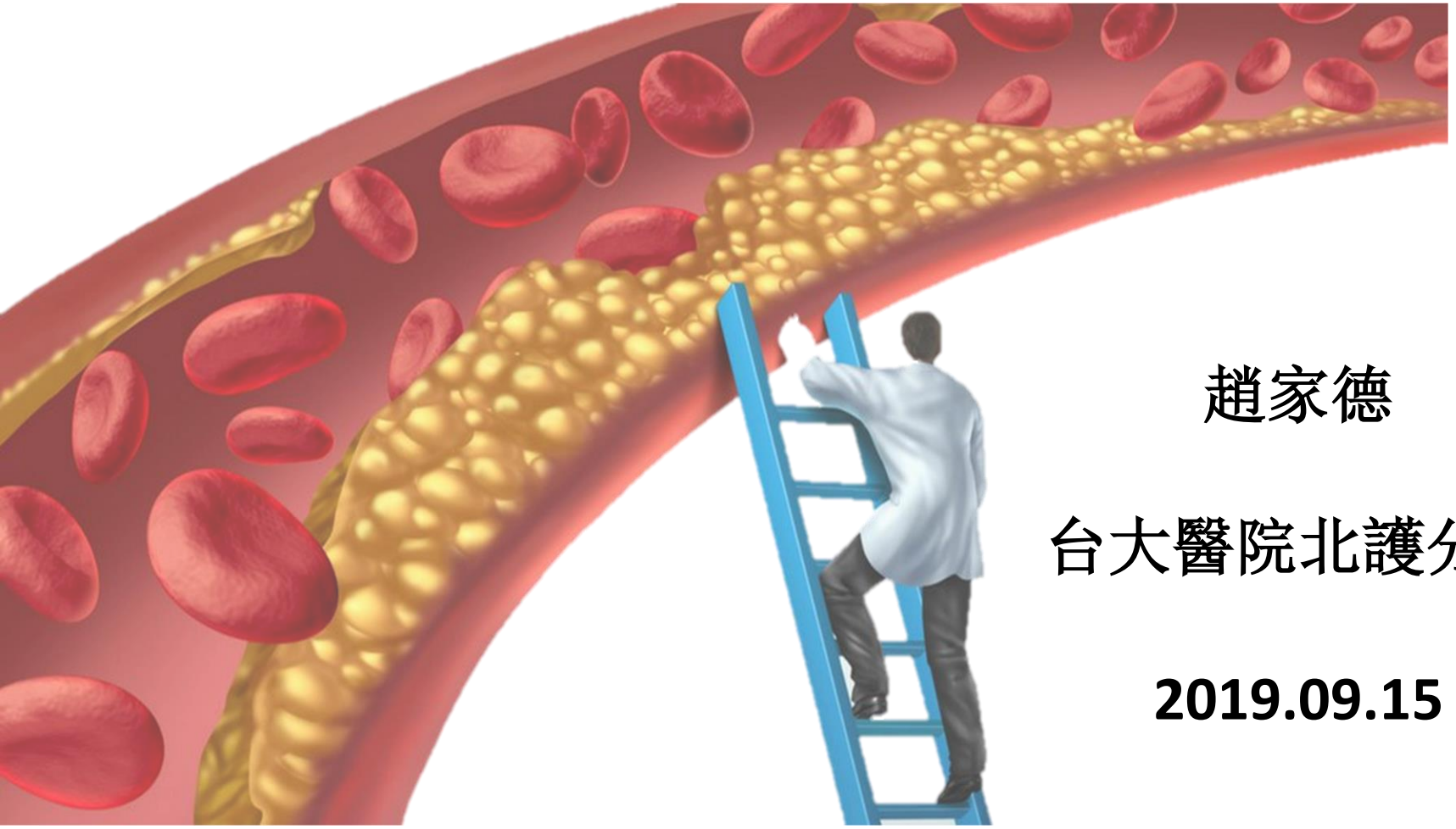
# Legacy Effect of Mevalotin in Primary Prevention



趙家德

台大醫院北護分院

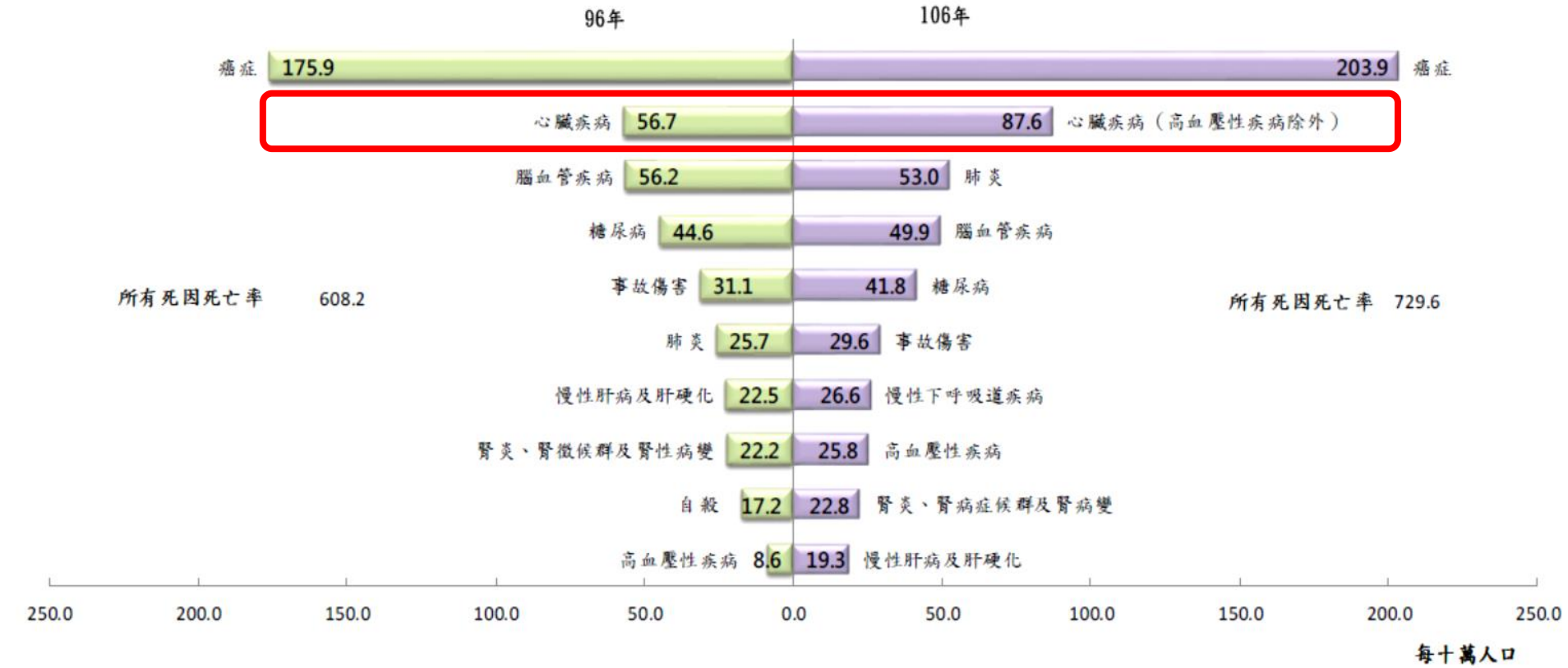
2019.09.15

# 大綱

- **The Earlier, The Better in Primary Prevention**
  - ✓ From Lipid-Control to Atherosclerosis Prevention
  - ✓ Early Intervention Provides more CV Risk Reduction
- Legacy Effect of Mevalotin in Primary Prevention
  - ✓ Lower CV Risk after 20-year of follow-up
- Challenges for Early Intervention- Medication adherence
  - ✓ High Tolerability
  - ✓ Less Adverse Effect
  - ✓ Long Term Safety

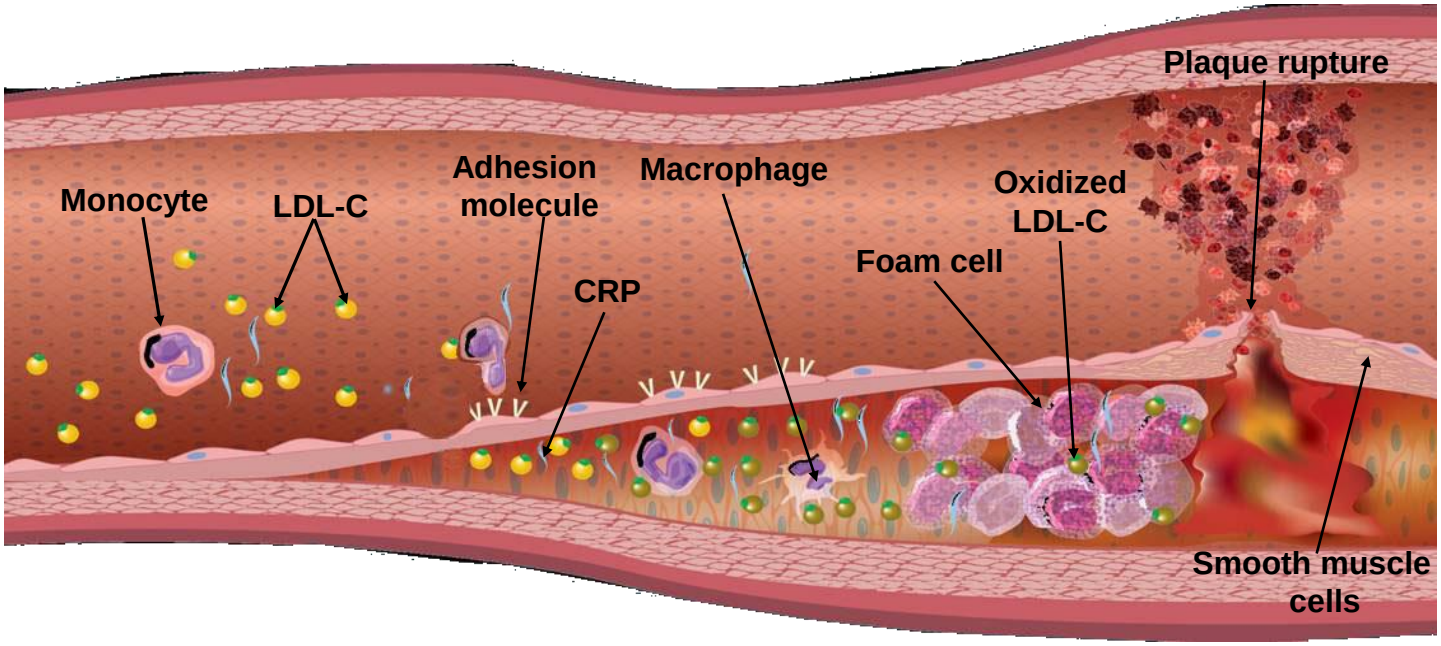
# 2017年台灣十大死因排名

**Cardiovascular disease is the secondary leading cause of death in Taiwan**



# 動脈硬化: A decade-long disease process

## Changing Nature of Lesions




**Ischemic Stroke**

**Myocardial Infarction**

**Cardiovascular Death**

Endothelial dysfunction → Inflammation → Oxidation → Plaque instability and thrombus

Libby P. Circulation. 2001;104:365-372; Ross R. N Engl J Med. 1999;340:115-126

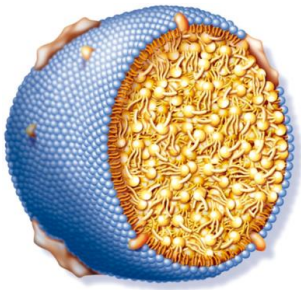
# Role of LDL in atherogenesis
## Pathological plausibility

Cellular remodelling

Release of bio-active lipids

Extracellular pathology

Lipoprotein retention
Deposits early micro- and later macro-cholesterol crystals.



Innate immunity

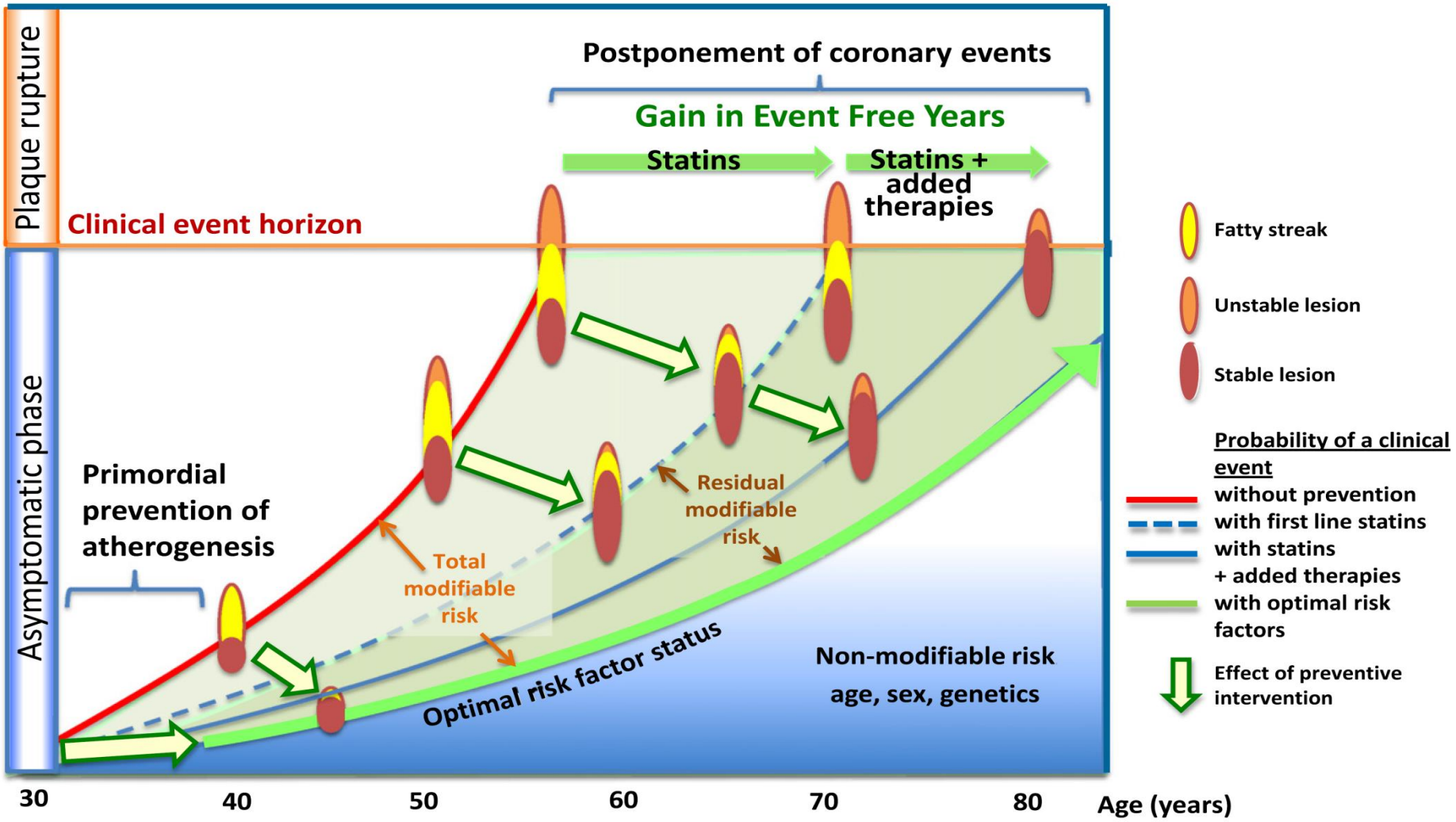
Initiates localised inflammation.
Macrophage recruitment.
Intracellular cholesterol accumulation.
Necrosis

Auto-immunity (apoB)

Adaptive immunity

Nature. 2011;473:317-325

# Reversibility of Plaque Decreases with Time…




Vascul Pharmacol. 2015 Aug;71:37-9.

