drug several times (n=246)

- For 64.1% of patients, initial treatment remained the same.

Park JE, Chiang CE, Munawar M, et al. Lipid-lowering treatment in hypercholesterolaemic patients: the CEPHEUS Pan-Asian survey. Eur J Prev Cardiol. 2012;19(4):781-794.

Initial statin potency were directly associated with goal attainment

Adjusted odds ratios for low-density lipoprotein cholesterol goal attainment among patients not at goal at baseline

Factor	Odds ratios (95% confidence interval)	P
Switched from initial statin (vs remained on initial statin)	0.859 (0.597-1.235)	0.4117
Up-titrated initial statin dose	1.015 (0.694-1.484)	0.9380
Down-titrated initial statin dose	1.254 (0.852-1.846)	0.2517

CHD = coronary heart disease; LDL-C = low density lipoprotein cholesterol

第一顆statin決定未來的達標

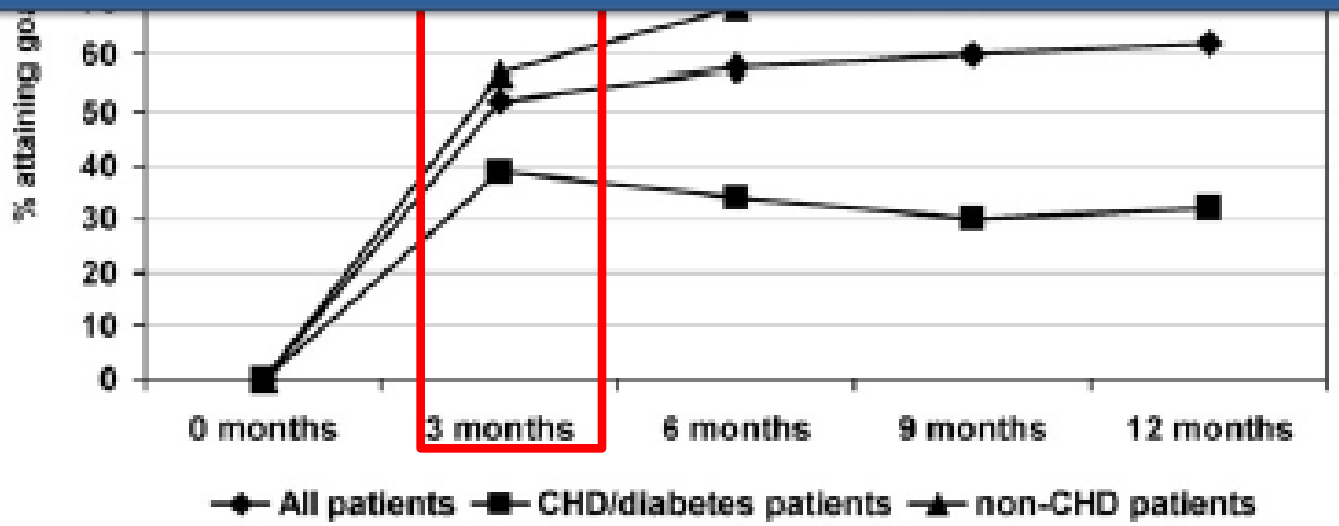
(起始治療選用的statin效能越高，達標率越高)

Curr Med Res Opin. 2008 Jul; 24(7): 1951-63

Turning Key to Get Goal

-把握前三個月黃金達標期，掌握先機

- 選擇高效能statin起始治療



Curr Med Res Opin. 2008 Jul; 24(7): 1951-63

如何一錠到底，一次到位

- ✓掌握前三個月的黃金治療期
- ✓協助病患達到血脂治療目標

Treat to Goal Vs. percentage reduction !

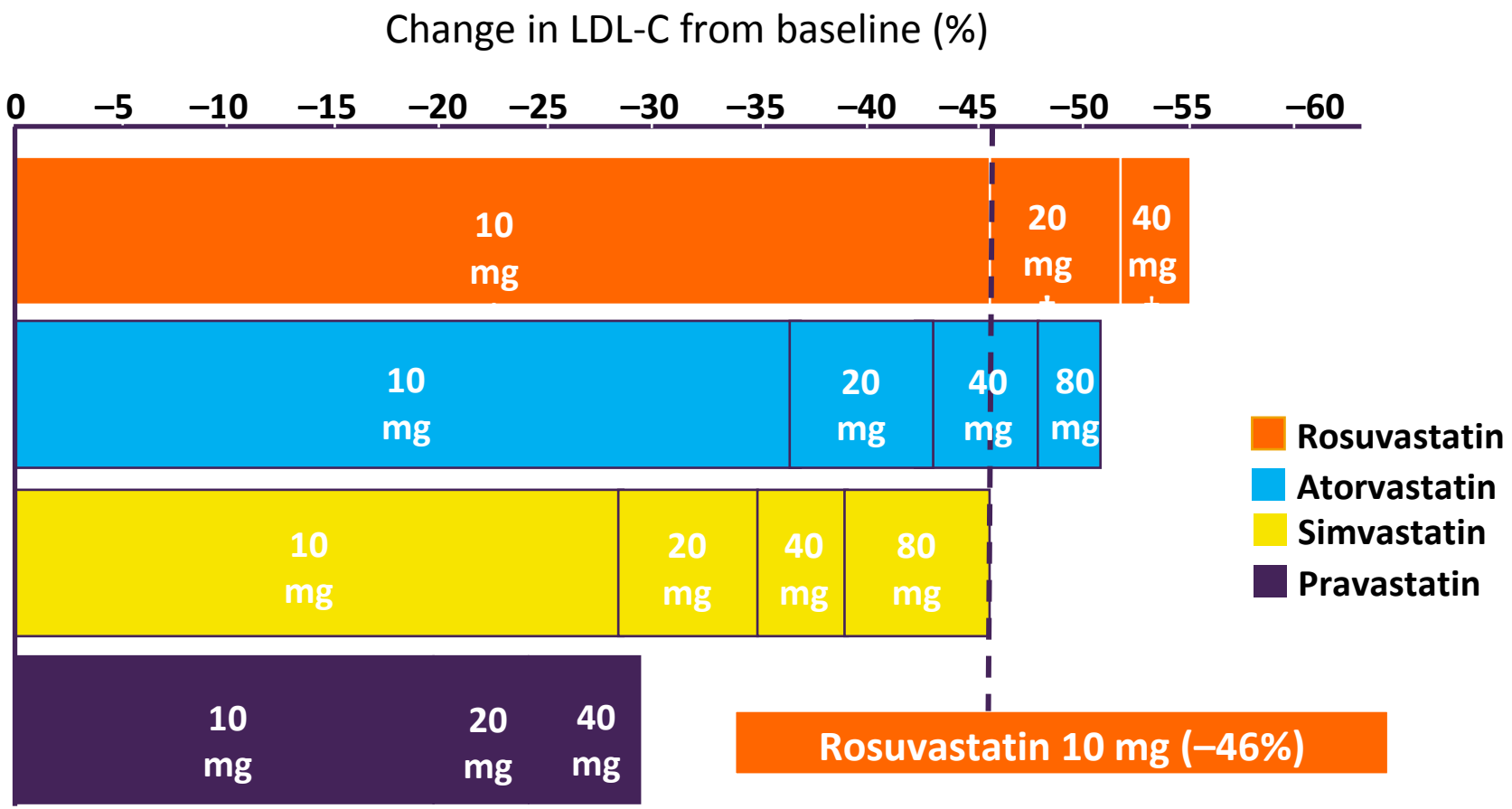
- LDL 160 --→ 100 mg/dL

  (160-100)/160 = 37.5%
  (moderate-intensity statin,
  e.g ATV 10-20 mg or RSV 5-10 mg)

- LDL 160-→ 70 mg/dL

  (160-70)/160 = 56.3%
  (high-intensity statin,
  eg. ATV 40-80 mg/dL or RSV 20-40 mg/dL)

選擇高效能statin協助病患一次達標



*p<0.002 vs atorvastatin 10 mg; simvastatin 10, 20, 40 mg; pravastatin 10, 20, 40 mg
†p<0.002 vs atorvastatin 20, 40 mg; simvastatin 20, 40, 80 mg; pravastatin 20, 40 mg
‡p<0.002 vs atorvastatin 40 mg; simvastatin 40, 80 mg; pravastatin 40 mg
Rosuvastatin 40mg & Atorvastatin 80mg is not available in Taiwan

Adapted from Jones PH et al. Am J Cardiol 2003;92:15

U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Home > Drugs > Drug Safety and Availability

Drugs

FDA Drug Safety Communication: New restrictions, contraindications, and dose limitations for Zocor (simvastatin) to reduce the risk of muscle injury

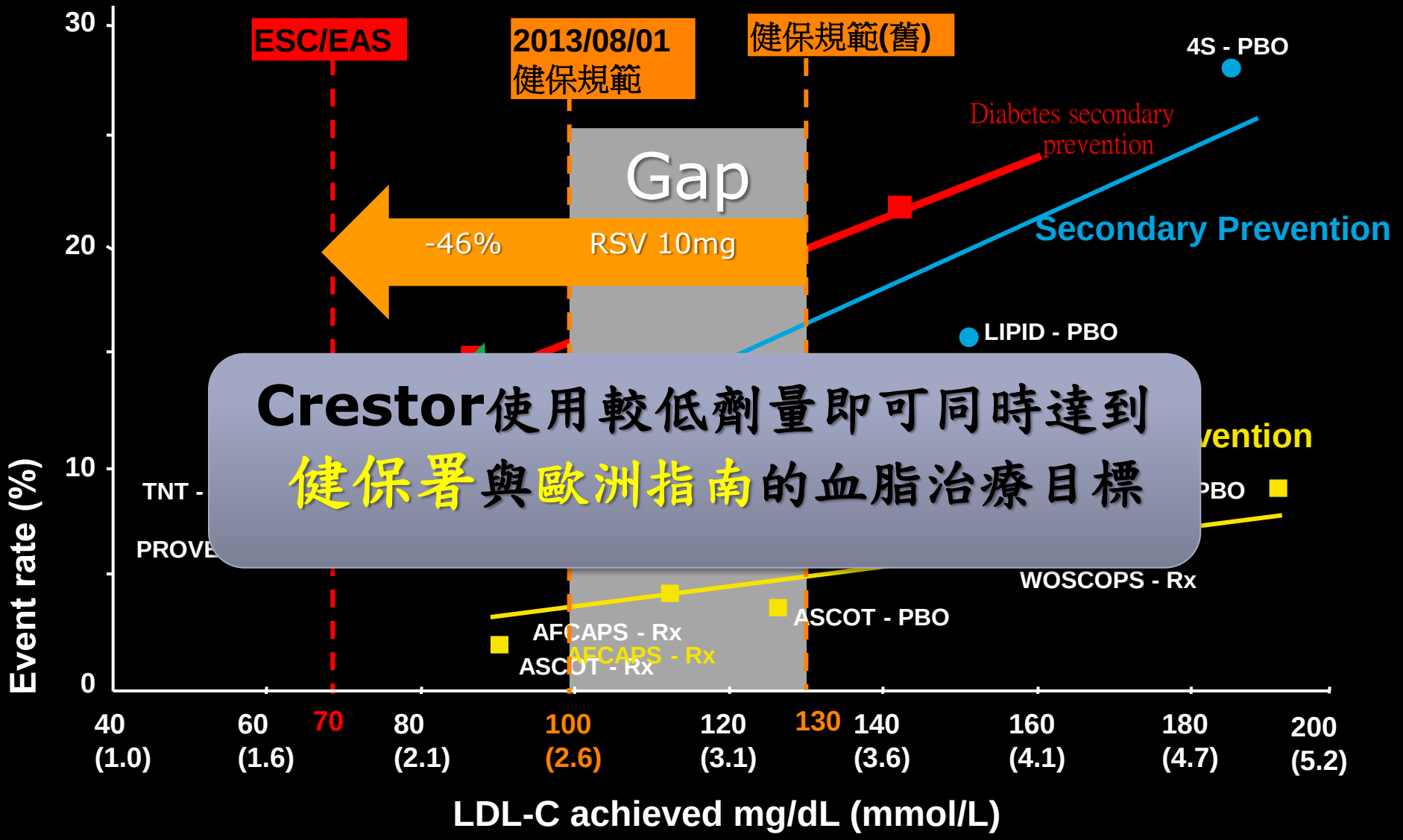
Safety Announcement

Relative LDL-lowering Efficacy of Statin and Statin-based Therapies

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%

Rosuva 10mg = atorva 40mg= simva 80mg

Patients with baseline LDL-C 100~130 mg/dL



Crestor使用較低劑量即可同時達到健保署與歐洲指南的血脂治療目標

Adapted from Rosensen, Exp Opin Emerg Drugs 2004;9:269;
LaRosa J et al, N Engl J Med, 2005;352:1425

