# Lipids & CVD prevention

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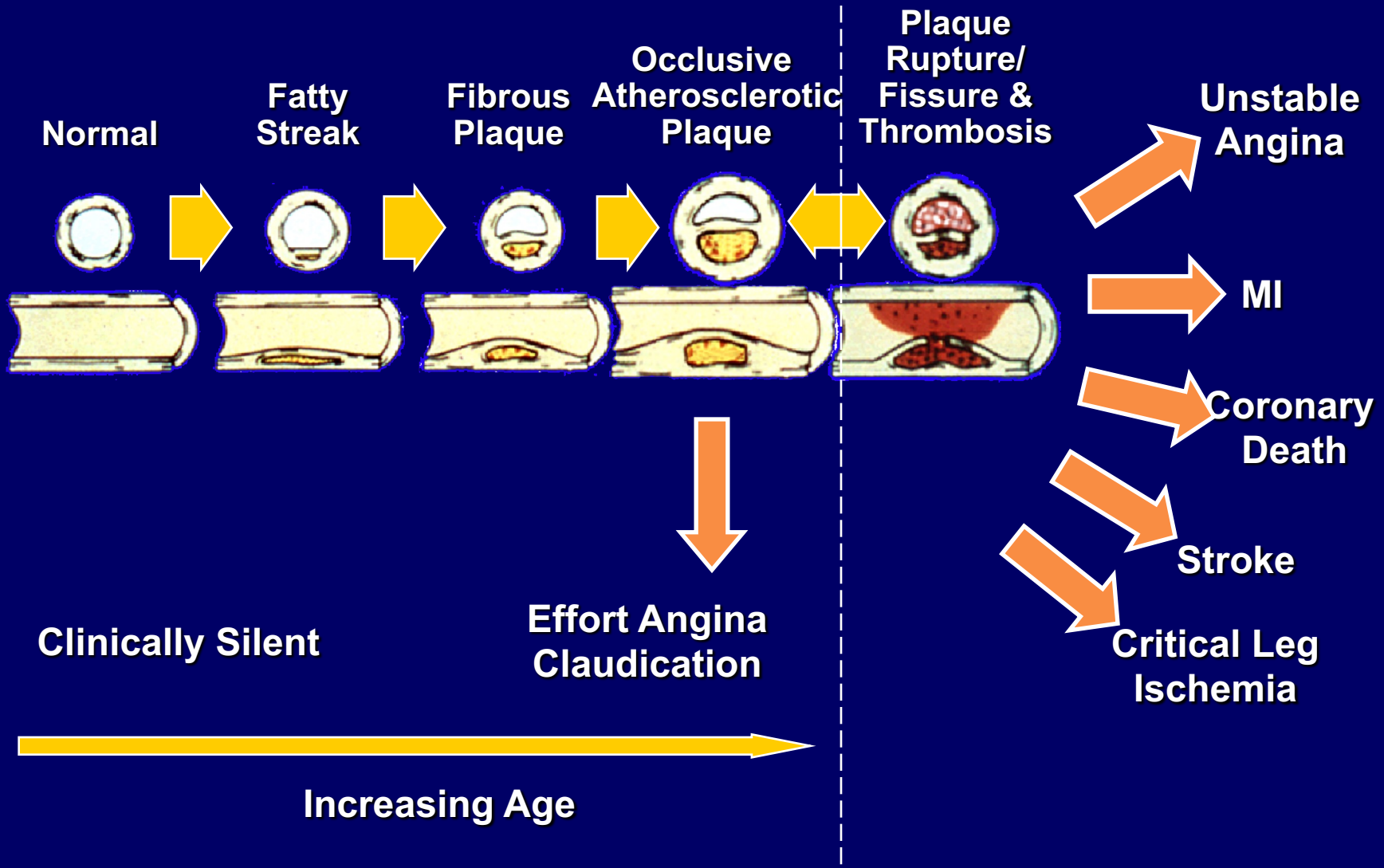
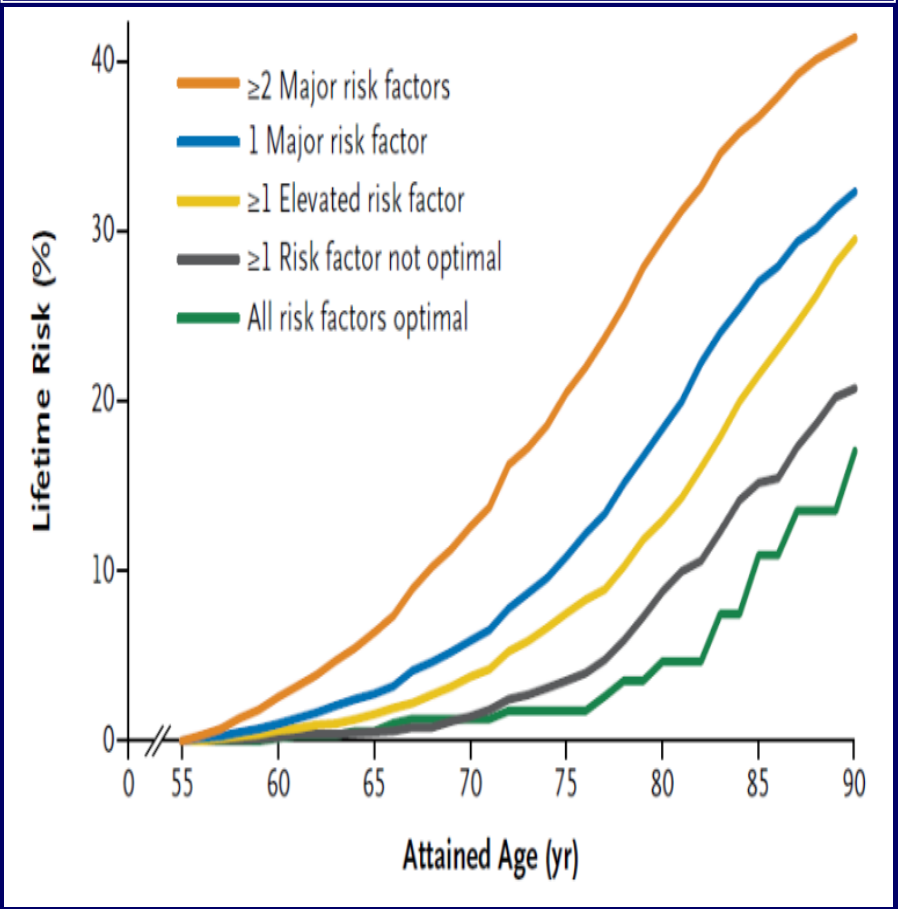
# Atherosclerosis: A Progressive Process