# LDL hypothesis –> LDL causality

Plaque amelioration → LDL reduction → Statin

Ezetimibe

PCSK9 inhibitors

Bile acid resin

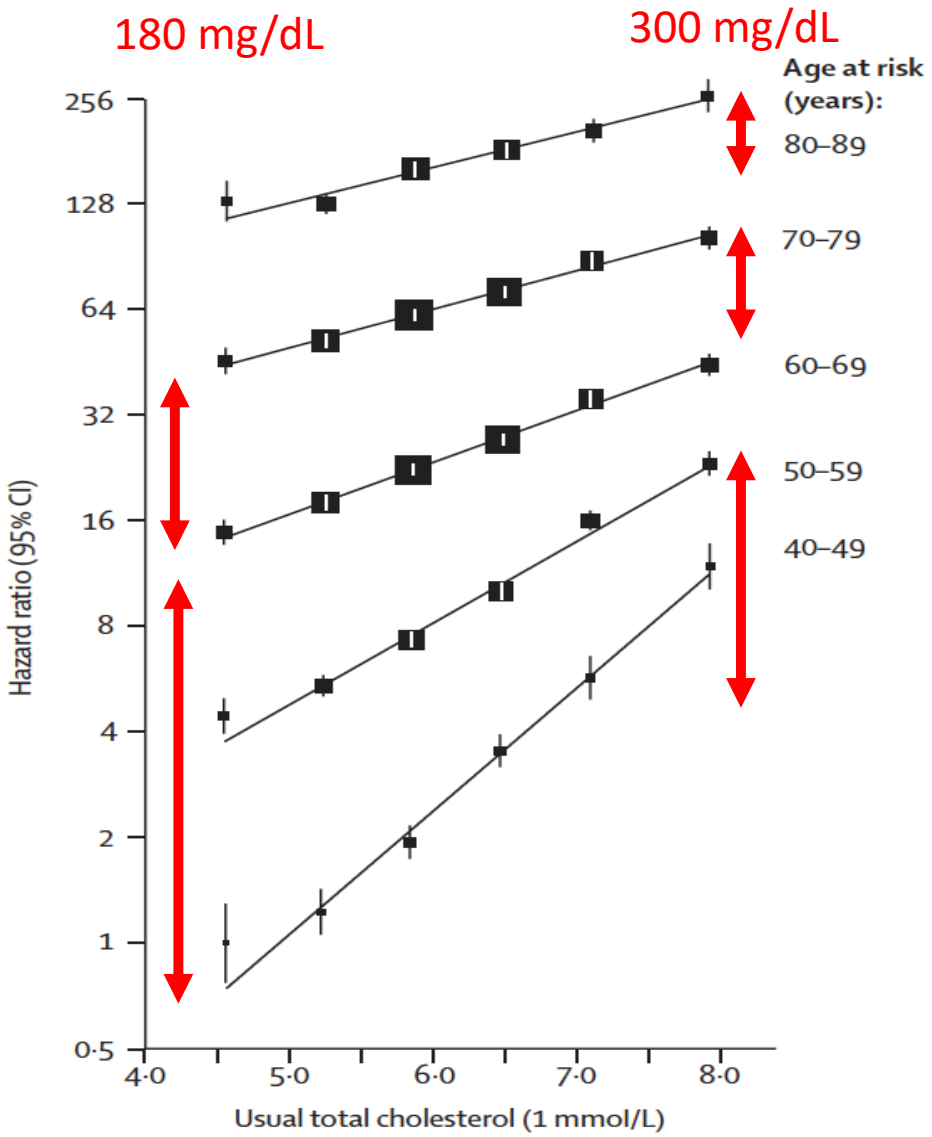
# The Levels of Prevention

| | **PRIMARY** Prevention | **SECONDARY** Prevention | **TERTIARY** Prevention |
|---|---|---|---|
| Definition | An intervention implemented before there is evidence of a disease or injury | An intervention implemented after a disease has begun, but before it is symptomatic. | An intervention implemented after a disease or injury is established |
| Intent | Reduce or eliminate causative risk factors (risk reduction) | Early identification (through screening) and treatment | Prevent sequelae (stop bad things from getting worse) |
| NAS Example | Prevent addiction from occurring<br><br>Prevent pregnancy | Screen pregnant women for substance use during prenatal visits and refer for treatment | Treat addicted women<br><br>Treat babies with NAS |

Adapted from: Centers for Disease Control and Prevention. A Framework for Assessing the Effectiveness of Disease and Injury Prevention. MMWR. 1992; 41(RR-3); 001. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/00016403.htm

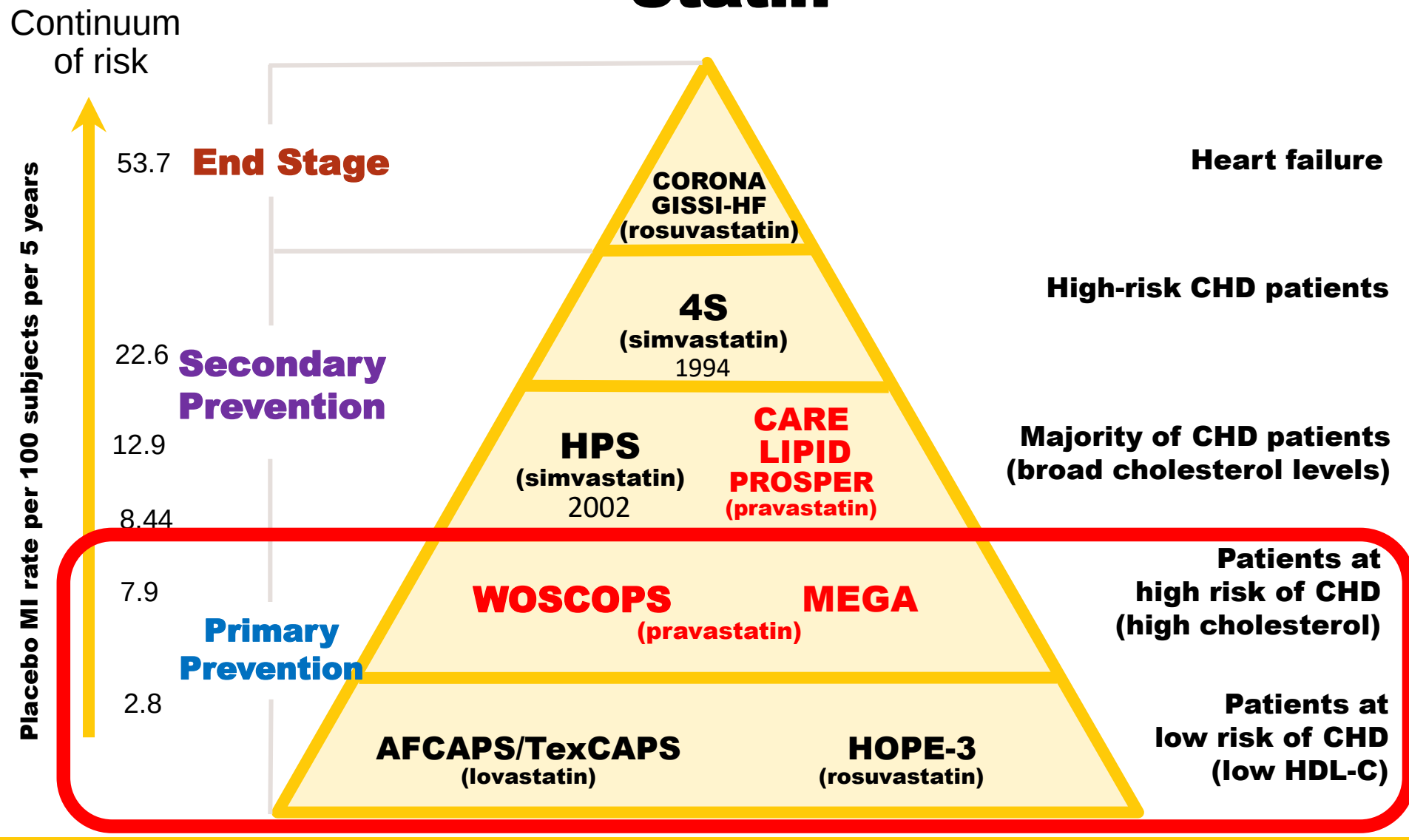
TENNESSEE DEPARTMENT OF HEALTH

# 及早介入治療，可以降低更多冠心病死亡風險




Lancet. 2007 Dec 1;370(9602):1829-39.

# Landmark Clinical CHD trials based on Statin



# OUTLINE

- The Earlier, The Better in Primary Prevention
  - ✓ From Lipid-Control to Atherosclerosis Prevention
  - ✓ Early Intervention Provides more CV Risk Reduction
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  - ✓ Long Term Safety

Oxford Bibliographies

*Your Best Research Starts Here*

Legacy effects are environmental changes resulting from antecedent human disturbances. The disturbance may be a result of changes in land use and land cover, fire regime, water diversions, introductions of chemicals or isotopes, other disruptions in natural systems, or combinations of these changes. Literally, "*legacy*" refers to an inherited condition. In the context of modern environmental

# The Legacy Effect in Type 2 Diabetes: Impact of Early Glycemic Control on Future Complications (The Diabetes & Aging Study)

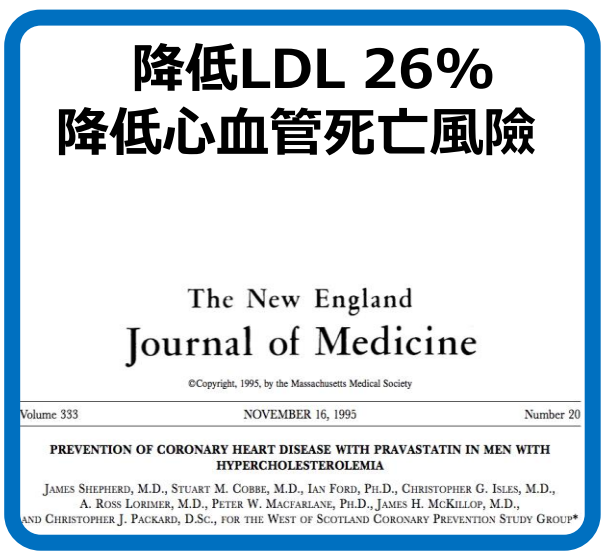
# Legacy Effect of Mevalotin in Primary Prevention

## WOSCOPS 20-year experience with pravastatin treatment

**Men without CHD**

- **Mevalotin 40mg/d** (n=3306)
- **Placebo** (n=3293)

| 5-yr Outcome | 15-yr Follow Up | 20-yr Follow Up |
|---|---|---|
| 降低LDL 26%<br>降低心血管死亡風險 | 持續降低心血管死亡風險 | 持續降低心血管死亡風險<br>長時間治療安全性 |
| 1995 NEJM | 2007 NEJM | 2016 CIRCULATION |


The New England Journal of Medicine

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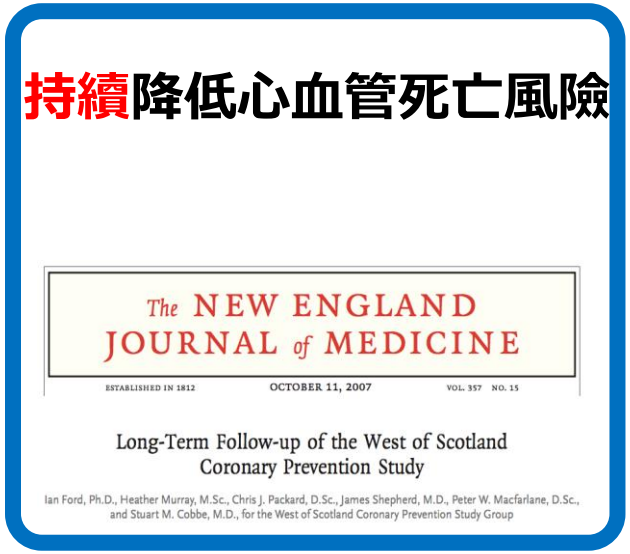
Volume 333 NOVEMBER 16, 1995 Number 20

PREVENTION OF CORONARY HEART DISEASE WITH PRAVASTATIN IN MEN WITH HYPERCHOLESTEROLEMIA

James Shepherd, M.D., Stuart M. Cobbe, M.D., Ian Ford, Ph.D., Christopher G. Isles, M.D., A. Ross Lorimer, M.D., Peter W. Macfarlane, Ph.D., James H. McKillop, M.D., and Christopher J. Packard, D.Sc., for the West of Scotland Coronary Prevention Study Group*


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 11, 2007 VOL. 357 NO. 15

Long-Term Follow-up of the West of Scotland Coronary Prevention Study

Ian Ford, Ph.D., Heather Murray, M.Sc., Chris J. Packard, D.Sc., James Shepherd, M.D., Peter W. Macfarlane, D.Sc., and Stuart M. Cobbe, M.D., for the West of Scotland Coronary Prevention Study Group