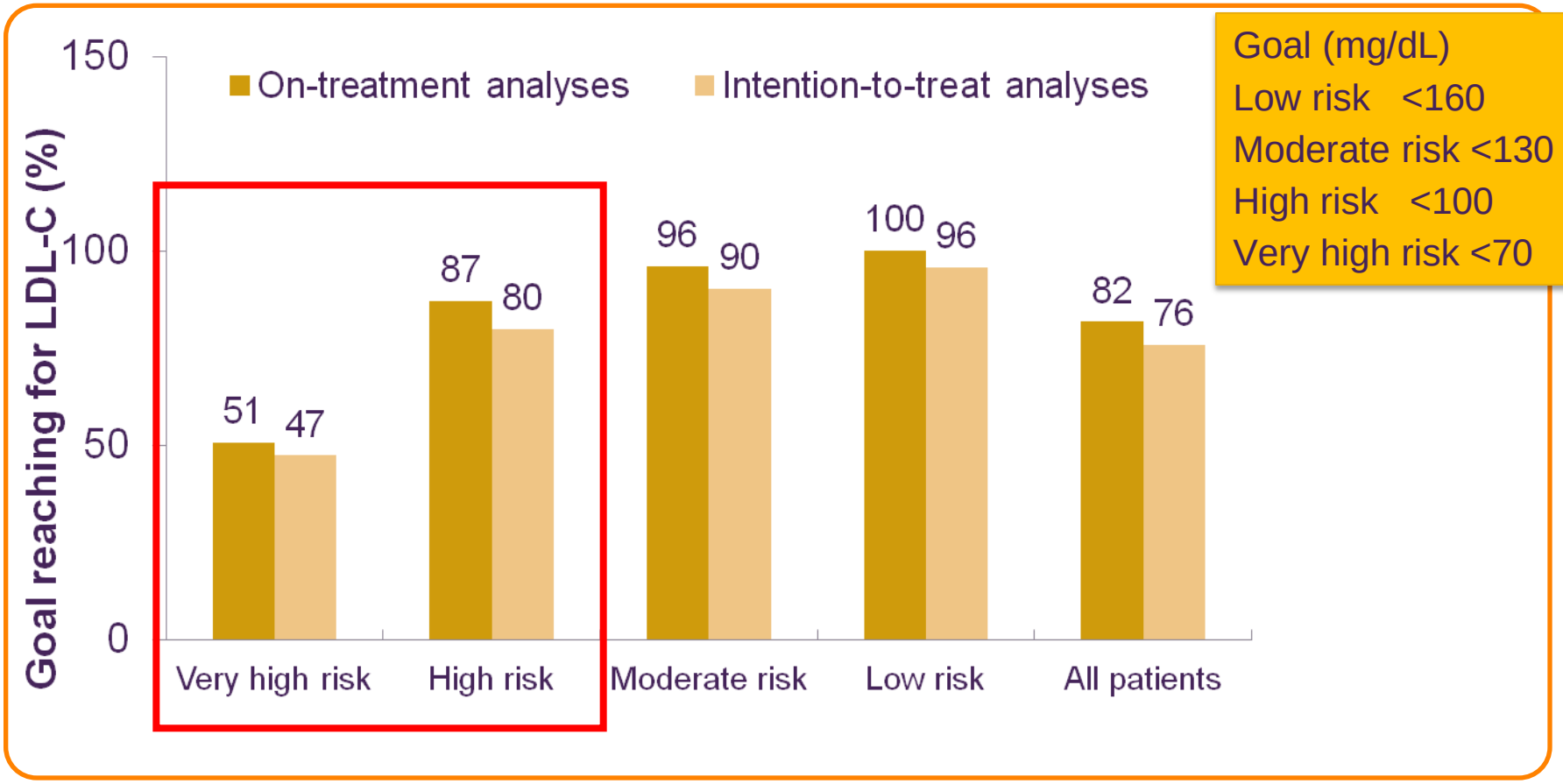
Statin Efficacy in diabetes patients to achieve LDL-C goal (T2DM)

	n	predicted probabilities	p-Value	Odds ratio	Lower CL	Upper CL
NCEP ATP III goal						
Rosuvastatin	239	87.28%				
Atorvastatin	1350	76.86%	<0.001	0.442	0.298	0.658
Simvastatin	546	68.66%	<0.001	0.275	0.180	0.420
Pravastatin	202	54.98%	<0.001	0.141	0.087	0.227
Lovastatin	332	55.30%	<0.001	0.143	0.091	0.224
Fluvastatin	61	61.26%	<0.001	0.189	0.095	0.375
NCEAP ATP III updated optional goals						
Rosuvastatin	244	82.16%				
Atorvastatin	1390	71.38%	<0.001	0.458	0.314	0.667
Simvastatin	570	63.67%	<0.001	0.293	0.195	0.438
Pravastatin	204	49.64%	<0.001	0.143	0.090	0.229
Lovastatin	341	49.64%	<0.001	0.143	0.092	0.222
Fluvastatin	61	57.16%	<0.001	0.208	0.106	0.409

CL=Confidence limit; NCEP ATP=National Cholesterol Education Program Adult Treatment Panel.

Adapted from Exp Opin Pharmacother 2008;9:669-76

Over 80% of Taiwan high risk patients can reach LDL-C goal 100mg/dl with rosuvastatin 10mg/day



Overall more than 75% of patients reached therapeutic goals with rosuvastatin therapy.

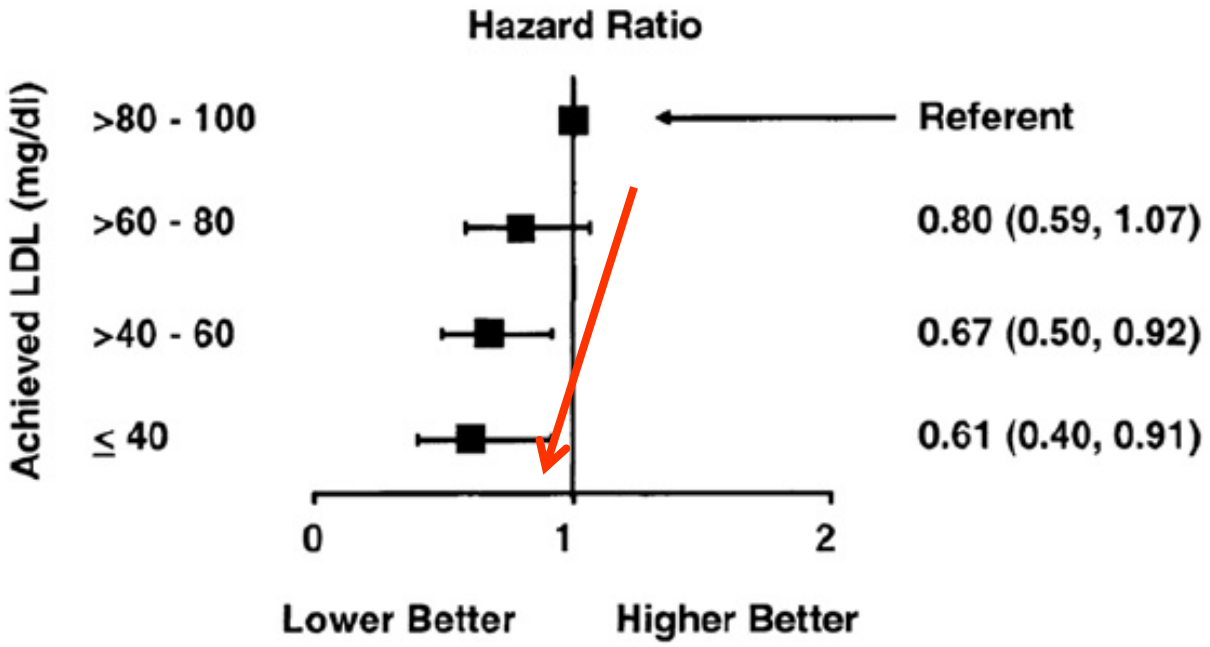
Adapted from Chiang CE, et al. J Chin Med Assoc. 2008;71:113–118.

Is lower still better if LDL-C<50mg/dL?

- ✓CV benefits
- ✓Safety

CV Benefit from PROVE IT study

Hazard Ratio for Primary Endpoint (PROVE IT-TIMI 22)



Wiviott SD, et al. J Am Coll Cardiol. 2005;46:1411-1416.

Safety from JUPITER study

Table 4 ALT or CK Elevation, Proteinuria, or Hematuria at Any Follow-Up Visit by Treatment Assignment and Attained LDL-C

	Placebo (n = 8,150)		Rosuvastatin: No LDL-C <50 mg/dl (n = 4,000)			Rosuvastatin: LDL-C <50 mg/dl (n = 4,154)			
	n	Rate	n	Rate	p Value vs. Placebo	n	Rate	p Value vs. Placebo	p Value vs. No LDL-C <50 mg/dl
ALT >3 × ULN	84	0.5	56	0.7	0.06	66	0.7	0.007	0.78
CK >10 × ULN	1	0.005	1	0.01	0.45	1	0.01	0.84	1.00
≥2+ proteinuria	387	2.2	210	2.5	0.01	251	2.6	0.13	0.29
≥2+ hematuria	531	3.0	295	3.6	0.008	346	3.7	0.003	0.56
eGFR change, ml/min/1.73 m^2, mean (SD)	−9.0 (13.5)		−9.1 (14.1)		0.004	−7.9 (13.1)		0.04	0.50

LDL-C<50 mg/dL 與LDL-C>50 mg/dL在**肌肉**、**肝臟**與**腎臟** 安全性相似

J Am Coll Cardiol 2011;57:1666–75)

ACC.12
61st Annual Scientific Session & Expo
ACC-i2 with TCT innovation in intervention

E1619
JACC March 27, 2012
Volume 59, Issue 13

Prevention

SAFETY PROFILE OF STATIN-TREATED PATIENTS WITH LDL-C < 30MG/DL

Background: While combinations of pharmacologic agents capable of reducing LDL-C well below recommended treatment guidelines are rapidly becoming available, safety and adverse event data in this setting is scarce.

Methods and Results: Of participants in the JUPITER trial with baseline LDL-C <130 mg/dL allocated to rosuvastatin 20 mg, 767 achieved at least one on-treatment LDLC <30 mg/dL during a median follow-up of 2 years, whereas 7,387 did not. Compared with participants with LDL ≥30 mg/dL on rosuvastatin, rates of any adverse event, myalgia, nervous system disorders, creatinine kinase elevations, liver function test abnormalities, or cancer were not significantly different among participants achieving LDL-C <30 mg/dL (all P values >0.05). In exploratory analyses evaluating a broad spectrum of potential adverse effects, an increase in total renal or urinary disorders was observed (adjusted relative risk (RR) 1.49, 95% CI 1.19-1.86) which appeared to primarily reflect an increase in hematuria (RR 2.20, 95% CI 1.47-3.28). Other hypothesis generating findings of uncertain pathobiology include possible increases in psychiatric (RR 1.43, 95% CI 1.09-1.88) and hepatobiliary disorders (RR 1.68, 95% CI 1.09-2.60).

Conclusions: In this post-hoc analysis of the JUPITER trial, achieving LDL-C levels <30 mg/dL appeared safe for the major side effects known to be associated with statin therapy. However, potential adverse effects on less well described pathways were suggested, indicating that close monitoring in future trials of very low LDL-C reduction is warranted.

Statin Safety Profile

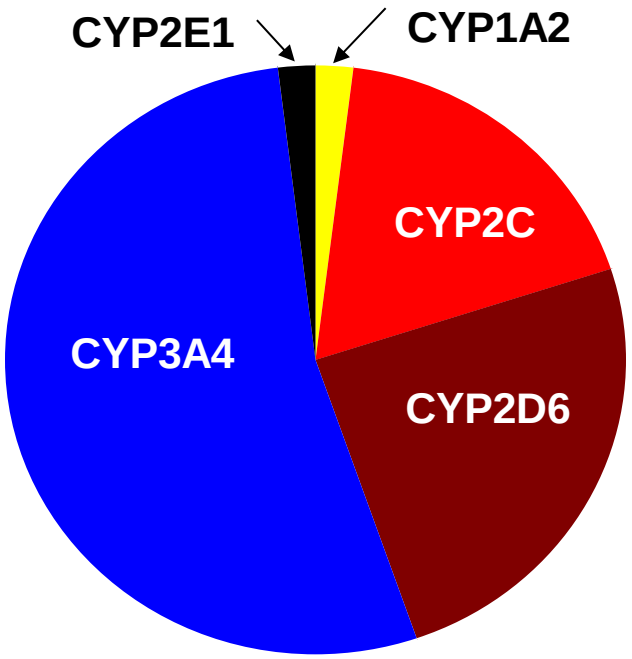
- ✓Drug- drug interaction
- ✓New-onset diabetes
- ✓LDL-C efficacy v.s. Dose

大部份的藥物是由 CYP3A4代謝

Relative Importance of P450s in Drug Metabolism

CYP3A4

- Simvastatin
- Atorvastatin
- Lovastatin
- Diltiazem
- Clopidogrel
- Amiodarone
- Cimetidine
- Ery/clarithromycin
- Ketoconazole
- Carbamazepine
- St John's wort
- Grapefruit juice



CPY2C9

- Rosuvastatin
- Fluvastatin
- Phenytoin
- Fluconazole
- Warfarin

Shimada T et al. *J Pharmacol Exp Ther* 1994;270(1):414.

藥物交互作用可能性

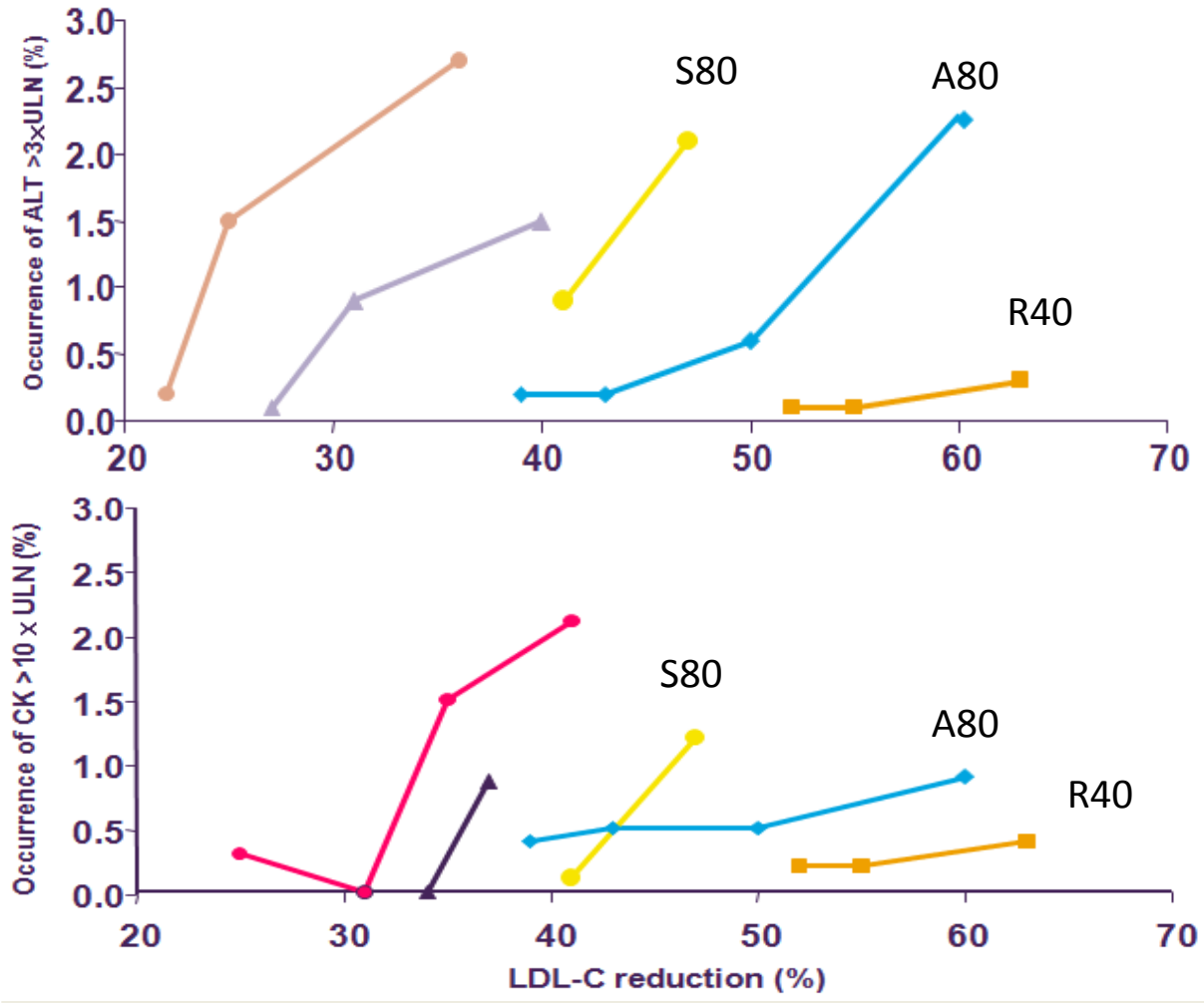
不同於某些statins藥物，CRESTOR與經由CYP 450 3A4代謝的藥物產生藥物交互作用的可能性較低

明顯經由 CYP450 3A4 代謝作用	
CRESTOR	no
atorvastatin	yes
simvastatin	yes
pravastatin	no

Reference:
1.Mc Taggart F et al. Am J Cardiol, 2001; 87(suppl): 288-328
2.Cziraky MJ et al. Am J Cardiol. 2001; 97(suppl): 61c-68c

Safety of Intensive-Dose Statin

Percentage changes in liver and muscle enzymes by percent LDL-C reduction[1]



Statin藥物不良反應發生率取決於藥物劑量，而非LDL-C efficacy

- Rosuvastatin (10, 20, 40 mg)
- Atorvastatin (10, 20, 40, 80 mg)
- Simvastatin (40, 80 mg)
- Lovastatin (20, 40, 80 mg)
- Fluvastatin (20, 40, 80 mg)
- Cerivastatin (0.2, 0.3, 0.4, 0.8 mg)
- Pravastatin (20, 40 mg)

Reference:
1. Davidson MH, Expert Opin Drug Saf 2004; 3(6): 547-557.
2. Jones P et al. Am J Cardiol 2003; 92: 152-160.

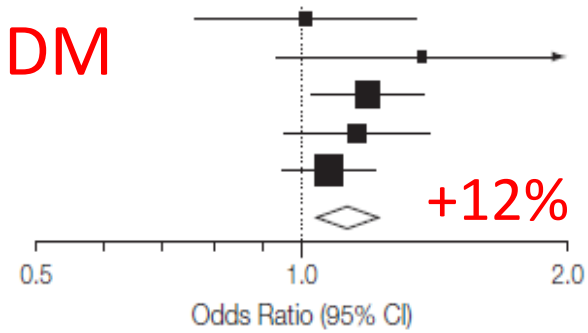
Rosuvastatin 40mg & Atorvastatin 80mg is not available in Taiwan

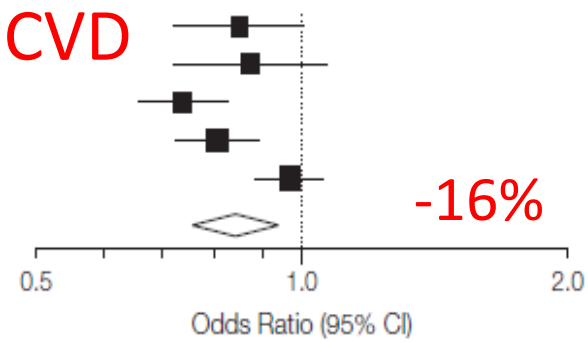
Statin-induced NODM: dose-dependent

Risk of Incident Diabetes With Intensive-Dose Compared With Moderate-Dose Statin Therapy

A Meta-analysis

	Cases/Total, No. (%)		
	Intensive Dose	Moderate Dose	OR (95% CI)
Incident Diabetes			
PROVE IT–TIMI 22,[18] 2004	101/1707 (5.9)	99/1688 (5.9)	1.01 (0.76-1.34)
A to Z,[17] 2004	65/1768 (3.7)	47/1736 (2.7)	1.37 (0.94-2.01)
TNT,[15] 2005	418/3798 (11.0)	358/3797 (9.4)	1.19 (1.02-1.38)
IDEAL,[16] 2005	240/3737 (6.4)	209/3724 (5.6)	1.15 (0.95-1.40)
SEARCH,[5] 2010	625/5398 (11.6)	587/5399 (10.9)	1.07 (0.95-1.21)
Pooled odds ratio	1449/16408 (8.8)	1300/16344 (8.0)	1.12 (1.04-1.22)
Heterogeneity: $I^2=0\%$; $P=.60$			
Incident CVD			
PROVE IT–TIMI 22,[18] 2004	315/1707 (18.4)	355/1688 (21.0)	0.85 (0.72-1.01)
A to Z,[17] 2004	212/1768 (12.0)	234/1736 (13.5)	0.87 (0.72-1.07)
TNT,[15] 2005	647/3798 (17.0)	830/3797 (21.9)	0.73 (0.65-0.82)
IDEAL,[16] 2005	776/3737 (20.8)	917/3724 (24.6)	0.80 (0.72-0.89)
SEARCH,[5] 2010	1184/5398 (21.9)	1214/5399 (22.5)	0.97 (0.88-1.06)
Pooled odds ratio	3134/16408 (19.1)	3550/16344 (21.7)	0.84 (0.75-0.94)
Heterogeneity: $I^2=74\%$; $P=.004$			

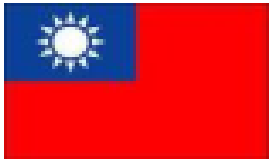




When expressed in absolute terms there was 1 additional case of diabetes for every 498 patients treated for 1 year compared with 1 fewer patient experiencing a cardiovascular event for every 155 patients treated for 1 year.

JAMA 2011;305:2556-64

Statins and New-Onset Diabetes: A Retrospective Longitudinal Cohort Study



Tsochiang Ma, PhD[1,*]; Liyun Tien, MHA[2]; Chih-Ling Fang, MPH[2]; Yi-Sheng Liou, MD[3,*]; and Gwo-Ping Jong, MD, PhD[4]

Patient with hypertension and dyslipidemia.
Follow-up:3.5 year

Drug Class	HR	95% CI	*P**
Pravastatin	1.30	1.13–1.56	0.0011
Fluvastatin	0.46	0.33–0.61	<0.0001
Lovastatin	0.70	0.59–0.83	<0.0001
Simvastatin	1.11	0.92–1.32	0.3028
Atorvastatin	1.15	0.96–1.35	0.5465
Rosuvastatin	0.54	0.39–0.76	0.0006

**P* values between NOD and non-NOD subjects.

Clin Ther. 2012 Sep;34(9):1977-83

The Long-Term Effect of Statins on the Risk of New-Onset Diabetes Mellitus in Elderly Taiwanese Patients with Hypertension and Dyslipidaemia

A Retrospective Longitudinal Cohort Study

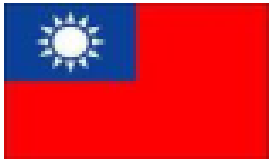
Tsochiang Ma,[1] Mu-Hsin Chang,[2] Liyun Tien,[3] Yi-Sheng Liou[4] and Gwo-Ping Jong[2]

Drug class	Adjusted[a]		
	HR	95% CI	p-Value[b]
Atorvastatin	0.77	0.72, 0.83	<0.0001
Lovastatin	1.36	1.24, 1.48	<0.0001
Simvastatin	1.30	1.14, 1.47	0.0001
Fluvastatin	1.00	0.87, 1.16	0.9510
Pravastatin	1.07	0.94, 1.23	0.3092
Rosuvastatin	0.66	0.52, 0.83	0.0006

Use vs non-use of the specified statin.