Circulation

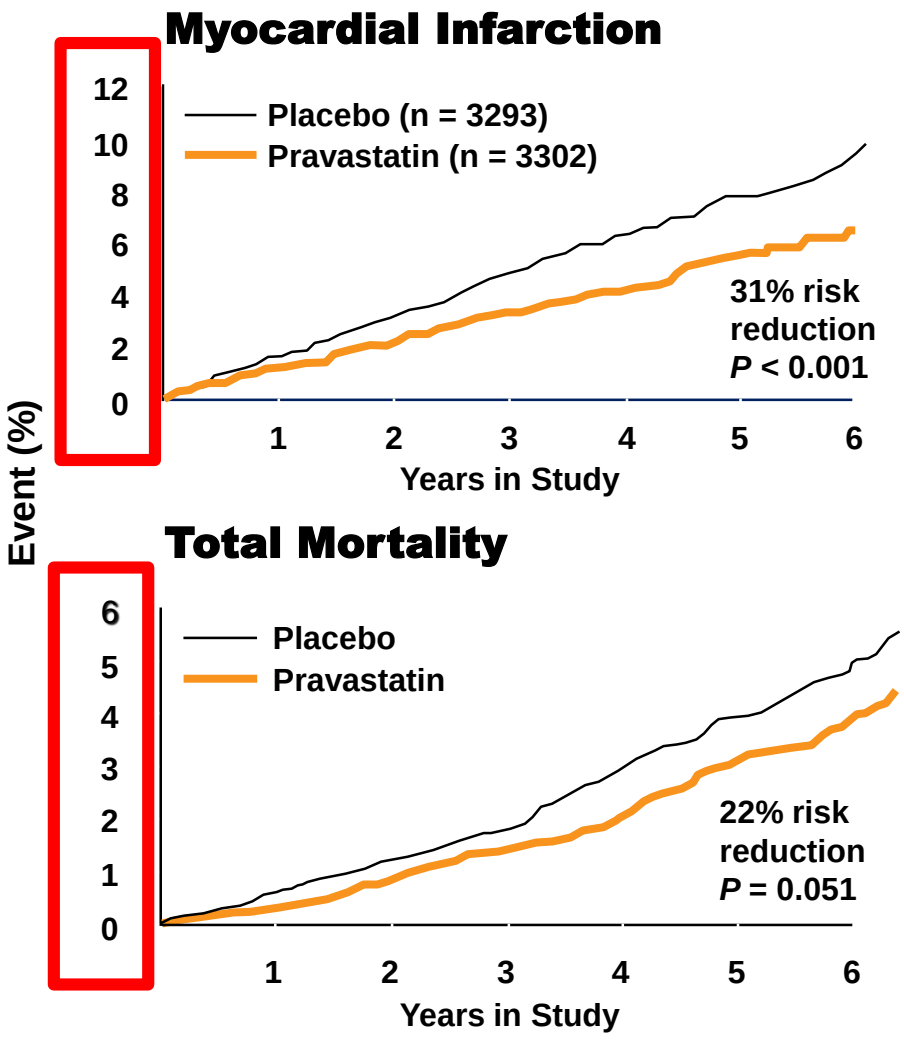
Long-Term Safety and Efficacy of Lowering Low-Density Lipoprotein Cholesterol With Statin Therapy

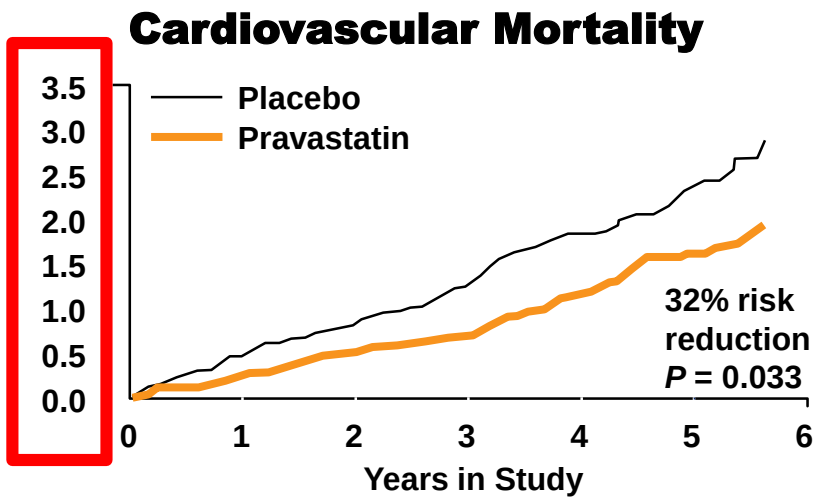
20-Year Follow-Up of West of Scotland Coronary Prevention Study

Ian Ford, PhD; Heather Murray, MSc; Colin McCowan, PhD; Chris J. Packard, DSc

N Engl J Med. 1995;333:1301-1307. N Engl J Med. 2007;357:1477-86. Circulation. 2016;133:1073-80

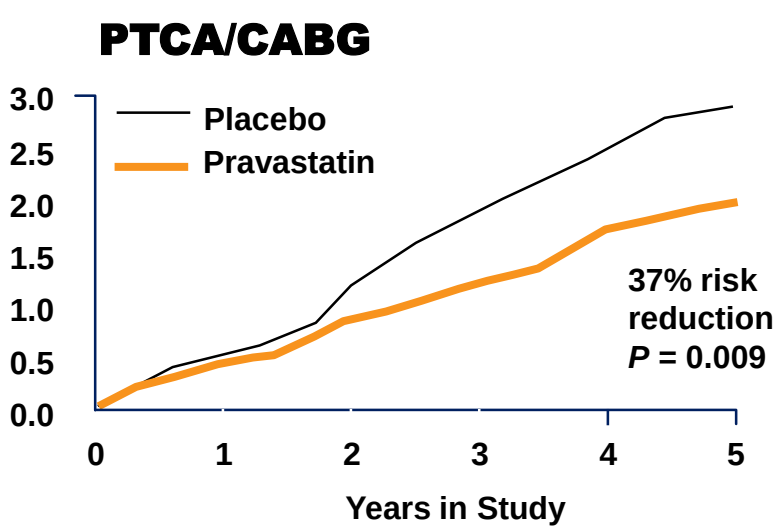
# Early Event Reduction with Mevalotin







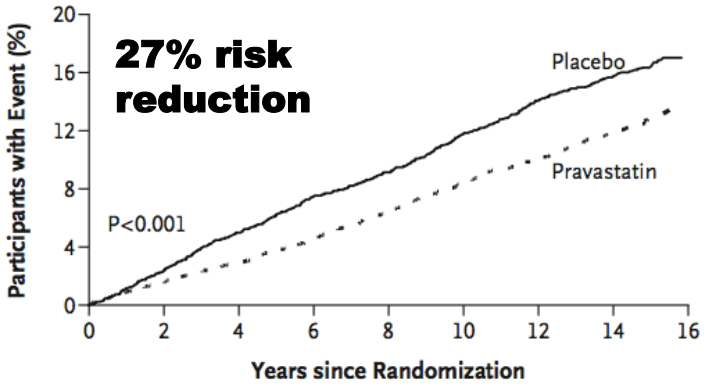



N Engl J Med. 1995;333:1301-1307.

# Mevalotin Use Offers Benefits 10 years After Trial End

## Nonfatal MI

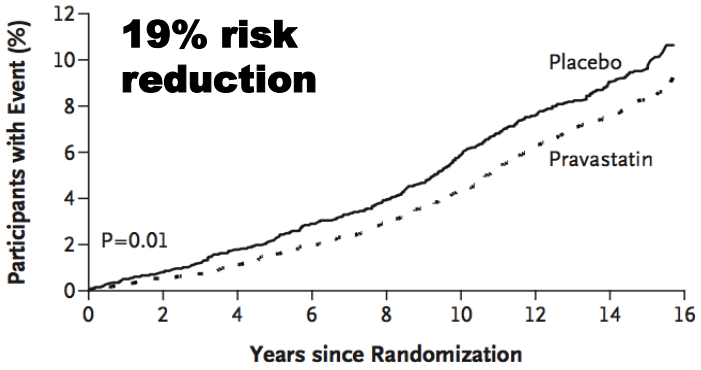
31%→




| No. at Risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Placebo | 3293 | 3199 | 3071 | 2953 | 2841 | 2691 | 2549 | 1903 |
| Pravastatin | 3302 | 3237 | 3157 | 3065 | 2943 | 2819 | 2675 | 2026 |

## Cardiovascular Mortality

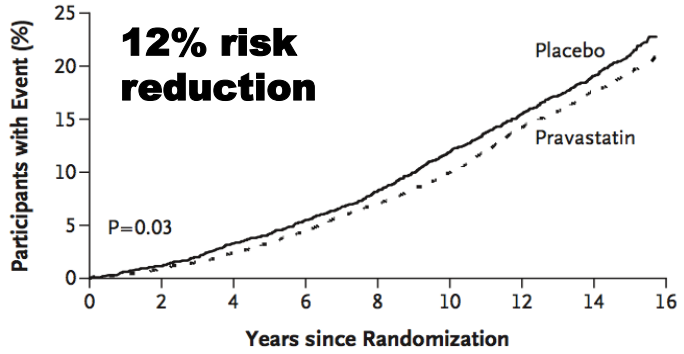
32%→




| No. at Risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Placebo | 3293 | 3254 | 3185 | 3113 | 3022 | 2902 | 2785 | 2114 |
| Pravastatin | 3302 | 3275 | 3223 | 3158 | 3068 | 2974 | 2835 | 2177 |

## All Cause Mortality

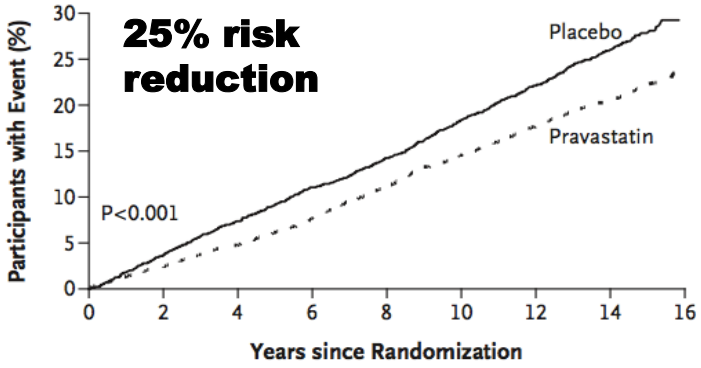
22%→




| No. at Risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Placebo | 3293 | 3254 | 3185 | 3113 | 3022 | 2902 | 2785 | 2114 |
| Pravastatin | 3302 | 3275 | 3223 | 3158 | 3068 | 2974 | 2835 | 2177 |

## CHD Mortality or Hospitalization

37%→

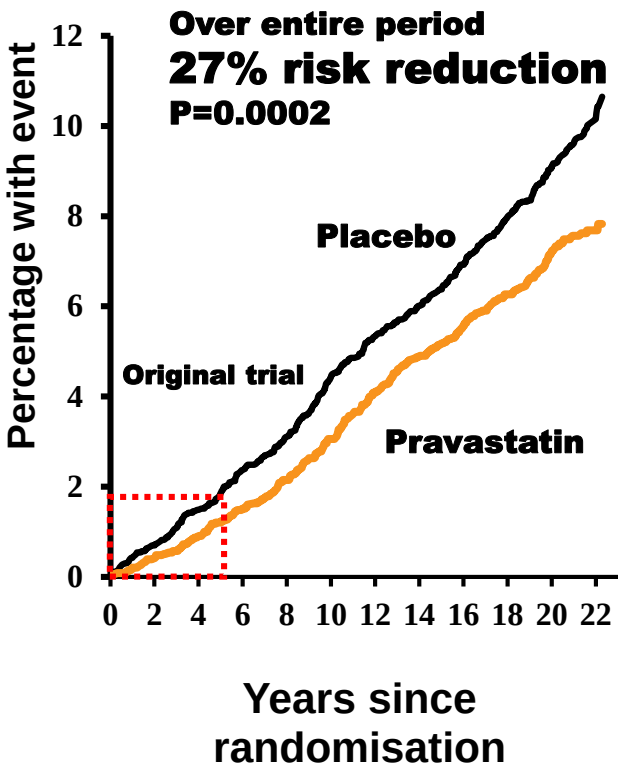



| No. at Risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Placebo | 3293 | 3156 | 2993 | 2839 | 2682 | 2486 | 2307 | 1661 |
| Pravastatin | 3302 | 3211 | 3100 | 2965 | 2800 | 2639 | 2454 | 1821 |

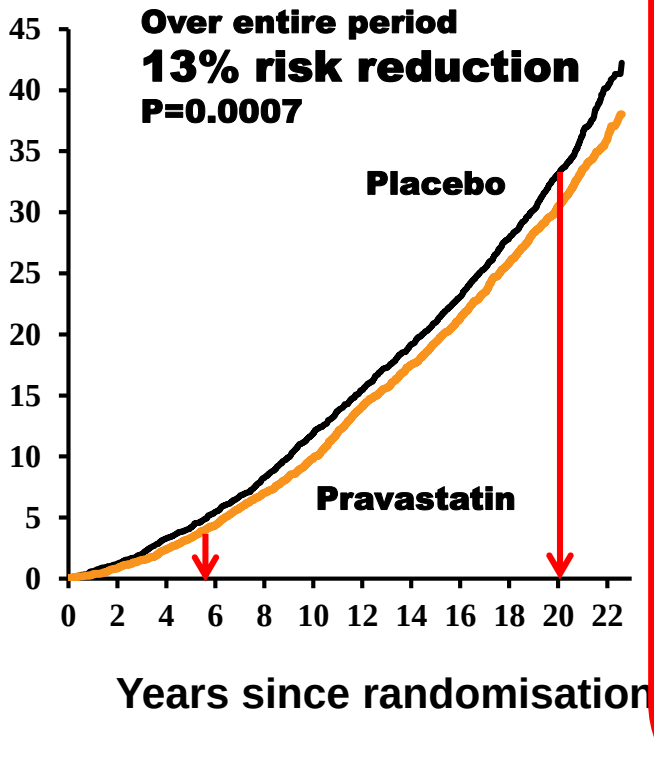
N Engl J Med. 2007;357:1477-86.

# Long Term Benefits of LDL Lowering with Mevalotin

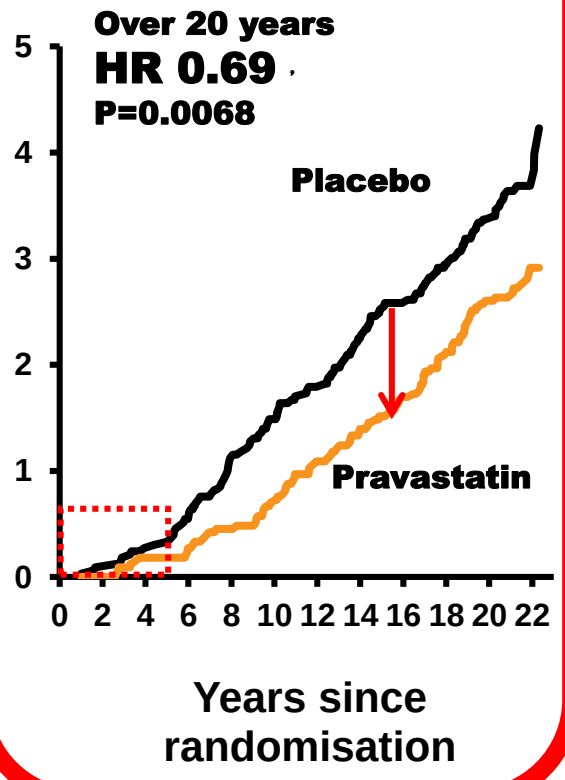
## CHD mortality




## All-cause mortality

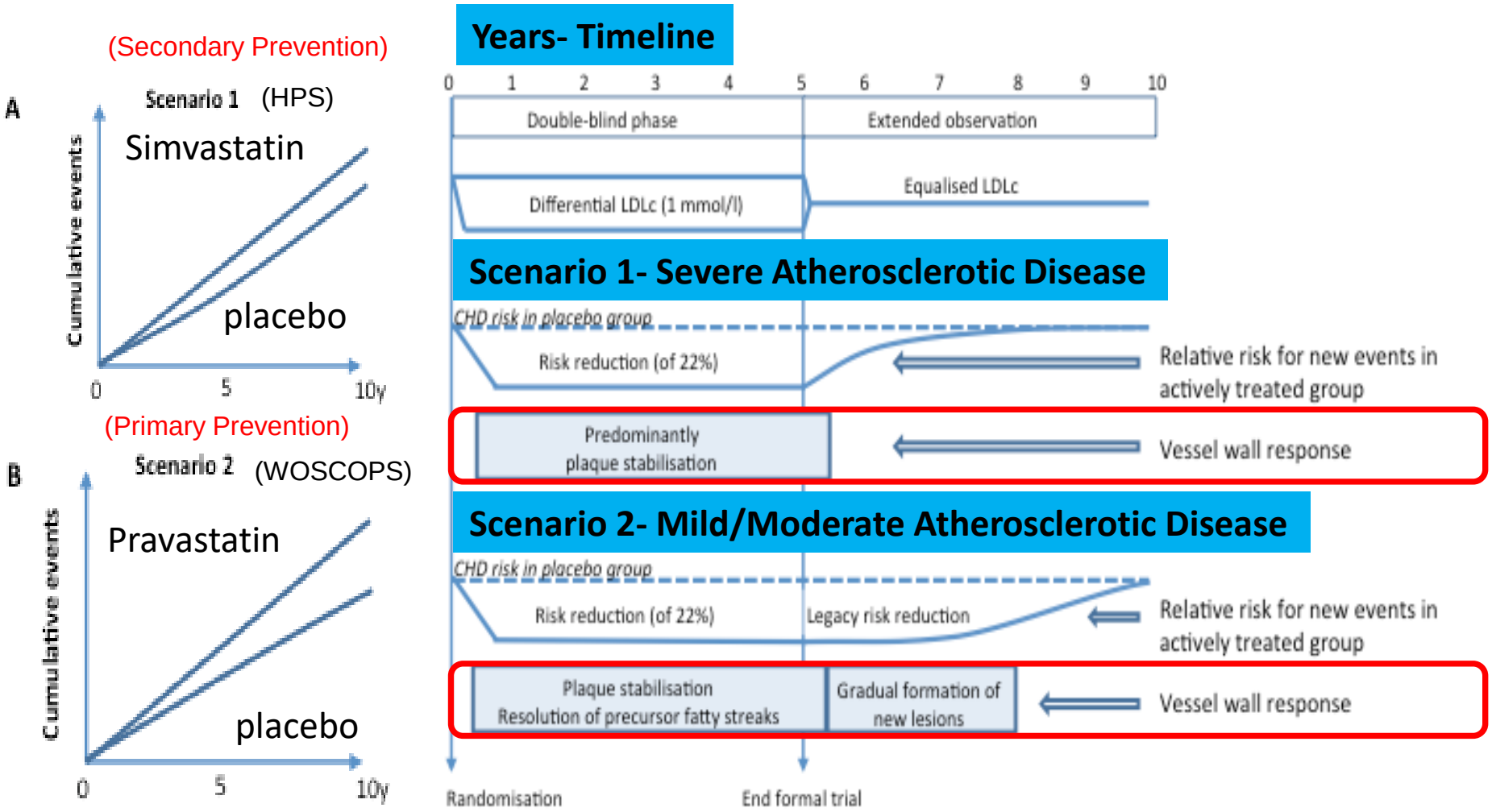



## Heart failure




Circulation. 2016;133:1073-80

# Primary vs. secondary prevention: 越早期介入LDL治療，長期心血管事件風險越低 (esp. Mevalotin)



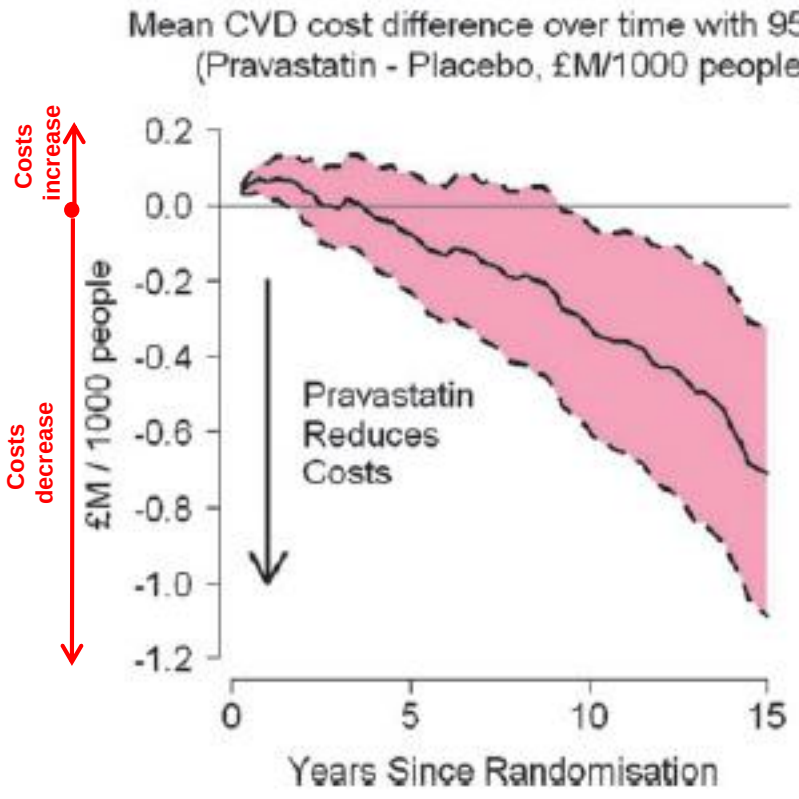

**Postpone, or even neutralize the risk!**

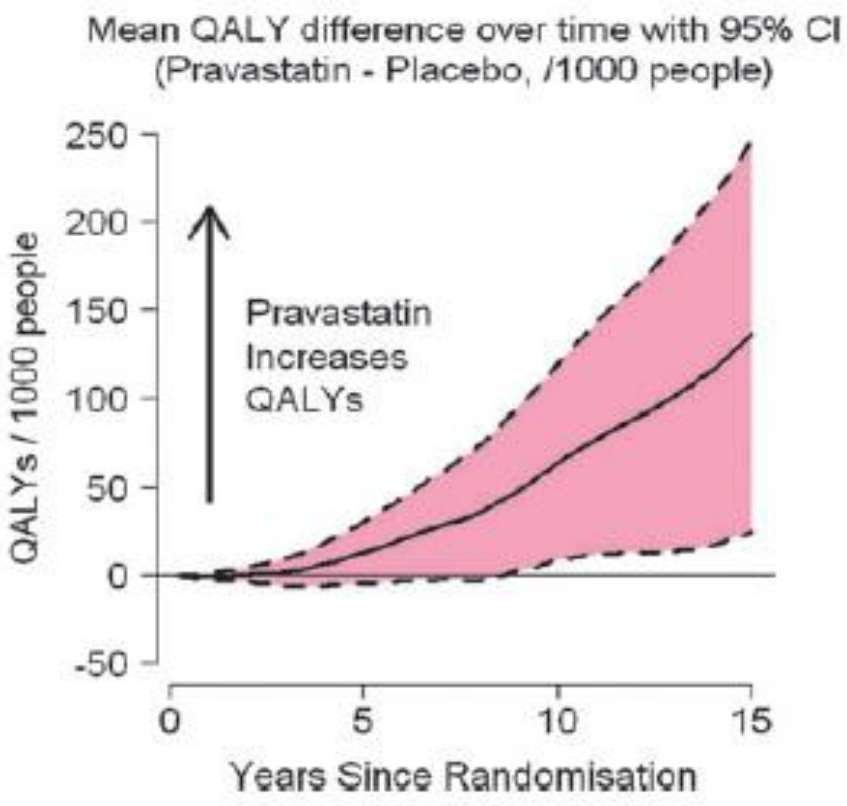
Curr Opin Lipidol. 2015;26;572-9

# 更多優勢：Primary prevention使用Mevalotin於具有CHD風險病患，有效節省醫療花費

**Five years treatment of 1000 patients with pravastatin (40 mg/day)**

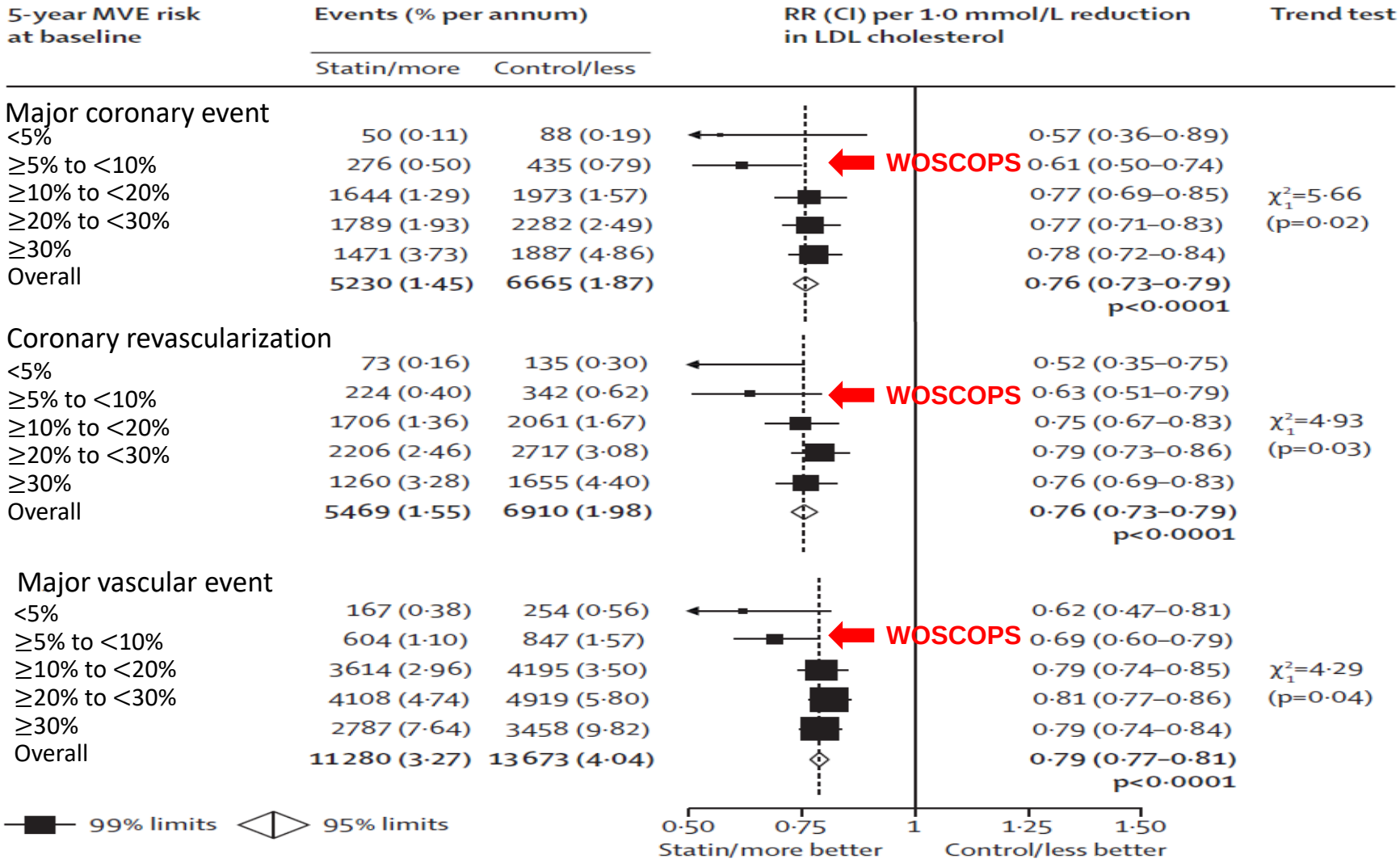
- **Saved the NHS £710 000 (P < 0.001)**
- **Gained 136 QALYs (P < 0.017)**
- **Reduced 163 fewer admissions**
- **Saved 1836 days in hospital**




Eur Heart J. 2014;35:290-8

# 在低CHD風險病人使用statin仍可有效降低心血管疾病事件風險




Lancet. 2012;380:581-90.