Drugs Aging. 2012;29:45-51

Comparison Among Statins



Parameter	Rosuva		Atorva		Prava		Fluva		Simva	
Half-life, h	19 (任何時間服用)		3~14 (任何時間服用)		1.8 (睡前服用)		1 (晚上服用)		3 (晚上服用)	
Metabolic enzyme (S, substrate; I, inhibitor)	2C9,2C19 (none)		3A4(S)		Sulfation (none)		2C9(I)		3A4(S)	
Food effect on bioavailability	None		↓13%		↓ 30%		↓15-25%		None	
Hepatoselectivity (log ratio)	3.3		2.2		3.3		1.3		0.54	
LDL-C reduction, %	*10 mg*	*46%*	10mg	37%	10mg	20%	80mg	30%	20mg	35%
	20mg	52%	20mg	43%	20mg	24%			40mg	39%
	40mg	55%	40mg	48%	40mg	30%			80mg	46%
HDL-C increase%	7.7%~10%		5.7%~2%		3.2%~5.5%		3.2%~5.5%		5.3%~6.8%	
TG reduction, %	20%~26%		20%~28%		8%~13%		8%~13%		11%~18%	
NHIA Price, NT$	*28(10mg)*		24.7(10mg) 42.2 (40mg)		28.3 (40mg)		21.1 (80mg)		36.4(40mg)	
Elimination, % Urine Feces	10 90		4 96		20 70		5 95		13 80	

Am J Med. 2004;116:408–416. Nicholis Sj. Et at. Am J Cardiol 2010; 105: 69-76. Data from different study

本比較表內之數據並非來源於單一試驗之直接比較，試驗間可能存在設計方法或患者特性等等不同。

Summary - Insights and Implications from NHI Lipid Guideline Change

- High-risk patients need LDL<70 mg/dL (<1.8 mmol/L)
- 健保署於2013/8/1起實施新的血脂藥品給付規定， 最主要的改變包括：
  - 針對心血管疾病或糖尿病患者起始藥物治療血脂值由≧130mg/dl降為≧100mg/dl，血脂目標值＜100mg/dl
  - 刪除達到治療目標需”減量至最低有效劑量” 之規定

ATV

RSV

- 根據研究顯示，使用CRESTOR能協助更多高危險病人群同時達到最新健保治療之LDL-C <100mg/dl與歐洲指南LDL-C <70mg/dl的目標。
- CRESTOR 以10mg的起始劑量即有優異的調控血脂效果，協助大多數患者達標，避免高劑量statin所產生的副作用


NEW
CHOLESTEROL
RECOMMENDATIONS
SOURCE:
AMERICAN HEART
ASSOCIATION
HEART DISEASE
DIABETES (TYPE 1 OR 2)
TAKE STATIN
10 YEAR RISK OVER 7.5%
BAD CHOLESTEROL OVER 190
CNN

AHA 2013 @ Dallas, Tx
New Cholesterol Guideline

10 Points to Remember on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

Provided by

AMERICAN COLLEGE *of* CARDIOLOGY

AHA/ACC 2013 New Cholesterol Guideline

- Level of evidence
- Who to Treat?
- Assess the Risk
- Intensity of Treatment?
- Non-Statin Lipid Lowering
- Target-based approach → Drug & Dose Approach
- Applying the guideline to specific patient groups

What's New?

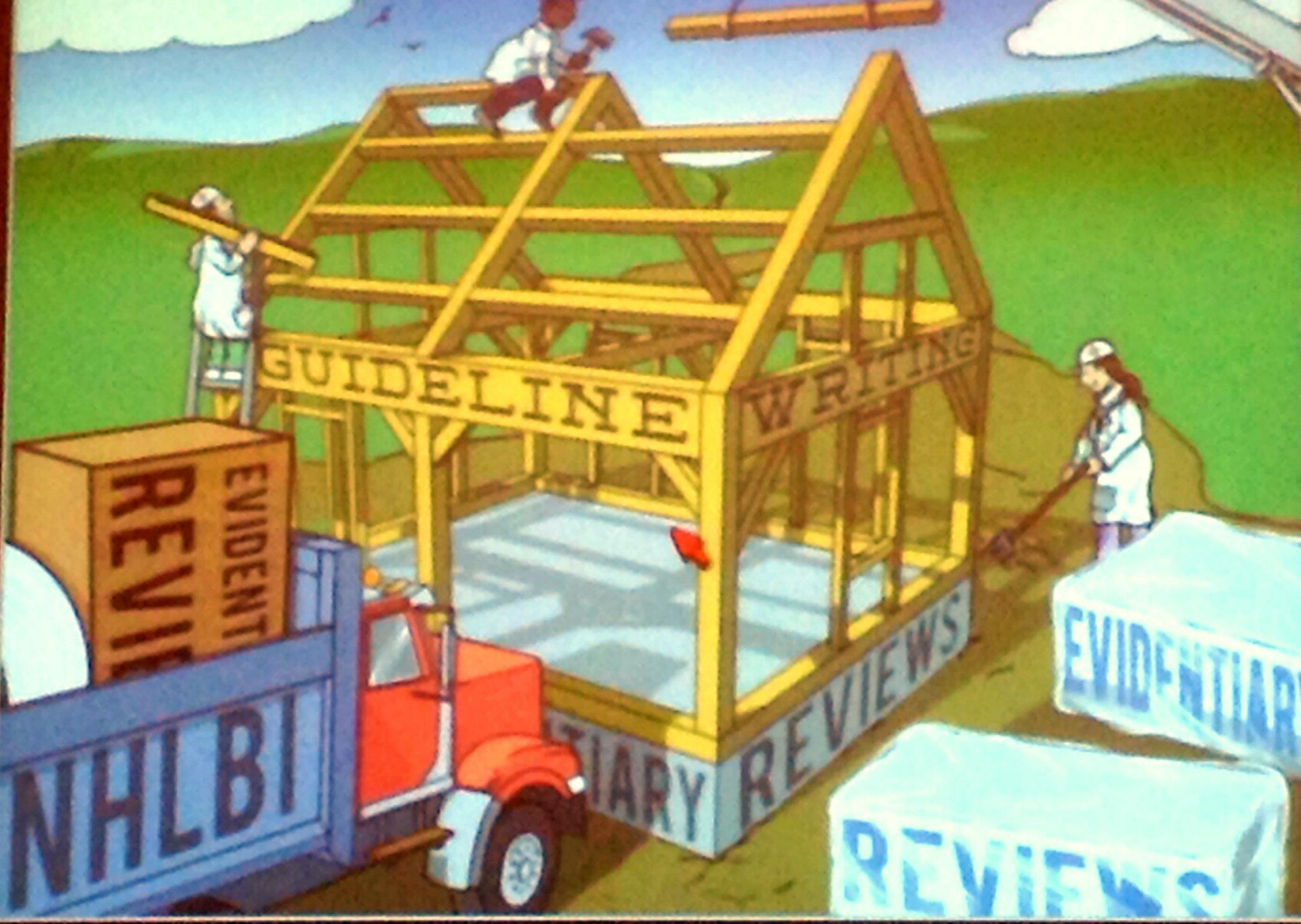
- New guidelines from the **American College of Cardiology** (ACC) and AHA, developed in conjunction with the **National Heart, Lung, and Blood Institute** (NHLBI), emphasized **abandoning** treating elevated LDL-cholesterol levels to a specific target, such as the older recommendations of <70 mg/dL or <100 mg/dL in secondary-prevention patients.
- Instead, the new guidelines emphasize treating risk, urging clinicians to treat patients with a moderate- or high-intensity statin depending on the patient's baseline risk for cardiovascular disease.


American
Heart
Association
SCIENTIFIC
SESSIONS
2013

Point 1

- The 2013 ACC/AHA Expert Panel included all 16 members of the National Heart, Lung, and Blood Institute (NHLI) Adult Treatment Panel (ATP) IV, and the document review included 23 expert reviewers and representatives of federal agencies.

- The expert panel recommendations arose from careful consideration of an extensive body of higher quality evidence derived from randomized controlled trials (RCTs), and systematic reviews and meta-analyses of RCTs.



Mike Mitka. *JAMA* August 14, 2013;310 (6):568-569

Point 2 Evidence-Based Medicine (EBM)

Through a rigorous process, four groups of individuals were identified for whom an extensive body of RCT evidence demonstrated a reduction in atherosclerotic cardiovascular disease (ASCVD) events (including coronary heart disease [CHD], cardiovascular deaths, and fatal and nonfatal strokes) with a good margin of safety from statin therapy:

Who To Treat? New US Guideline - 4 major Statin Benefit Groups

Group 1

Clinical ASCVD
CHD, Stroke and PAD
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)

Stone NJ, et al. J Am Coll Cardiol 2013 Nov. 7. Epub ahead of print

Point 2 (cont.)

Four Statin Benefit Groups:

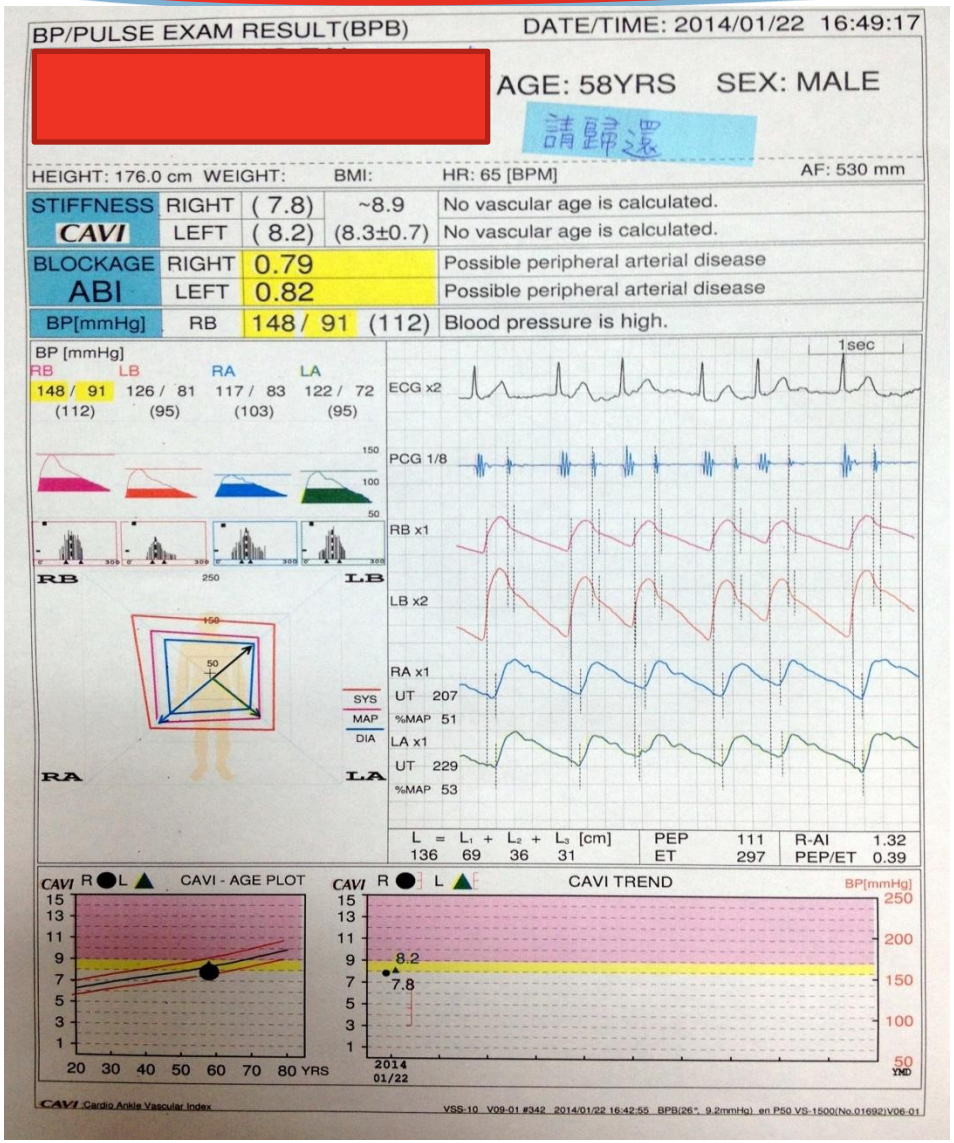
- Individuals **with clinical ASCVD** (acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin) without New York Heart Association (NYHA) class II-IV heart failure or receiving hemodialysis.