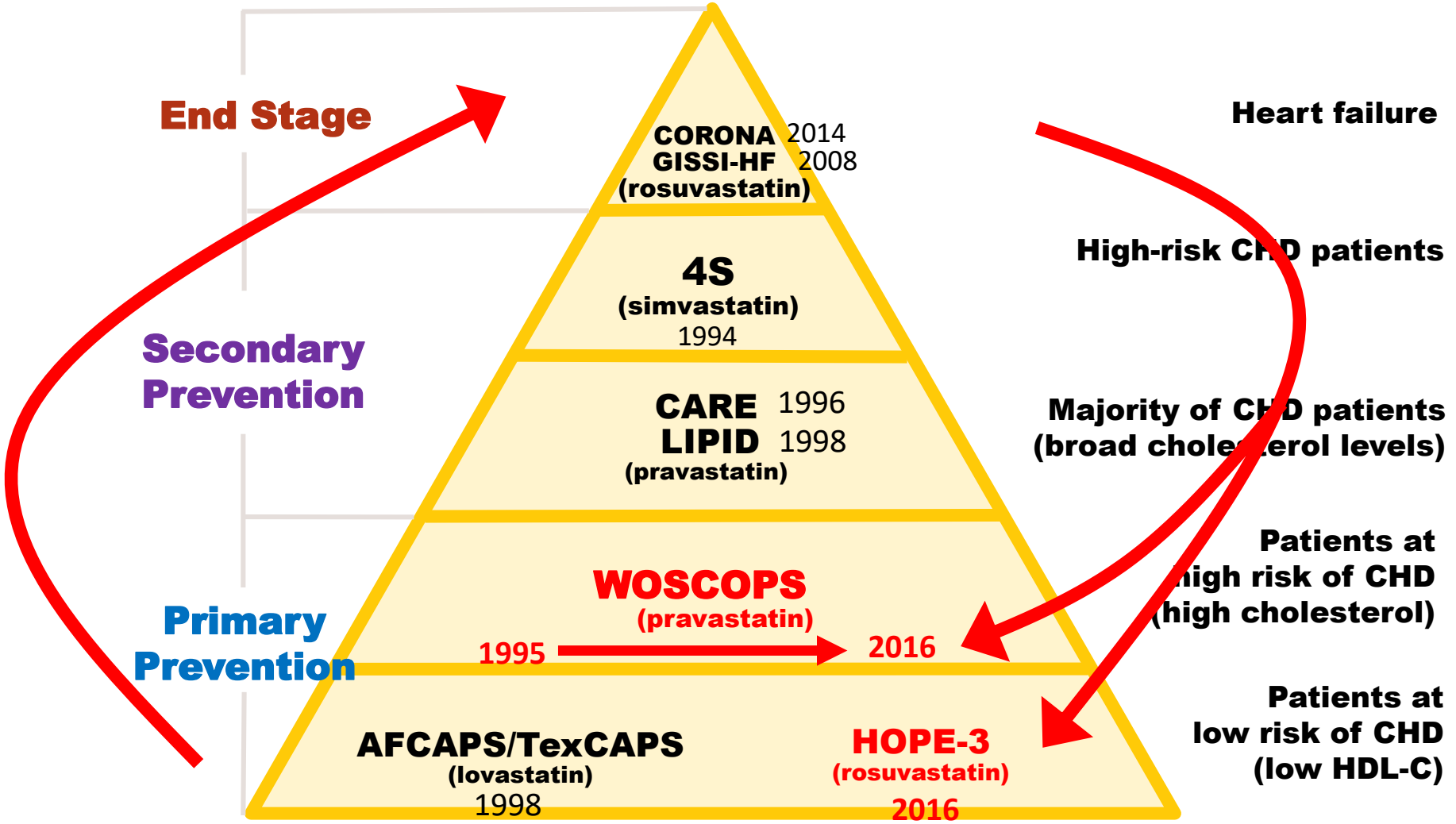
# Brief Summary

- 早期介入治療，降低更多心血管死亡風險
- 20年追蹤，Mevalotin可以持續降低心血管死亡風險

    1. 27% CHD Mortality
    2. 13% All-Caused Mortality
    3. 31% Heart Failure hospitalization

- 及早使用Mevalotin/Pravastatin，長期心血管事件風險降低

# Landmark Clinical CHD Event Trials




BACK
TO THE FUTURE
IN CONCERT

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  - ✓ Early Intervention Provides more CV Risk Reduction
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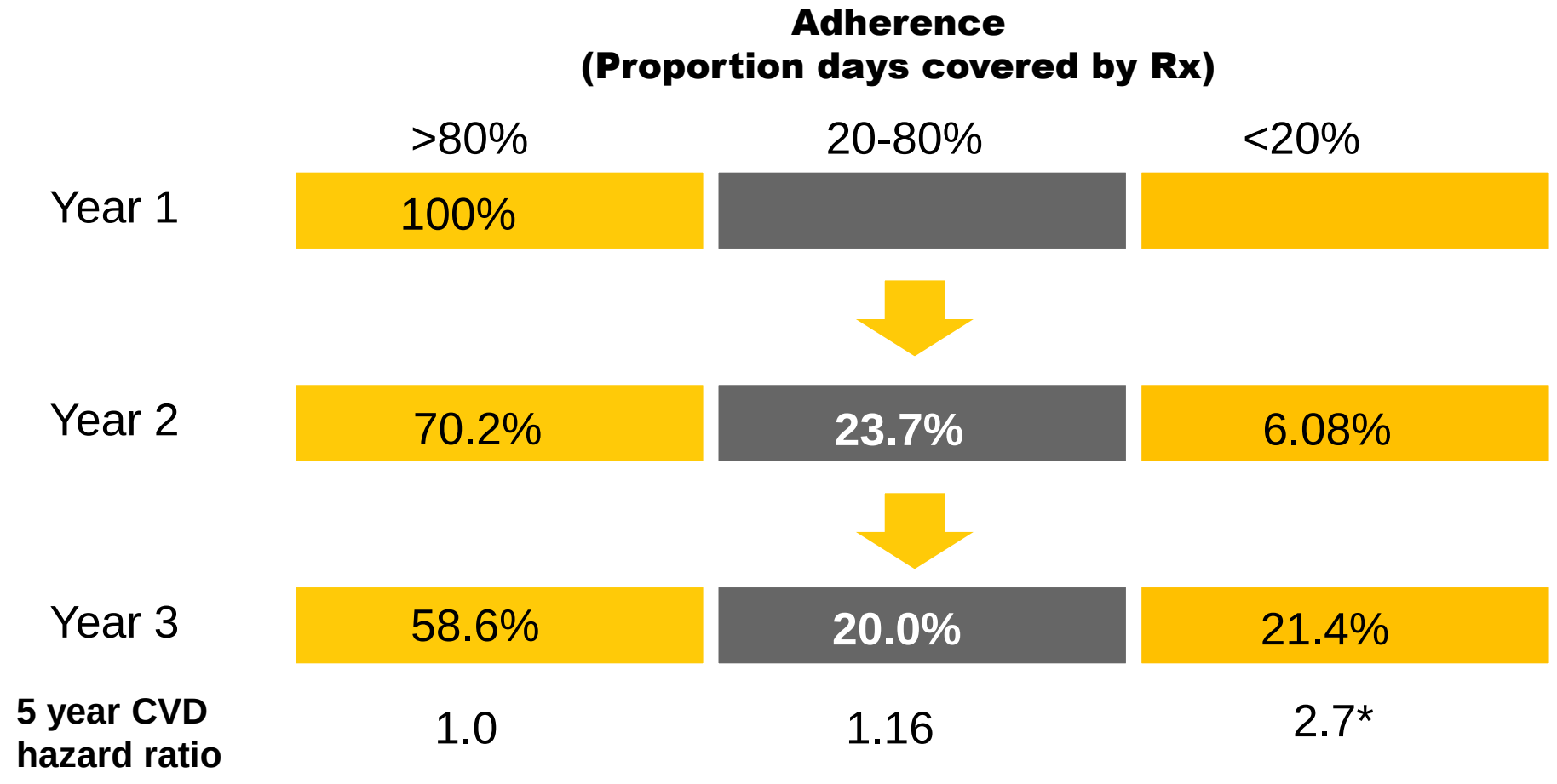
- **Challenges for Early Intervention- Medication adherence**
  - ✓ **High Tolerability**
  - ✓ **Less Adverse Effect**
  - ✓ **Long Term Safety**

# Statin類藥物服藥順從性隨時間而變差

- US Prescription claims database - Asymptomatic patients prescribed statin (n=11,126)
- Yearly adherence changes in initially good compliers to statin




J Manag Care Pharm. 2014;20:51-7.

# Mevalotin不良副作用較少；耐受度更佳!

## Comparative Tolerability and Harms of Individual Statins
### A Study-Level Network Meta-Analysis of 246 955 Participants From 135 Randomized Controlled Trials

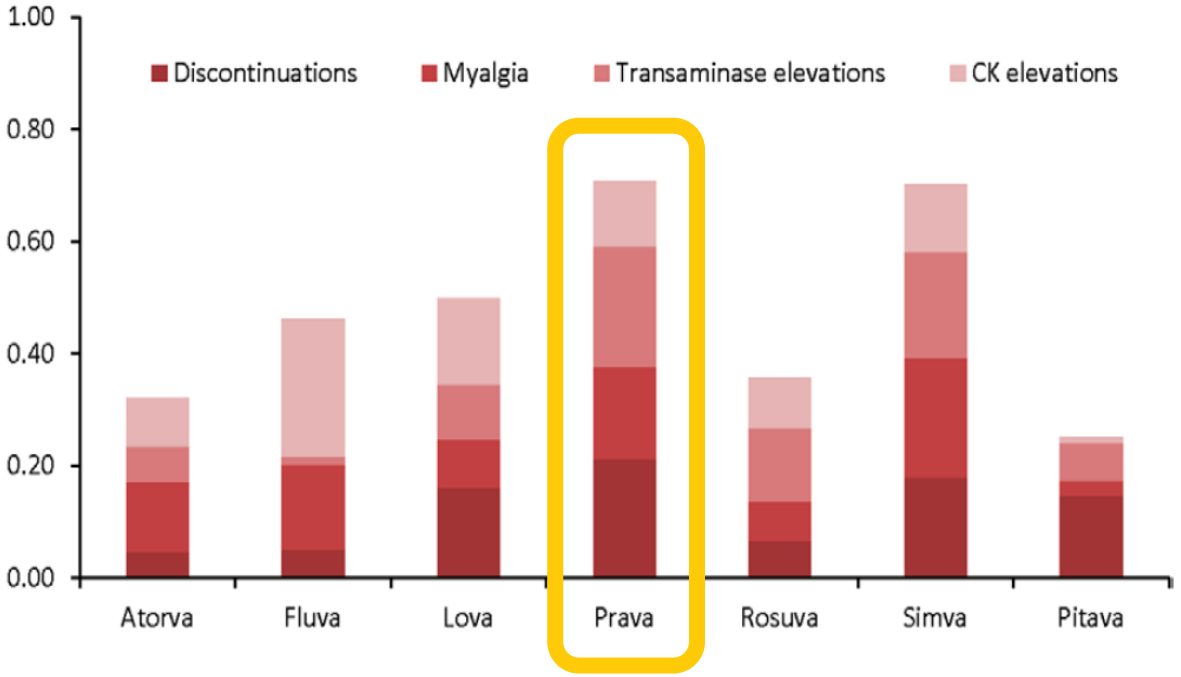



**Figure 6.** Overall ranking of individual statins in placebo-controlled and active-comparator trials of participants by their overall probability to be the best treatment in terms of discontinuations because of adverse events, myalgia, hepatic transaminase elevation, and CK elevation. In addition to the overall score for each statin, the relative contribution of each of the 4 outcomes to the overall score is also shown. Each statin was scored with points up to a maximum of 0.25 for each outcome (overall maximum score: 1.00). Higher scores indicate a better tolerability and safety profile. CK indicates creatine kinase.

*Higher scores indicate a better tolerability and safety

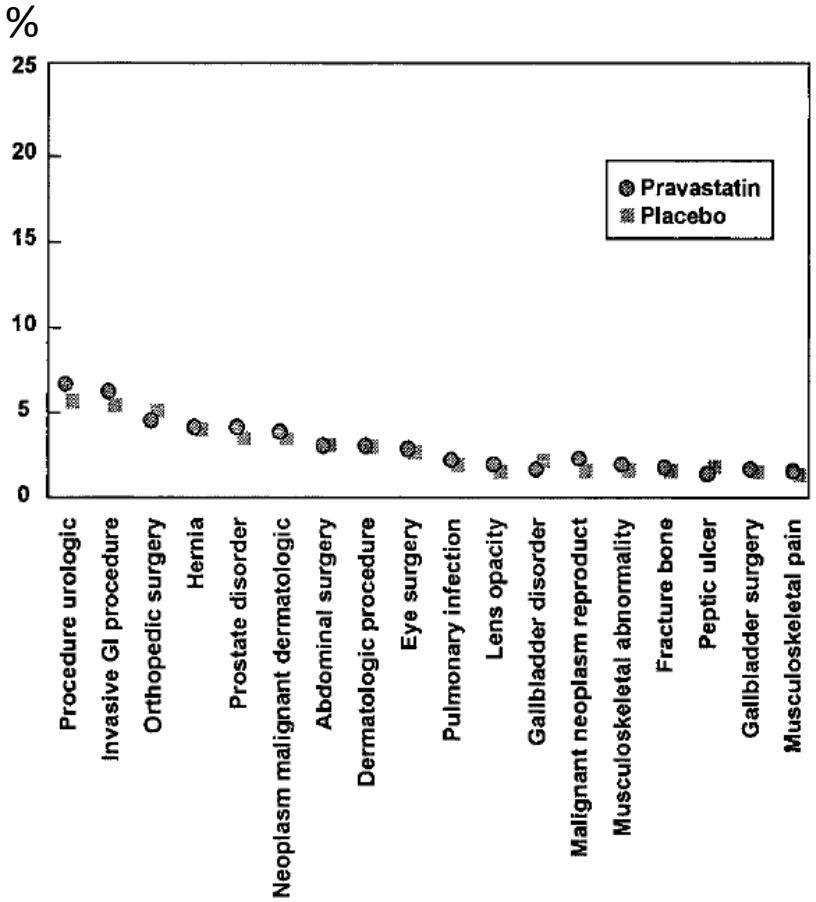
Circ Cardiovasc Qual Outcomes. 2013;6:390-9

五洲製藥的理念

# 先講求不傷身體
# 再講求效果

# Mevalotin的non-CV AE 發生率和Placebo相同

## Combined，individual subject level data from WOSCOPS，CARE and LIPID




- 19,592 subjects randomised to placebo or pravastatin 40mg/day
- 5 years in-trial follow-up
- > 112,000 patient-years exposure

**TABLE 3. Serum Chemistry Abnormalities**

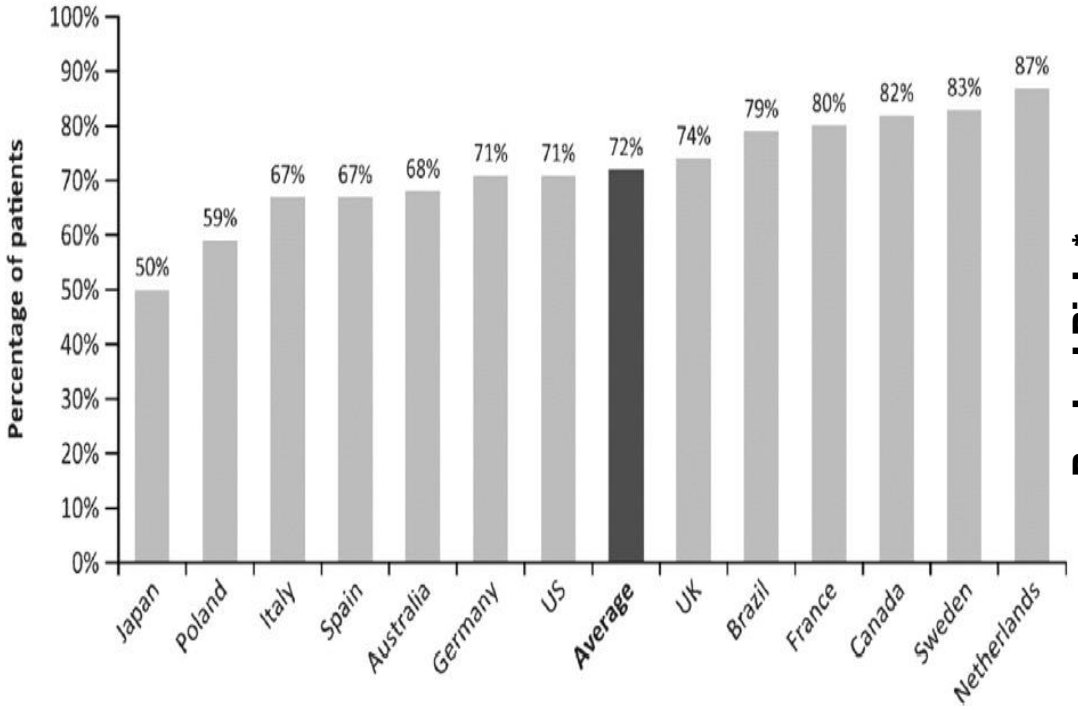
| | ALT Abnormalities | | | CPK Abnormalities | | |
|---|---|---|---|---|---|---|
| | Pravastatin 40 mg (n=9185), n (%) | Placebo (n=9152), n (%) | 95% CI of Difference | Pravastatin 40 mg (n=5245), n (%) | Placebo (n=5233), n (%) | 95% CI of Difference |
| Any value >1.5×ULN | 804 (8.8) | 746 (8.2) | −0.21, 1.42 | 587 (11.2) | 563 (10.8) | −0.78, 1.65 |
| >1.5×ULN to ≤3×ULN | 676 (7.4) | 615 (6.7) | −0.11, 1.39 | 480 (9.2) | 460 (8.8) | −0.75, 1.48 |
| >3×ULN to ≤5×ULN | 84 (0.9) | 90 (1.0) | −0.36, 0.22 | 84 (1.6) | 79 (1.5) | −0.40, 0.59 |
| >5×ULN to ≤7×ULN | 24 (0.3) | 19 (0.2) | −0.10, 0.21 | 8 (0.2) | 16 (0.3) | −0.36, 0.05 |
| >7×ULN to ≤9×ULN | 6 (<0.1) | 9 (<0.1) | −0.13, 0.06 | 6 (0.1) | 6 (0.1) | −0.15, 0.15 |
| >9×ULN | 14 (0.2) | 13 (0.1) | −0.11, 0.13 | 9 (0.2) | 2 (<0.1) | −0.02, 0.28 |

ULN=upper limit of normal.

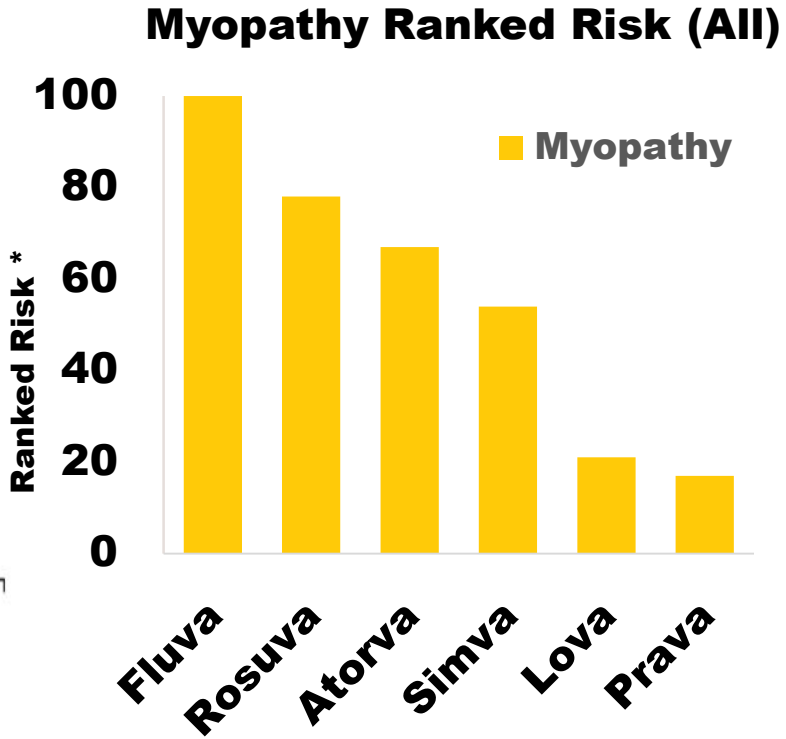
Circulation. 2002;105:2341-6.

# FDA AERS database: Mevalotin 有較低的Myopathy發生率

- Survey involving 60 clinicians per country, 12 countries and 90 clinicians in the US was conducted.
- An average of 72% of patients with potential SAS were reported to present with muscle-related symptoms (50-87%).




**Proportion of patients newly prescribed statins reported to present with potential statin-associated muscle symptoms.**



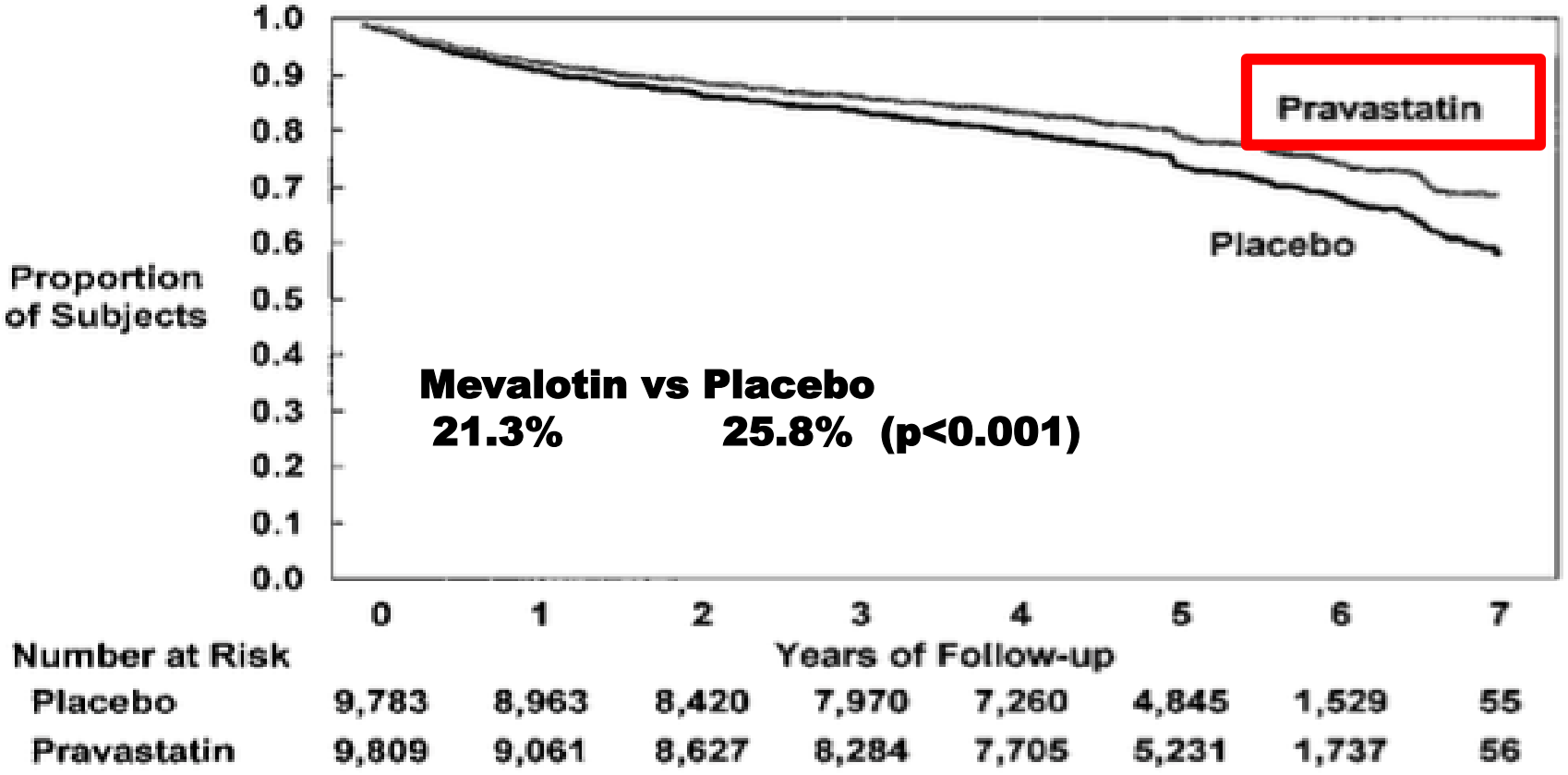

*In each category，the statin with the highest risk rate was designated as having a ‘‘ranked risk’’ value of 100.

Atherosclerosis. 2016;245:111-7.

PLOS ONE 2012;7:e42866.

# Mevalotin 中斷治療的比例較Placebo更低

- Placebo: discontinue due to an AE related to the cardiovascular endocrine/metabolic, and general body systems.
- After exclude CV event related discontinuation, the discontinuation rate of placebo is still higher than Mevalotin.




Circulation. 2002;105:2341-6.

# Statin Use and Cancer Risk: A Comprehensive Review

**Denise M. Boudreau, RPh, PhD [Scientific Investigator, Associate Professor]** ,
Group Health Research Institute, Seattle, WA, USA and University of Washington School of Pharmacy, Seattle, WA, USA

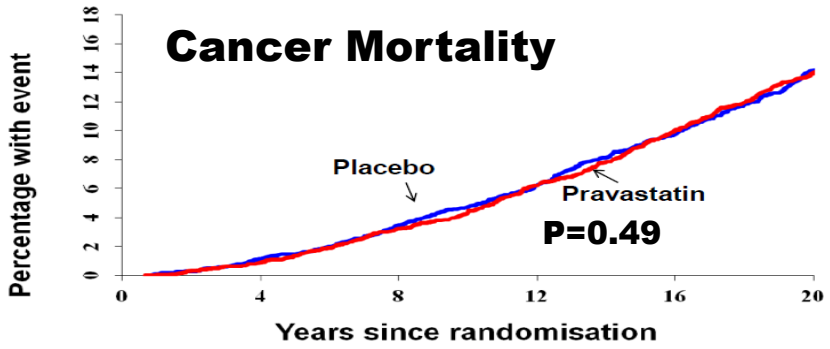
**Onchee Yu, MS [Biostatistician]**, and
Group Health Research Institute, Seattle, WA, USA

**Jeanene Johnson [Research Assistant]**
Group Health Research Institute, Seattle, WA, USA

**Importance of the Field—**HMG-CoA inhibitors (statins), a class of drugs that reduce cholesterol, are used to manage and prevent coronary heart disease. They are among the most commonly prescribed drugs worldwide. Contrary to early concerns over the carcinogenicity of statins, a growing body of evidence suggests statins may in fact have a chemopreventive potential against cancer.

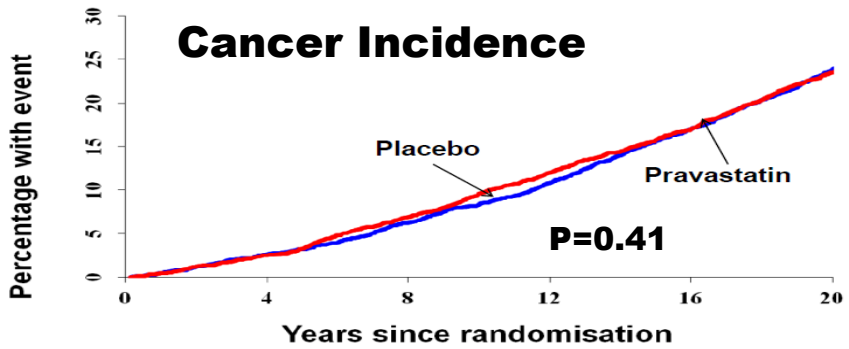
Expert Opin Drug Saf 2010;9:603-21.