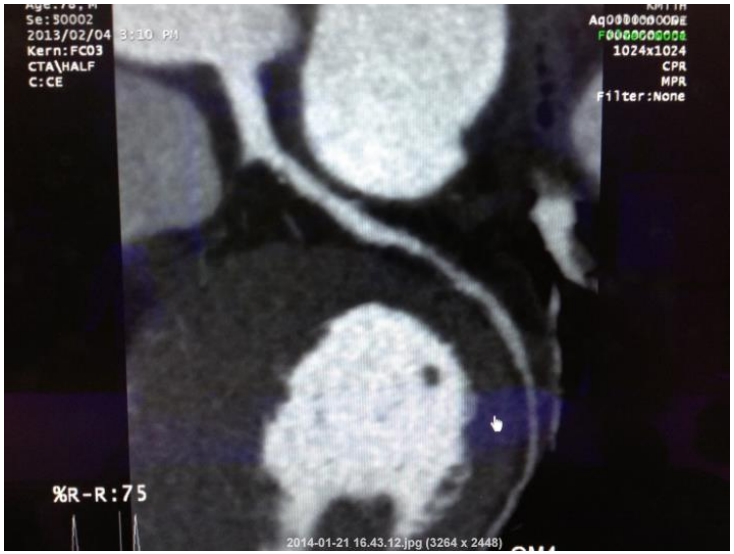
- Individuals with primary elevations of low-density lipoprotein cholesterol (LDL-C) ≥**190** mg/dl.

- Individuals 40-75 years of age with **diabetes**, and LDL-C 70-189 mg/dl without clinical ASCVD.

- Individuals without clinical ASCVD or diabetes, who are 40-75 years of age with LDL-C 70-189 mg/dl, and have an estimated **10-year ASCVD risk of 7.5% or higher.**

PAOD or statin-induced Myalgia?





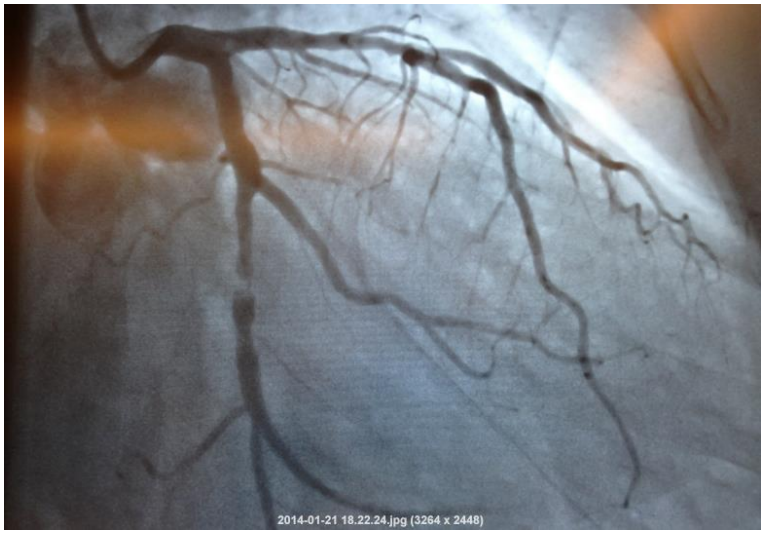


Figure 2. Major recommendations for statin therapy for ASCVD prevention

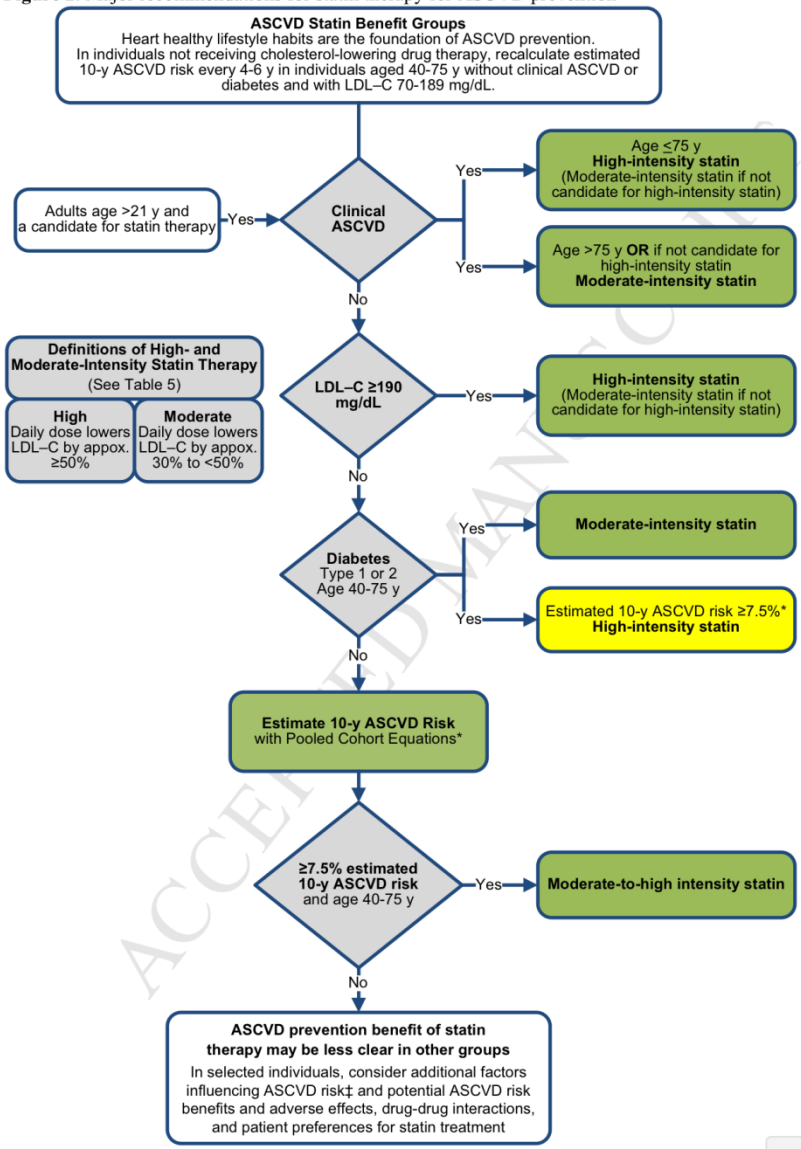
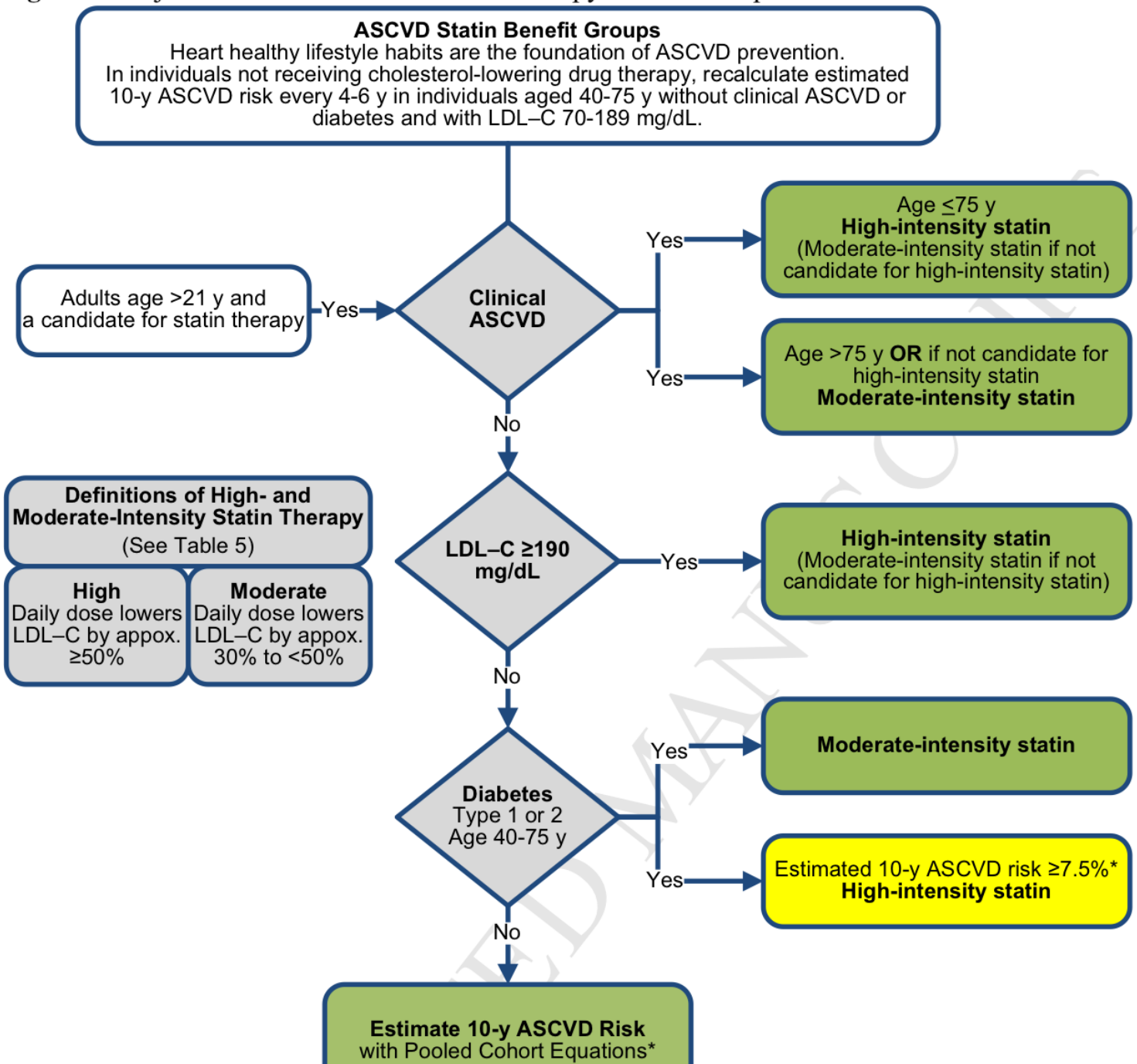
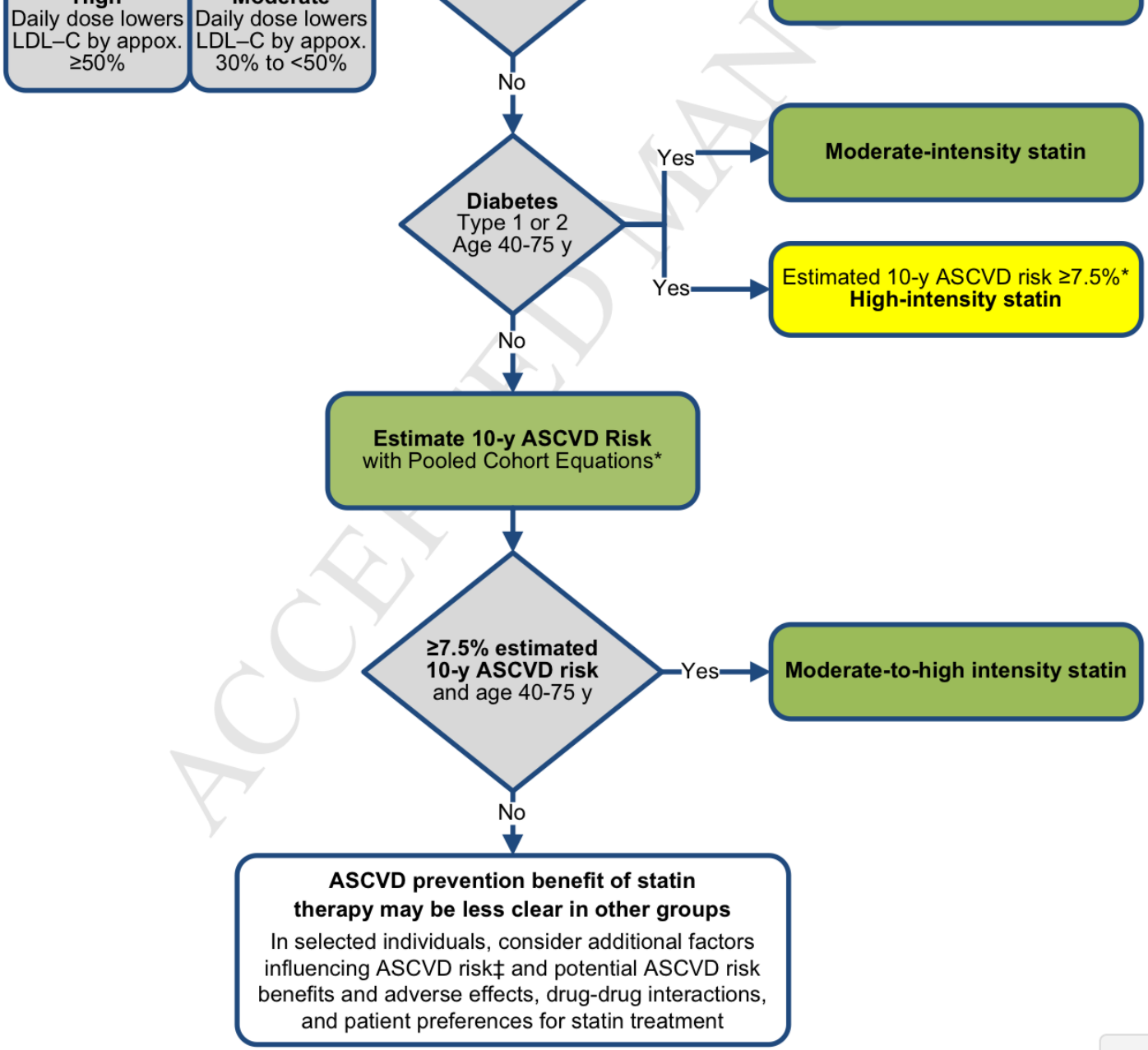


Figure 2. Major recommendations for statin therapy for ASCVD prevention





Point 3 全新的心血管風險計算工具

Individuals in the fourth group can be identified by using the new Pooled Cohort Equations for ASCVD risk prediction, developed by the Risk Assessment Work Group.

Download website:
http://my.americanheeart.org/cvriskcalculator

FRAMINGHAM RISK SCORE to predict 10 year ABSOLUTE RISK of CHD EVENT

ST ALBANS & HEMEL HEMPSTEAD NHS TRUST : CARDIOLOGY DEPARTMENT

This risk assessment only applies to assessment for **PRIMARY PREVENTION of CHD**, in people who do not have evidence of established vascular disease.
Patients who *already* have evidence of vascular disease usually have a >20% risk of further events of over 10 years, and require vigorous **SECONDARY PREVENTION**.
People with a Family History of premature vascular disease are at higher risk than predicted; Southern Europeans and some Asians may have a lower risk in relation to standard risk factors.

STEP 1: Add scores by sex for Age, Total Cholesterol, HDL-Cholesterol, BP, Diabetes and Smoking. (If HDL unknown, assume 1.1 in Males, 1.4 in Females)

Age	M	F
30-34	- 1	- 9
35-39	0	- 4
40-44	1	0
45-49	2	3
50-54	3	6
55-59	4	7
60-64	5	8
65-69	6	8
70-74	7	8

Total Cholesterol	M	F
< 4.1	- 3	- 2
4.1 – 5.1	0	0
5.2 – 6.2	1	1
6.3 – 7.1	2	1
7.2	3	3

HDL Cholesterol	M	F
< 0.9	2	5
0.9 - 1.16	1	2
1.17 - 1.29	0	1
1.30 - 1.55	0	0
≥1.56	- 2	- 3

Systolic BP	Diastolic BP				
Male	<80	80-84	85-89	90-99	≥100
<120	0	0	1	2	3
120-129	0	0	1	2	3
130-139	1	1	1	2	3
140-159	2	2	2	2	3
≥160	3	3	3	3	3
Female	<80	80-84	85-89	90-99	≥100
<120	- 3	0	0	2	3
120-129	0	0	0	2	3
130-139	0	0	0	2	3
140-159	2	2	2	2	3
≥160	3	3	3	3	3

If Systolic and Diastolic BP fall into different categories, use score from higher category

Diabetes	M	F
No	0	0
Yes	2	4

Smoking	M	F
No	0	0
Yes	2	2

Categorisation of 10 year Risk of CHD Event	
Very Low risk	< 10%
Low risk	< 15%
Moderate risk	15-20%
High risk	> 20%

STEP 2: Use total score to determine Predicted 10 year Absolute Risk of CHD Event (Coronary Death, Myocardial Infarction, Angina) by sex

Total Score	≤-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	3	14	15	16	≥17
10 year Risk: Male		<2%	3%	3%	4%	5%	7%	8%	10%	13%	16%	20%	25%	31%	37%	45%	53%	53%	53%	53%
10 year Risk: Female	<1%	2%	2%	2%	3%	3%	4%	4%	5%	6%	7%	8%	10%	11%	13%	15%	18%	20%	24%	27%

STEP 3: Compare Predicted 10 year Absolute Risk with "Average" and "Ideal" 10 year Risks, to give Relative Risks

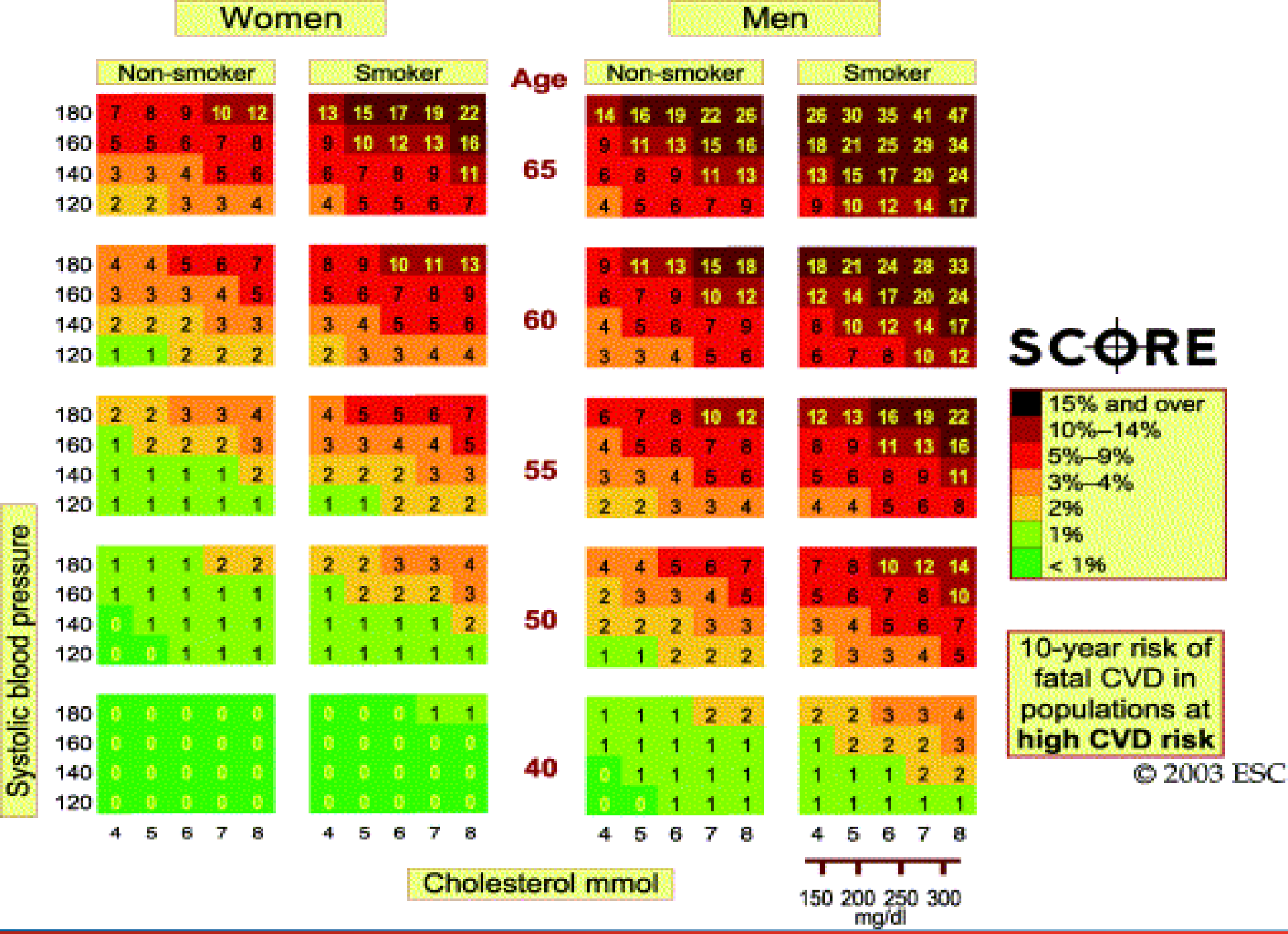
Age	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	65 - 69	70 - 74
"Average" Male	3%	5%	7%	11%	14%	16%	21%	25%	30%
"Ideal" Male	2%	3%	4%	4%	6%	7%	9%	11%	14%
"Average" Female	< 1%	< 1%	2%	5%	8%	12%	12%	13%	14%
"Ideal" Female	< 1%	1%	2%	3%	5%	7%	8%	8%	8%

"Ideal" risk represents
Total Cholesterol = 4.1 - 5.1
HDL = 1.2 (Male), 1.4 (Female)
BP < 120/80
No Diabetes, Non Smoker

People with an absolute risk of ≥20% should be considered for treatment: with a Statin to achieve a Total Cholesterol <5 and/or LDL cholesterol <3.2
with anti-hypertensives to achieve a BP ≤160/90 (ideally ≤140/80)

from Wilson PWF, et al Prediction of coronary heart disease using risk factor categories. Circulation 1998;97:1837-47

Dr John Bayliss


Women
Men
Non-smoker
Smoker
Non-smoker
Smoker
Age
65
60
55
50
40
180 160 140 120
7 8 9 10 12
5 5 6 7 8
3 3 4 5 6
2 2 3 3 4
13 15 17 19 22
9 10 12 13 16
6 7 8 9 11
4 5 5 6 7
14 16 19 22 26
9 11 13 15 16
6 6 9 11 13
4 5 6 7 9
26 30 35 41 47
18 21 25 29 34
13 15 17 20 24
9 10 12 14 17
4 4 5 6 7
3 3 3 4 5
2 2 2 3 3
1 1 2 2 2
8 9 10 11 13
5 6 7 8 9
3 4 5 5 6
2 3 3 4 4
9 11 13 15 18
6 7 9 10 12
4 5 6 7 9
3 3 4 5 6
18 21 24 28 33
12 14 17 20 24
8 10 12 14 17
6 7 8 10 12
2 2 3 3 4
1 2 2 2 3
1 1 1 1 2
1 1 1 1 1
4 5 5 6 7
3 3 4 4 5
2 2 2 3 3
1 1 2 2 2
6 7 8 10 12
4 5 6 7 8
3 3 4 5 6
2 2 3 3 4
12 13 16 19 22
8 9 11 13 16
5 6 8 9 11
4 4 5 6 8
1 1 1 2 2
1 1 1 1 1
0 1 1 1 1
0 0 1 1 1
2 2 3 3 4
1 2 2 2 3
1 1 1 1 2
1 1 1 1 1
4 4 5 6 7
2 3 3 4 5
2 2 2 3 3
1 1 2 2 2
7 8 10 12 14
5 6 7 8 10
3 4 5 6 7
2 3 3 4 5
0 0 0 0 0
0 0 0 0 0
0 0 0 0 0
0 0 0 0 0
0 0 0 1 1
0 0 0 0 0
0 0 0 0 0
0 0 0 0 0
1 1 1 2 2
1 1 1 1 1
0 1 1 1 1
0 0 1 1 1
2 2 3 3 4
1 2 2 2 3
1 1 1 1 2
1 1 1 1 1
4 5 6 7 8
Systolic blood pressure
Cholesterol mmol
150 200 250 300
mg/dl
SCORE
15% and over
10%–14%
5%–9%
3%–4%
2%
1%
< 1%
10-year risk of fatal CVD in populations at high CVD risk
© 2003 ESC

Why Pooled Cohort Equations?