# 20年長期追蹤，Mevalotin並未增加癌症風險




Numbers at risk:

| | | | | | | |
|---|---|---|---|---|---|---|
| Placebo | 3293 | 3185 | 3021 | 2785 | 2501 | 2203 |
| Pravastatin | 3302 | 3223 | 3069 | 2838 | 2598 | 2295 |




Numbers at risk:

| | | | | | | |
|---|---|---|---|---|---|---|
| Placebo | 3293 | 3138 | 2923 | 2647 | 2317 | 1448 |
| Pravastatin | 3302 | 3172 | 2952 | 2658 | 2377 | 1548 |

| Endpoint | Placebo，number (%) with event Total n=3293 | Pravastatin，number (%) with event Total n=3302 | Adjusted Hazard Ratio (95% Confidence Interval) | P- Value |
|---|---|---|---|---|
| All cancers | 816 ( 24.8%) | 809 ( 24.5%) | 0.96 ( 0.87， 1.06) | 0.41 |
| Colorectal cancer | 140 ( 4.25%) | 127 ( 3.85%) | 0.87 ( 0.68， 1.10) | 0.25 |
| Lung cancer | 202 ( 6.13%) | 187 ( 5.66%) | 0.89 ( 0.73， 1.08) | 0.24 |
| Prostate cancer | 170 ( 5.16%) | 186 ( 5.63%) | 1.05 ( 0.85， 1.29) | 0.65 |
| Upper GI cancer | 77 ( 2.34%) | 87 ( 2.63%) | 1.09 ( 0.80， 1.48) | 0.60 |
| Urinary tract cancer | 97 ( 2.95%) | 99 ( 3.00%) | 0.99 ( 0.75， 1.31) | 0.93 |
| Other cancer | 160 ( 4.86%) | 157 ( 4.75%) | 0.95 ( 0.76， 1.18) | 0.62 |
| All non-CVD deaths | 757 ( 23.0%) | 731 ( 22.1%) | 0.92 ( 0.83， 1.02) | 0.12 |

Circulation. 2016;133:1073-80

BMJ Open Diabetes Research & Care

# Statin use and risk of developing diabetes: results from the Diabetes Prevention Program

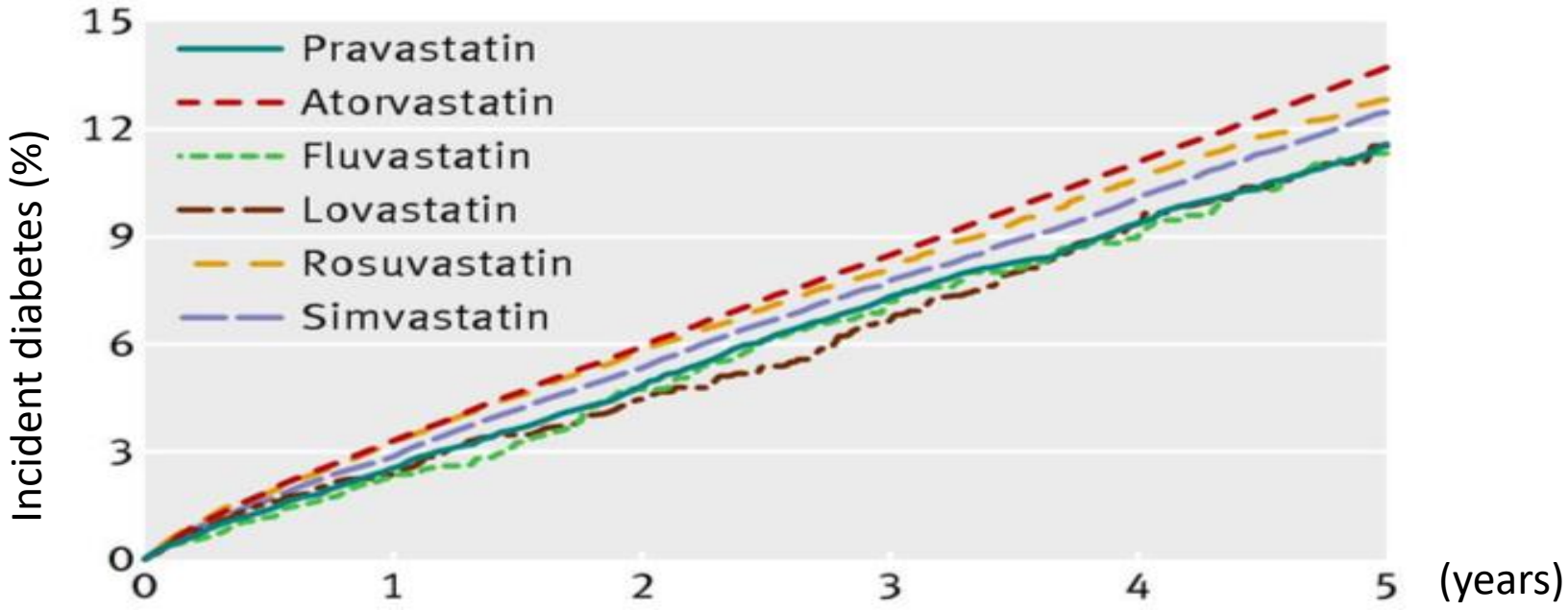
Table 2 HR (95% CI) for diabetes associated with statin use at visit prior to diabetes diagnosis

| Adjusted models | Pooled | Placebo | Metformin | Lifestyle |
|---|---|---|---|---|
| Model 1: demographic | **1.36 (1.17 to1.59)** | 1.21 (0.93 to 1.57) | **1.33 (1.02 to 1.73)** | **1.59 (1.21 to 2.10)** |
| Model 2: 1+baseline diabetes risk factors | **1.35 (1.15 to1.57)** | 1.18 (0.90 to 1.54) | **1.37 (1.05 to 1.78)** | **1.53 (1.16 to 2.03)** |
| Model 3: 2+updated statin confounders | **1.27 (1.08 to1.50)** | 1.15 (0.87 to 1.53) | 1.31 (0.99 to 1.73) | **1.36 (1.00 to 1.86)** |
| Model 4: 2+updated diabetes risk factors | **1.27 (1.08 to1.49)** | 1.19 (0.91 to 1.55) | **1.36 (1.04 to 1.76)** | **1.37 (1.04 to 1.81)** |
| Model 5: fully adjusted | **1.27 (1.08 to1.50)** | 1.20 (0.90 to 1.59) | **1.33 (1.01 to 1.76)** | **1.43 (1.06 to 1.94)** |

## What is already known about this subject?

- In observational studies, statin use has been associated with increased risk for diabetes.
- Data from randomized statin trials also suggest incident diabetes is increased.

# Mevalotin 的新生糖尿病風險低

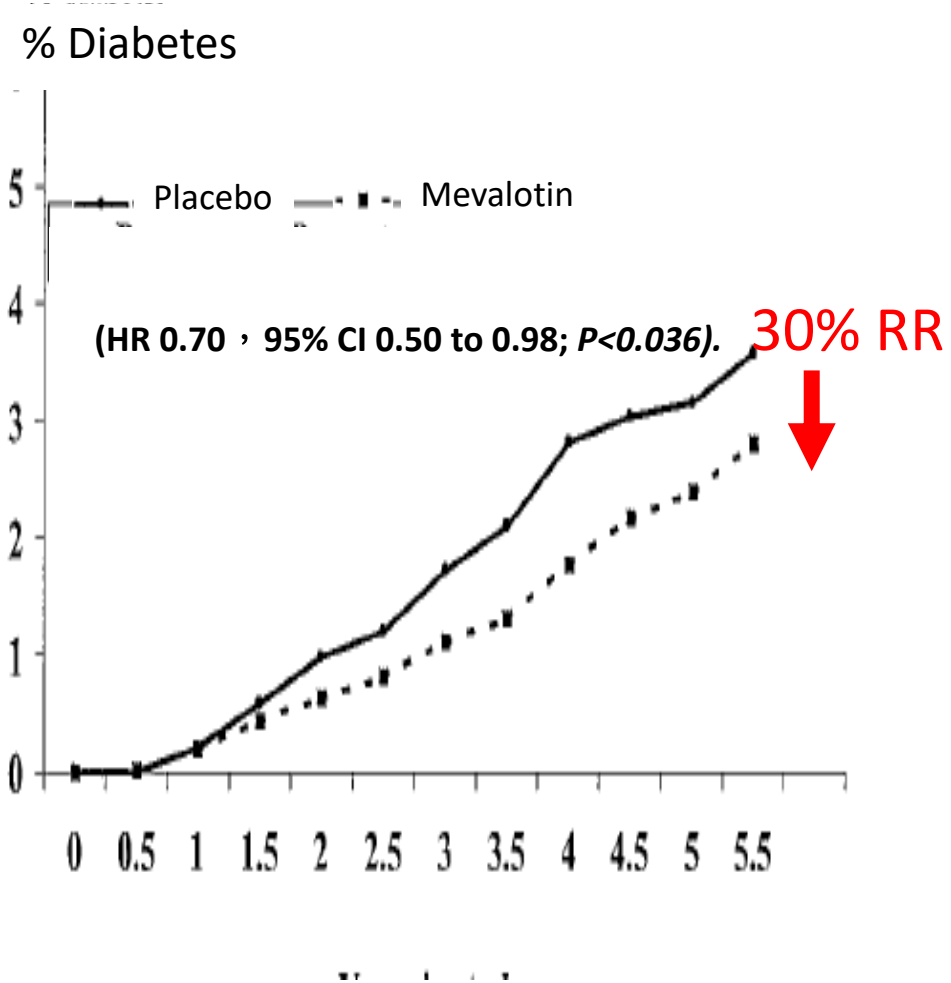


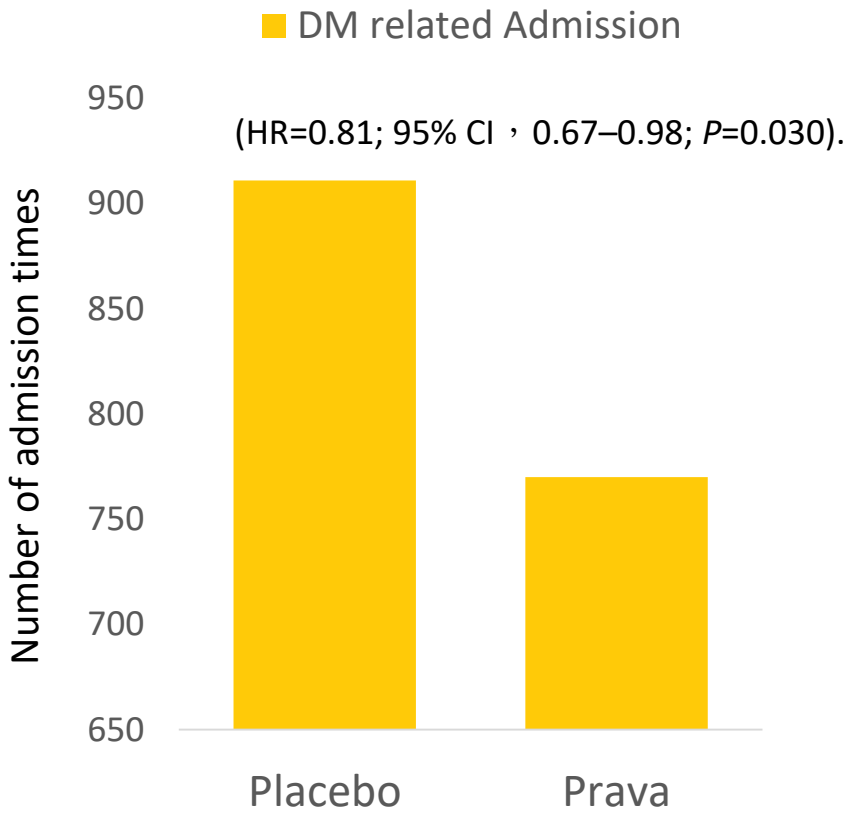

| Statin | No of patients | No of outcomes | Median (IQR) follow-up (person days) | No of outcomes per 1000 person years | HR (95% CI) | | Number needed to treat to harm |
|---|---|---|---|---|---|---|---|
| | | | | | Unadjusted | Adjusted* | |
| Pravastatin | 38 470 | 1713 | 236 (90-1080) | 27.07 | Reference | Reference | — |
| Atorvastatin | 268 254 | 18 303 | 360 (89-1256) | 37.28 | 1.39 (1.33 to 1.46) | 1.21 (1.15 to 1.27) | 140 |
| Fluvastatin | 5636 | 193 | 188 (66-732) | 24.99 | 0.90 (0.78 to 1.05) | 0.91 (0.79 to 1.06) | — |
| Lovastatin | 6287 | 260 | 207 (90-927) | 27.06 | 0.99 (0.87 to 1.13) | 1.03 (0.90 to 1.17) | — |
| Rosuvastatin | 76 774 | 4565 | 300 (50-796) | 42.35 | 1.53 (1.45 to 1.62) | 1.15 (1.08 to 1.22) | 202 |
| Simvastatin | 75 829 | 4477 | 323 (90-1355) | 31.84 | 1.19 (1.13 to 1.26) | 1.11 (1.05 to 1.18) | 261 |

*Adjusted for age，sex，year of cohort entry，recent acute coronary syndrome，chronic coronary artery disease，Charlson score，previous use of diuretic (thiazide)，nitroglycerin，angiotensin receptor blocker，β blocker，hormones and analogues.

BMJ 2013;346:f2610

# WOSCOPS trial: Mevalotin 顯著降低新生糖尿病風險



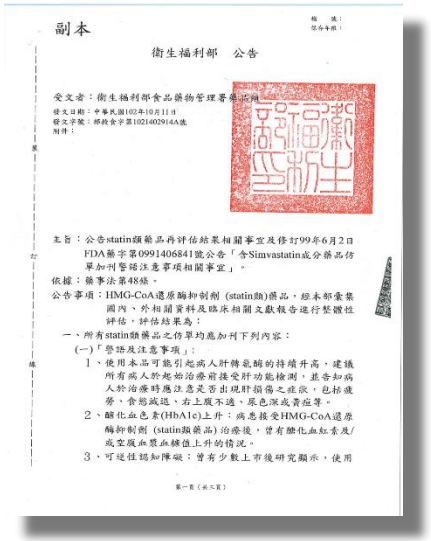

Circulation. 2001;103:357-62.