- Framingham risk score: applied to non-hispanic whites, focus on coronary hard endpoints
- European SCORE
- Hispanic whites? Asians ?, American indians?

(IIb indication to use)

10 year ASCVD risk calculator (Pooled Cohort Equation)

Risk factor	
sex	M or F
age	years
Race	AA or WH
Total cholesterol	mg/dL
HDL-cholesterol	mg/dL
Systolic blood pressure	mmHg
Treatment of HT	Y or N
diabetes	Y or N
Smoker	Y or N

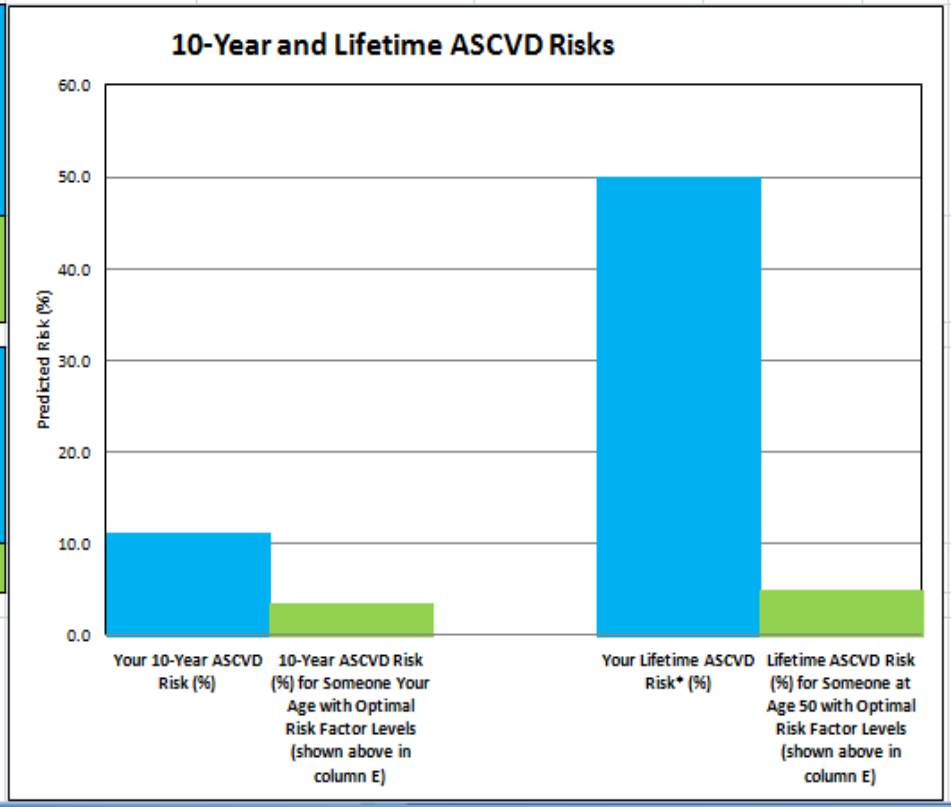
no family history,
no TG,
no WC or BMI

Hard end points: non-fatal MI, coronary death, fatal or non-fatal stroke

http://my.americanheart.org/cvriskcalculator

C5 fx WH

	A	B	C	D	E	F	H
1			Enter patient values in this column				
2	**Risk Factor**	**Units**	**Value**	Acceptable range of values	Optimal values		
3	**Sex**	M (for males) or F (for females)	M	M or F			
4	**Age**	years	55	20-79			
5	**Race**	AA (for African Americans) or WH (for whites or others)	WH	AA or WH			
6	**Total Cholesterol**	mg/dL	200	130-320	170		
7	**HDL-Cholesterol**	mg/dL	40	20-100	50		
8	**Systolic Blood Pressure**	mm Hg	120	90-200	110		
9	**Treatment for High Blood Pressure**	Y (for yes) or N (for no)	N	Y or N	N		
10	**Diabetes**	Y (for yes) or N (for no)	N	Y or N	N		
11	**Smoker**	Y (for yes) or N (for no)	Y	Y or N	N		
12							
13	**Your 10-Year ASCVD Risk (%)**	**11.3**					
14	10-Year ASCVD Risk (%) for Someone Your Age with Optimal Risk Factor Levels (shown above in column E)	**3.6**					
15							
16	**Your Lifetime ASCVD Risk* (%)**	**50.0**					
17	Lifetime ASCVD Risk (%) for Someone at Age 50 with Optimal Risk Factor Levels (shown above in	**5.0**					
18							



*This is the lifetime ASCVD risk for an individual at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from different approaches. While 10-year risk

Point 4 Therapeutic Lifestyle Modification

- Lifestyle modification
  (i.e., adhering to a heart healthy diet, regular exercise habits, avoidance of tobacco products, and maintenance of a healthy weight)
  ---- > remains a critical component of health promotion and ASCVD risk reduction, both prior to and in concert with the use of cholesterol-lowering drug therapies.

Point 5 No LDL Goal, Non-Statin Therapy?

- There is no evidence to support continued use of specific LDL-C and/or non–high-density lipoprotein cholesterol (non–HDL-C) treatment targets.

- The appropriate intensity of statin therapy should be used to reduce risk in those most likely to benefit.

- Non-statin therapies, whether alone or in addition to statins, do not provide acceptable ASCVD risk reduction benefits compared to their potential for adverse effects in the routine prevention of ASCVD.

Statin-intensity groups

- High-intensity: on average lowers LDL–C by approximately ≥50%,
- Moderate-intensity: lowers LDL–C by approximately 30% to <50%,
- Lower-intensity: lowers LDL–C by <30%

High - Moderate - and Low - Intensity Statin Therapy

Statin in bold were evaluated in randomized controlled trials; those in *italic* were not

Table 5. High- Moderate- and Low-Intensity Statin Therapy (Used in the RCTs reviewed by the Expert Panel)*

High-Intensity Statin Therapy	Moderate-Intensity Statin Therapy	Low-Intensity Statin Therapy
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*

Specific statins and doses are noted in bold that were evaluated in RCTs (17,18,46-48,64-67,69-78) included in CQ1, CQ2 and the CTT 2010 meta-analysis included in CQ3 (20). All of these RCTs demonstrated a reduction in major cardiovascular events. Statins and doses that are approved by the U.S. FDA but were not tested in the RCTs reviewed are listed in *italics*.

*Individual responses to statin therapy varied in the RCTs and should be expected to vary in clinical practice. There might be a biologic basis for a less-than-average response.

†Evidence from 1 RCT only: down-titration if unable to tolerate atorvastatin 80 mg in IDEAL (47).

‡Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.

Lipid Trials Published Since 2002

- Major Statin Trials
  - HPS
  - PROVE-IT, A to Z
  - ALLHAT
  - PROSPER
  - ASCOT-LLA
  - MEGA
  - TNT, IDEAL
  - CORONA, GSSI
  - JUPITER
  - 4D, AURODA, SHARP
  - SPARCL
- NonStatin Trials
  - FIELD
  - ACCORD
  - AIM-HIGH
  - HPS-THRIVE
  - Awaiting **IMPROVE-IT**

Clinical trials of fibrates & niacin in the statin era

- **FIELD Trial**
  - *No benefit of fenofibrate on cardiac death + MI in 9,765 patients with diabetes followed for 5 years*
- **ACCORD Lipid Trial**
  - *No benefit of fenofibrate added to simvastatin on cardiac death, MI and stroke in 5,518 patients followed for 4.7 years*
- **AIM-HIGH**
  - *No benefit of niacin added to high-dose simvastatin in 3,414 patients with CAD followed for 3 years*
- **HPS2-THRIVE**
  - *No benefit of niacin/laropiprant added to simvastatin in 25,673 high-risk patients followed for 3.9 years*

Point 6 Risk-engine Categories by PCE

This guideline recommends use of the new Pooled Cohort Equations (PCE) to estimate 10-year ASCVD risk in both white and black men and women.

By more accurately identifying higher risk individuals for statin therapy, the guideline focuses statin therapy on those most likely to *benefit*.

It also indicates, based on RCT data, those high-risk groups that may not benefit.

Table 2. What's New in the Guideline?*

1	***Focus on ASCVD Risk Reduction: 4 statin benefit groups*** • Based on a comprehensive set of data from RCTs that identified 4 statin benefit groups which focus efforts to reduce ASCVD events in secondary and primary prevention. • Identifies high-intensity and moderate-intensity statin therapy for use in secondary and primary prevention.
2	***A New Perspective on LDL–C and/or Non-HDL–C Treatment Goals*** • The Expert Panel was unable to find RCT evidence to support continued use of specific LDL–C and/or non-HDL–C treatment targets. • The appropriate intensity of statin therapy should be used to reduce ASCVD risk in *those most likely to benefit*. • Nonstatin therapies do not provide acceptable ASCVD risk reduction benefits compared to their potential for adverse effects in the routine prevention of ASCVD.
3	***Global Risk Assessment for Primary Prevention*** • This guideline recommends use of the new Pooled Cohort Equations to estimate 10-year ASCVD risk in both white and black men and women. • By more accurately identifying higher risk individuals for statin therapy, the guideline focuses statin therapy on *those most likely to benefit*. • It also indicates, based on RCT data, those high-risk groups that may not benefit. • Before initiating statin therapy, this guideline recommends a discussion by clinician and patients.
4	***Safety Recommendations*** • This guideline used RCTs to identify important safety considerations in individuals receiving treatment of blood cholesterol to reduce ASCVD risk. • Using RCTs to determine statin adverse effects facilitates understanding of the net benefit from statin therapy. • Provides expert guidance on management of statin-associated adverse effects, including muscle symptoms.
5	***Role of Biomarkers and Noninvasive Tests*** • Treatment decisions in selected individuals who are not included in the 4 statin benefit groups may be informed by other factors as recommended by the Risk Assessment Work Group guideline.

Not in the 4 major statin benefit groups- additional factors

- primary LDL–C ≥160 mg/dL or other evidence of genetic hyperlipidemias,
- 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
- hs-CRP >2 mg/L,
- CAC score ≥300 Agatston units
- ABI <0.9
- or elevated lifetime risk of ASCVD.

Carotid Intima Thickness (Carotid IMT) is NOT included/recommended!!!

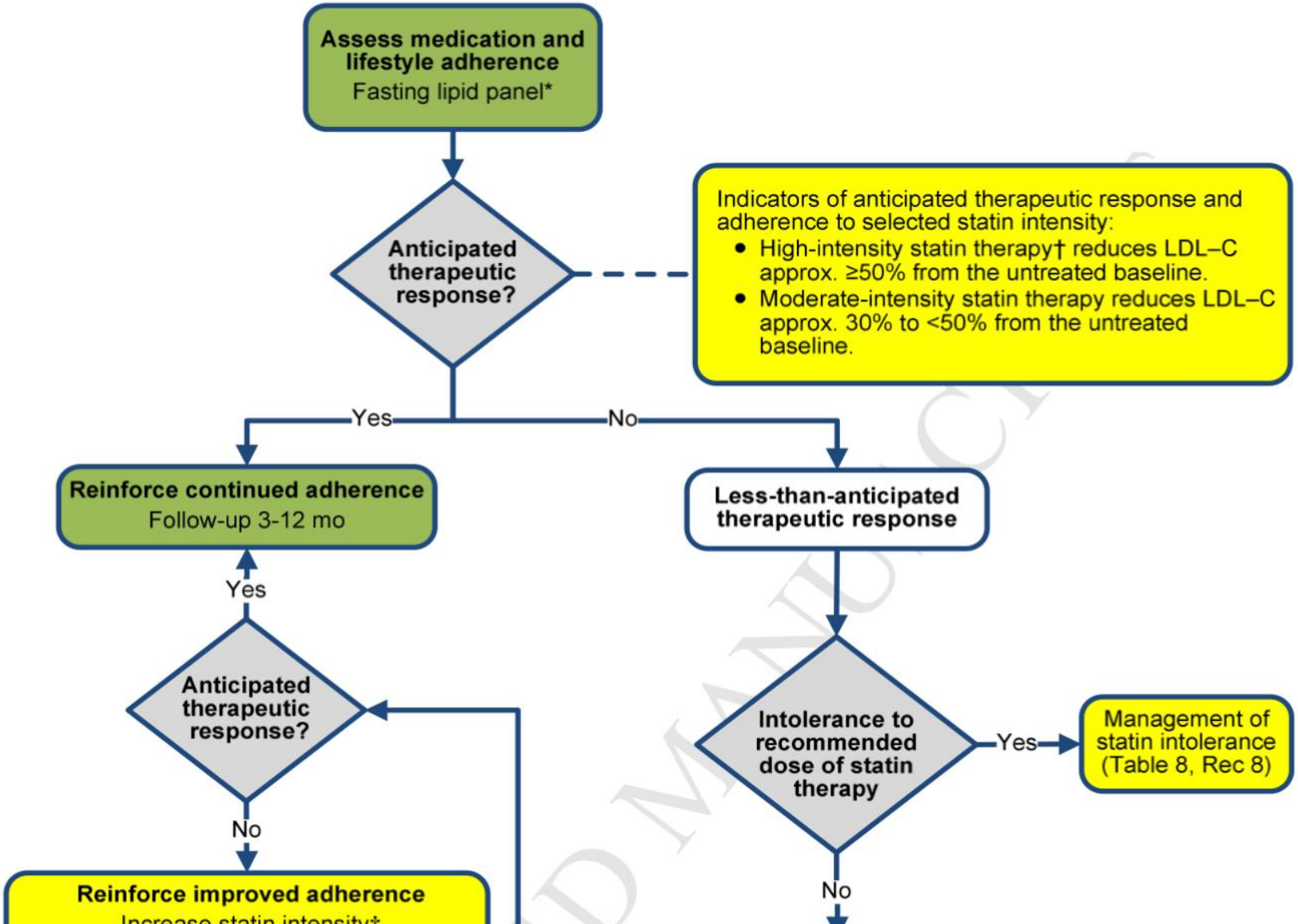
Additional factors

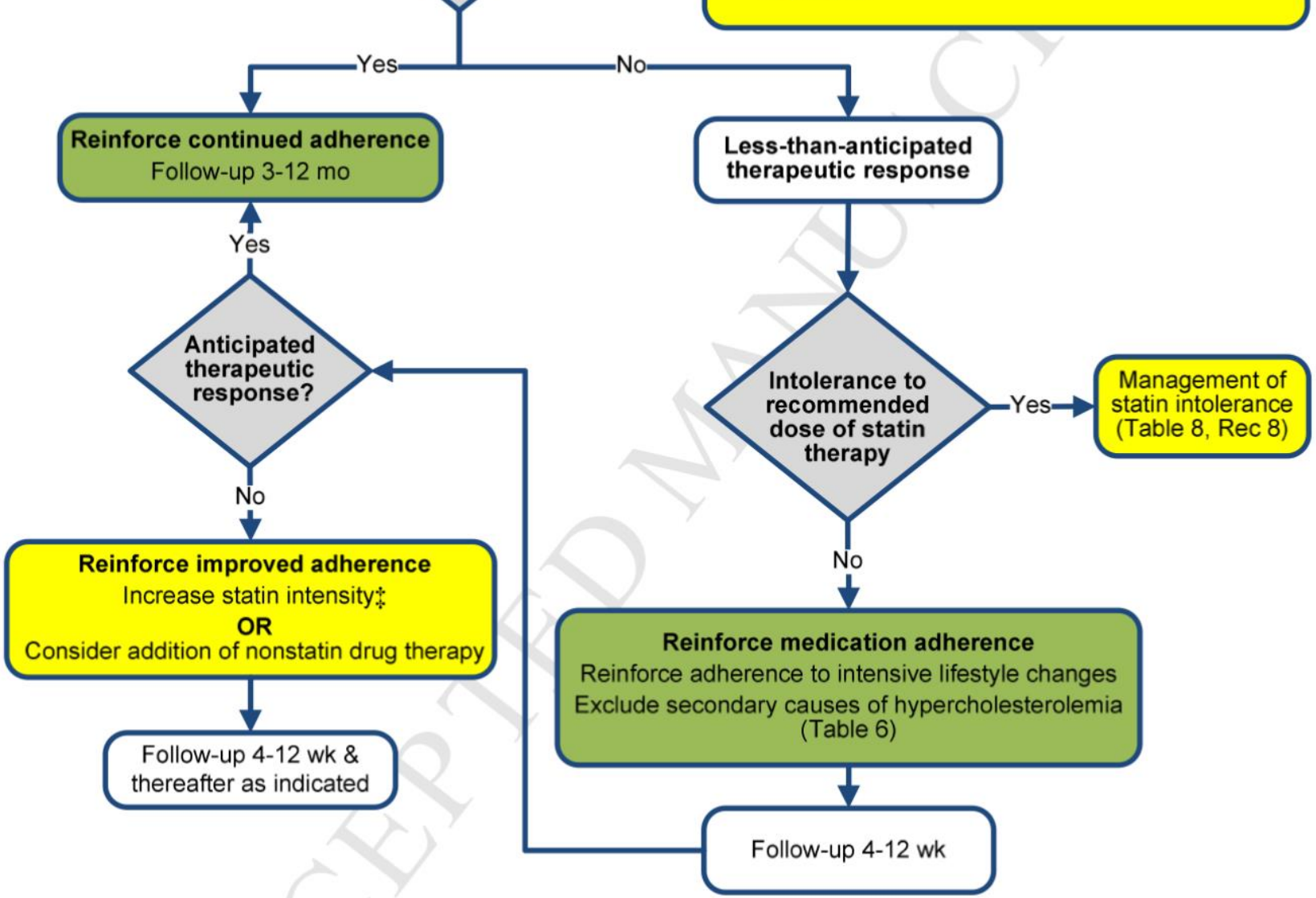
根據2013 ACC/AHA 新血脂治療指引準則，不符合四大重點治療族群的患者，臨床醫師可以參考其他因子，包括：

Measure	Support Revising Risk Assessment Upward	Do Not Support Revising Risk Assessment
Family history of premature CVD	Male <55 years of age Female <65 years of age (1st degree relative)	Occurrences at older ages only (if any)
hs-CRP	≥2 mg/L	<2 mg/L
CAC score	≥300 Agatston units or ≥75th percentile for age, sex, and ethnicity*	<300 Agatston units and <75 percentile for age, sex, and ethnicity*
ABI	<0.9	≥0.9

Carotid Intima Thickness (Carotid IMT) is NOT included/recommended

Figure 5. Statin Therapy: Monitoring therapeutic response and adherence





Colors correspond to the class of recommendations in the ACC/AHA Table 1.

*Fasting lipid panel preferred. In a nonfasting individual, a nonfasting non-HDL–C >220 mg/dL may indicate genetic hypercholesterolemia that requires further evaluation or a secondary etiology. If nonfasting triglycerides are >500 mg/dL, a fasting lipid panel is required.

†In those already on a statin, in whom baseline LDL–C is unknown, an LDL–C <100 mg/dL was observed in most individuals receiving high-intensity statin therapy in RCTs.

‡See Section 6.3.1.

Point 7

- No recommendations are made to inform treatment decisions in selected individuals who are not included in the four statin benefit groups.

- In these individuals whose 10-year risk is <7.5% or when the decision is unclear, other factors including :
  - family history of premature ASCVD,
  - LDL-C >160 mg/dl,
  - high-sensitivity C-reactive protein ≥2 mg/dl,
  - coronary calcium score ≥300 Agatston units or ≥75th percentile for age, sex, ethnicity,
  - ankle-brachial index <0.9, or
  - elevated lifetime risk of ASCVD ;

  …..may be used to enhance the treatment decision making.

Point 8

- High-intensity statin therapy is defined as a daily dose that lowers LDL-C by ≥50% and moderate-intensity by 30% to <50%.

- All patients with ASCVD who are age ≤75 years, as well as patients >75 years, should receive high-intensity statin therapy;

- if not a candidate for high-intensity, should receive moderate-intensity statin therapy.

Point 9

- Those with an LDL-C ≥190 mg/dl should receive high-intensity or moderate-intensity statin therapy, if not a candidate for high-intensity statin therapy.

- Addition of other cholesterol-lowering agents can be considered to further lower LDL-C.

- Diabetes with a 10-year ASCVD ≥7.5% should receive high-intensity statins and <7.5% moderate-intensity statin therapy.

- Persons 40-75 years with a ≥7.5% 10-year ASCVD risk should receive moderate- to high-intensity statin therapy.

Point 10

- The following are **no** longer considered appropriate strategies: **treat to target, lower is best.**

- The new guideline recommends: treat to level of ASCVD risk, based upon **estimated 10-year or** lifetime risk of ASCVD.

- The guidelines provided **no** recommendations for initiating or discontinuing statins in NYHA class II-IV ischemic systolic heart failure patients or those on maintenance hemodialysis.

Conclusion

- The new US cholesterol guidelines are designed o target patients at higher risk who have been shown in clinical trials to benefit from statin
- The 4 groups are patients with known ASCVD, patients with diabetes, patient with very high-LDL-C, and patients with a 10-year risk score of more than 7.5%
- High-intensity statin therapy (atorvastatin 40-80 mg or rosuvastatin 20-40 mg) is recommended for most of hose patients; moderate-intensity for the remainder
- Treatment target have been eliminated
- The guideline emphasize that treatment decisions must be based on a physician-patient discussion, and that treatment maybe indicated for some patients not in the 4 categories.

Insight & Implication

- Identify Four statin-benefit groups and using high- or moderate-intensity statin
- Statin is favored, not only for lipid-lowering, but for atherosclerotic risk cutting
- Regular lipid profile monitoring is not recommended as routine because target goal is no longer existed
- Surrogate markers, e.g. hs-CRP or CAC, are not advocated and their use should be reduced
- New Pool Cohort Equation might increase statin user
- ApoB? Small dense LDL? Electronegative LDL?
- What to monitor? Patient adherence? Adverse effect?
- Let's build our own risk-engine categories, guideline & consensus

NEW TAIWAN NHI GUIDELINE (2013/8/1~)

心血管疾病或糖尿病患者的起始治療值由 LDL-C ≧130 降至100 mg/dL

附件一	非藥物治療	起始藥物治療血脂值	血脂目標值	處方規定
心血管疾病或糖尿病患者	與藥物治療可並行	TC≧160mg/dL 或 LDL -C≧100mg/dL	TC＜160mg/dL 或 LDL -C＜100mg/dL	第一年應每3-6個月抽血檢查一次，第二年以後應至少每6-12個月抽血檢查一次，同時請注意副作用之產生如肝功能異常，橫紋肌溶解症。
2個危險因子或以上	給藥前應有3-6個月非藥物治療	TC≧200mg/dL 或 LDL -C≧130mg/dL	TC＜200mg/dL 或 LDL -C＜130mg/dL	
1個危險因子	給藥前應有3-6個月非藥物治療	TC≧240mg/dL 或 LDL -C≧160mg/dL	TC＜240mg/dL 或 LDL -C＜160mg/dL	
0個危險因子	給藥前應有3-6個月非藥物治療	LDL -C≧190mg/dL	LDL -C＜190mg/dL	

心血管疾病定義：
（一）冠狀動脈粥狀硬化病人：心絞痛病人，有心導管證實或缺氧性心電圖變化或負荷性試驗陽性反應者(附檢查報告)
（二）缺血型腦血管疾病病人包含：
1. 腦梗塞。
2. 暫時性腦缺血患者(TIA)。（診斷須由神經科醫師確立）
3. 有症狀之頸動脈狹窄。（診斷須由神經科醫師確立）

危險因子定義：
1. 高血壓
2. 男性≧45歲，女性≧55歲或停經者
3. 有早發性冠心病家族史(男性≦55歲，女性≦65歲)
4. HDL-C<40mg/dL
5. 吸菸(因吸菸而符合起步治療準則之個案，若未戒菸而要求藥物治療，應以自費治療)。

Source: Taiwan NHIA

Thank You For Your Attention!