# 含pravastatin成分藥品得免刊載醣化血色素上升之危險性

## 衛生福利部公告[2013-10-11]

1.**所有statin類藥品**之仿單均應加刊

(一)「警語及注意事項」：
1.使用本品可能引起病人肝轉胺胸持續升高
2.**糖化血色素(HbA1c)及/或空腹血漿血糖值上升**
3.可逆性認知障礙


副本

衛生福利部　公告

受文者：衛生福利部食品藥物管理署(北)

發文日期：中華民國102年10月11日
發文字號：部授食字第1021402914A號
附件：

主旨：公告statin類藥品再評估結果相關事宜及修訂99年6月2日FDA藥字第0991406841號公告「含Simvastatin成分藥品仿單加刊警語注意事項相關事宜」。

依據：藥事法第48條。

公告事項：HMG-CoA還原酶抑制劑（statin類）藥品，經本部彙集國內、外相關資料及臨床相關文獻報告進行整體性評估，評估結果為：

一、所有statin類藥品之仿單均應加刊下列內容：

(一)「警語及注意事項」：

1、使用本品可能引起病人肝轉氨酶的持續升高，建議所有病人於起始治療前接受肝功能檢測，甚告知病人於治療時應注意是否出現肝損傷之症狀，包括疲勞、食慾減退、右上腹不適、尿色深或黃疸等。

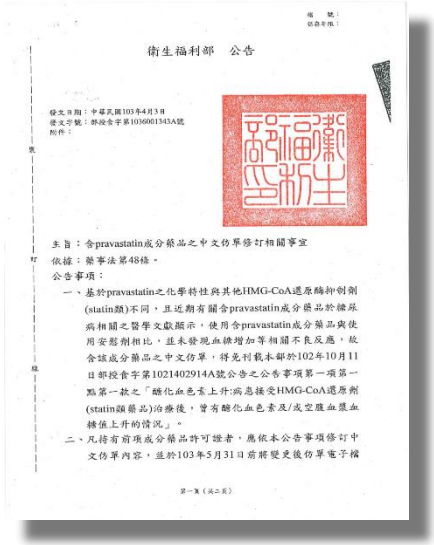
2、醣化血色素(HbA1c)上升：病患接受HMG-CoA還原酶抑制劑（statin類藥品）治療後，曾有醣化血紅素及/或空腹血漿血糖值上升的情況。

3、可逆性認知障礙：曾有少數上市後研究顯示，使用

第一頁（共二頁）

## 衛生福利部公告[2014-4-3]

基於**pravastatin**之**化學特性與其他HMG-CoA還原酶抑制劑(statin類)不同**，且近期有關含pravastatin成分藥品於糖尿病相關之醫學文獻顯示，使用含pravastatin成分藥品與使用安慰劑相比，**並未發現血糖增加等相關不良反應**，故中文仿單**得免刊載**衛福部於102年10月11日公告之公告事項第一項第一點第一款之「醣化血色素上升：病患接受HMG-CoA還原酶抑制劑(statin類)治療後，曾有醣化血色素及/或空腹血漿血糖值上升的情況」的警語。


衛生福利部　公告

發文日期：中華民國103年4月3日
發文字號：部授食字第1036001543A號
附件：

主旨：含pravastatin成分藥品之中文仿單修訂相關事宜

依據：藥事法第48條。

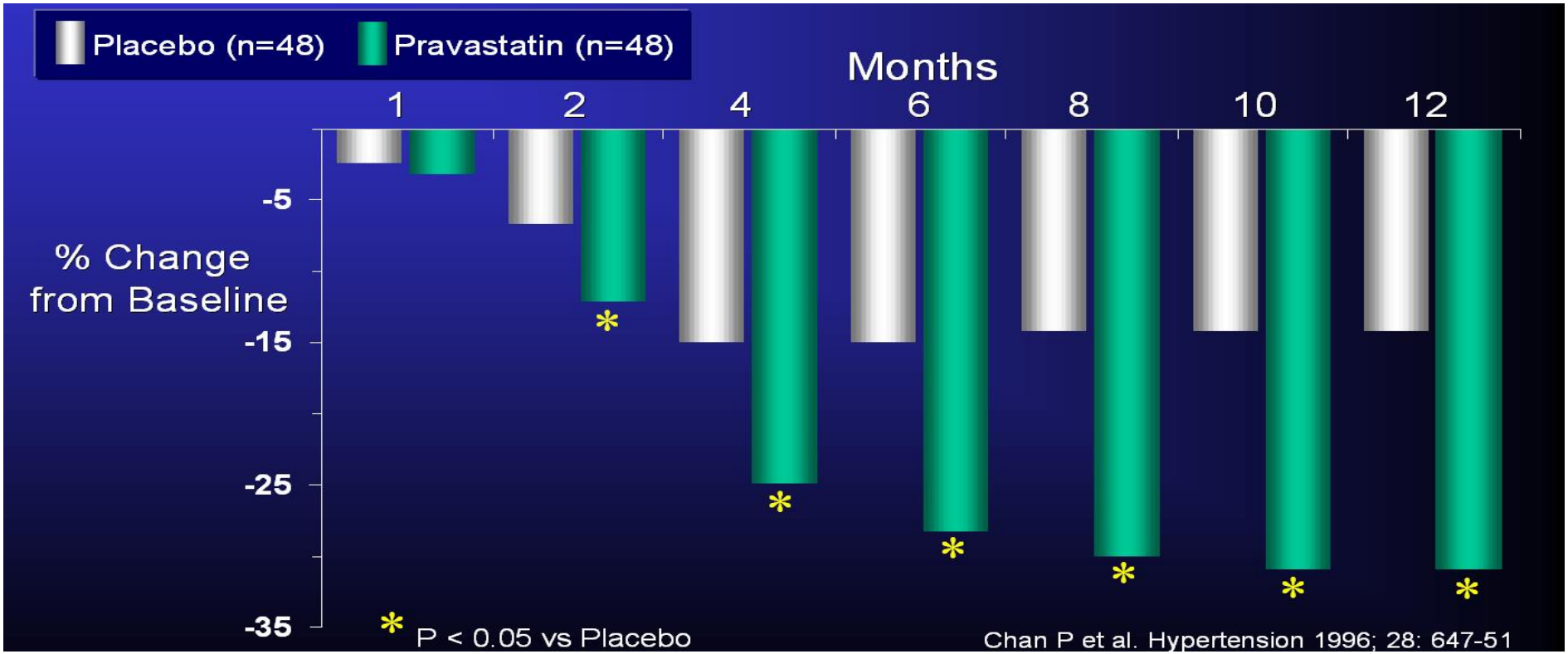
公告事項：

一、基於pravastatin之化學特性與其他HMG-CoA還原酶抑制劑(statin類)不同，且近期有關含pravastatin成分藥品於糖尿病相關之醫學文獻顯示，使用含pravastatin成分藥品與使用安慰劑相比，並未發現血糖增加等相關不良反應，故含該成分藥品之中文仿單，得免刊載本部於102年10月11日部授食字第1021402914A號公告之公告事項第一項第一點第一款之「醣化血色素上升：病患接受HMG-CoA還原酶抑制劑(statin類藥品)治療後，曾有醣化血色素及/或空腹血漿血糖值上升的情況」。

二、凡持有前項成分藥品許可證者，應依本公告事項修訂中文仿單內容，並於103年5月31日前將變更後仿單電子檔

第一頁（共二頁）

# Mevalotin顯著降低insulin level




Hypertension. 1996;28:647-51

# Mevalotin不經CYP450代謝，較少藥物交互作用

| Statin | Pravastatin (Mevalotin®) | Rosuvastatin (Crestor®) | Pitavastatin (Livalo®) | Fluvastatin (Lescol®) | Atorvastatin (Lipitor®) | Simvastatin (Zocor®) | Lovastatin (Mevacor®) |
|---|---|---|---|---|---|---|---|
| CYP metabolism | NONE | CYP2C9 | | | CYP3A4 | | |
| Solubility (log P) | Water (-0.84) | Water (-0.33) | Lipid (1.49) | Lipid (1.27) | Lipid (1.11) | Lipid (1.6) | Lipid (1.7) |

## CYP2C9 substrate

- **Pain-NSAID**
  Celecoxib Diclofenac
  Ibuprofen Naproxen
  Piroxicam
- **Diabetic medications**
  Glipizide Tolbutamide
- **Hypertension-ARB**
  Irbesartan Lorsartan
- **Anticoagulant**
  Warfarin

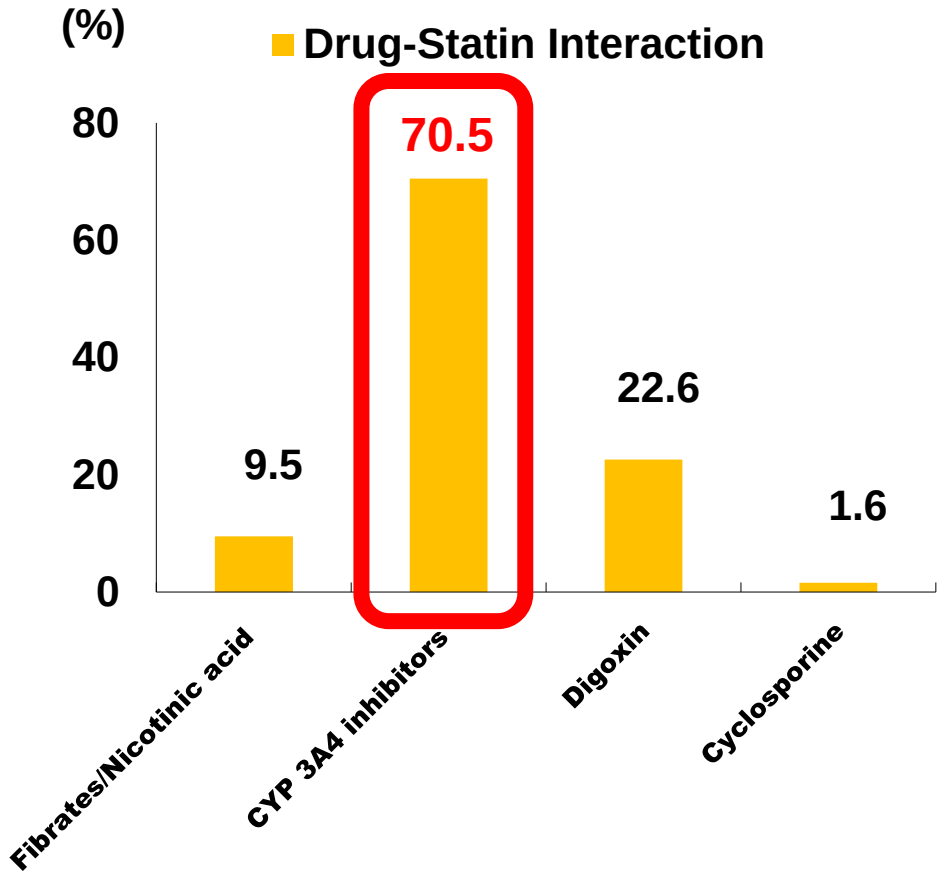
## CYP3A4 substrate

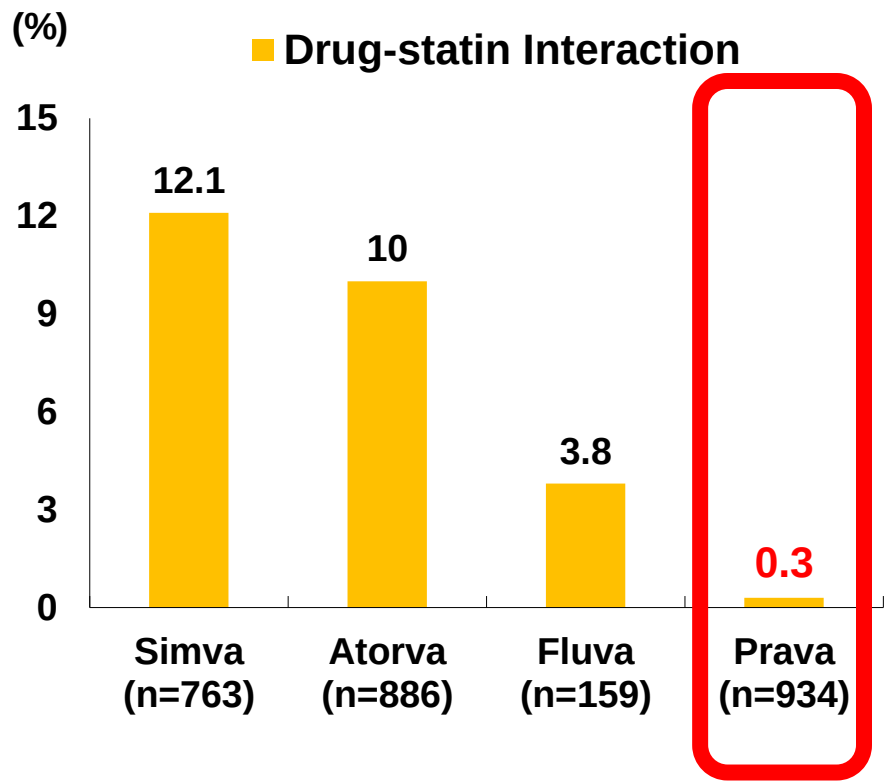
- **Anti-hypertensives-CCB**
  Amlodipine Dilitiazem
  Felodipine Nifedipine
  Nisoldipine Nitrendipine
  Verapamil
- **Anticoagulant**
  Apixaban Rivaroxaban
  Phenprocoumon
- **Antibiotic-Macrolide**
  Clarithromycin Erythromicin

Arterioscler Thromb Vasc Biol. 2019;39:e38-e81

# Mevalotin不經CYP450代謝，較少藥物交互作用

- This study included 2742 ambulatory statin-treated patients.
- CYP 3A4 inhibitors accounts for 70.5% of the drug interaction event.
- The proportion of patients with a potential drug-statin interaction was 12.1% for simvastatin，10.0% for atorvastatin, 3.8% for fluvastatin and 0.3% for pravastatin.




Drug Saf. 2005;28:263-75.

# Summary

## The Earlier, The Better

- 早期介入治療，降低更多心血管死亡風險

## Long term CV Risk Reduction

- 降低27%CHD死亡風險
- 降低31% Heart Failure 住院風險

**MEVALOTIN**

## Cost Effective

- 5年治療，每年省下71萬英鎊醫療花費
- 減少住院次數
- 縮短住院時間

## Long term Safety

- 較少副作用，較高服藥依順性
- 有效降低新生糖尿病風險
- 較少藥物交互作用

# Thank you for your attention