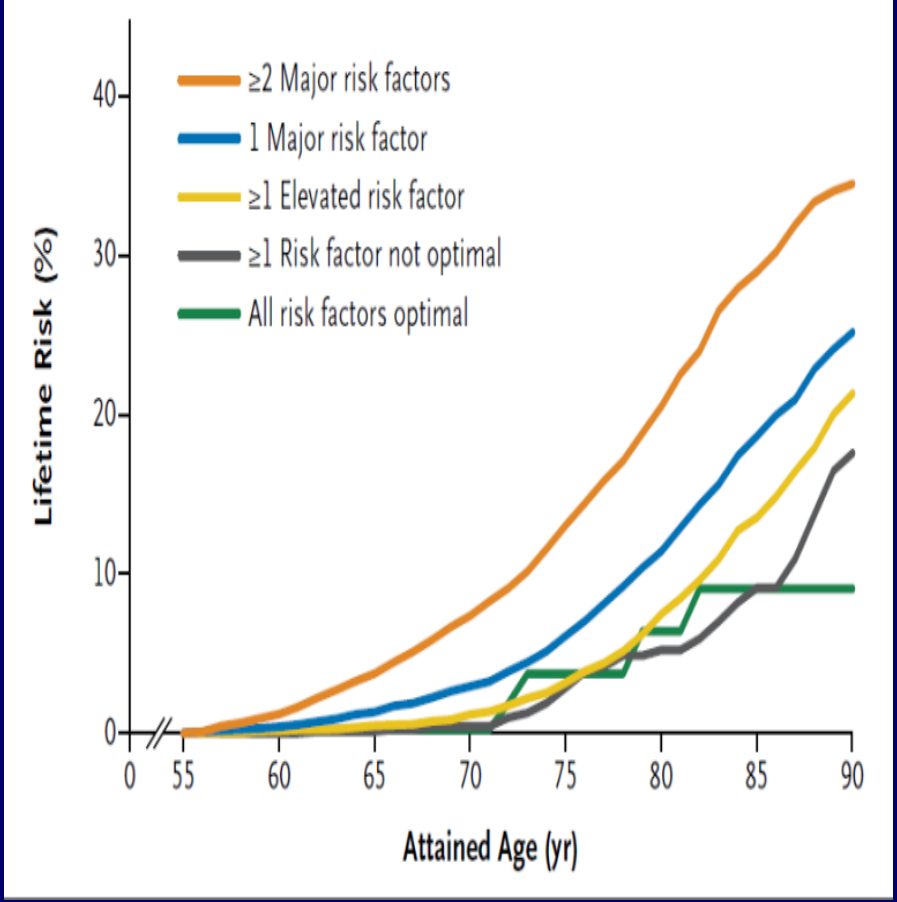

Courtesy of P Ganz.

# Lifetime risk of CVD & parameters of optimal health

## Men



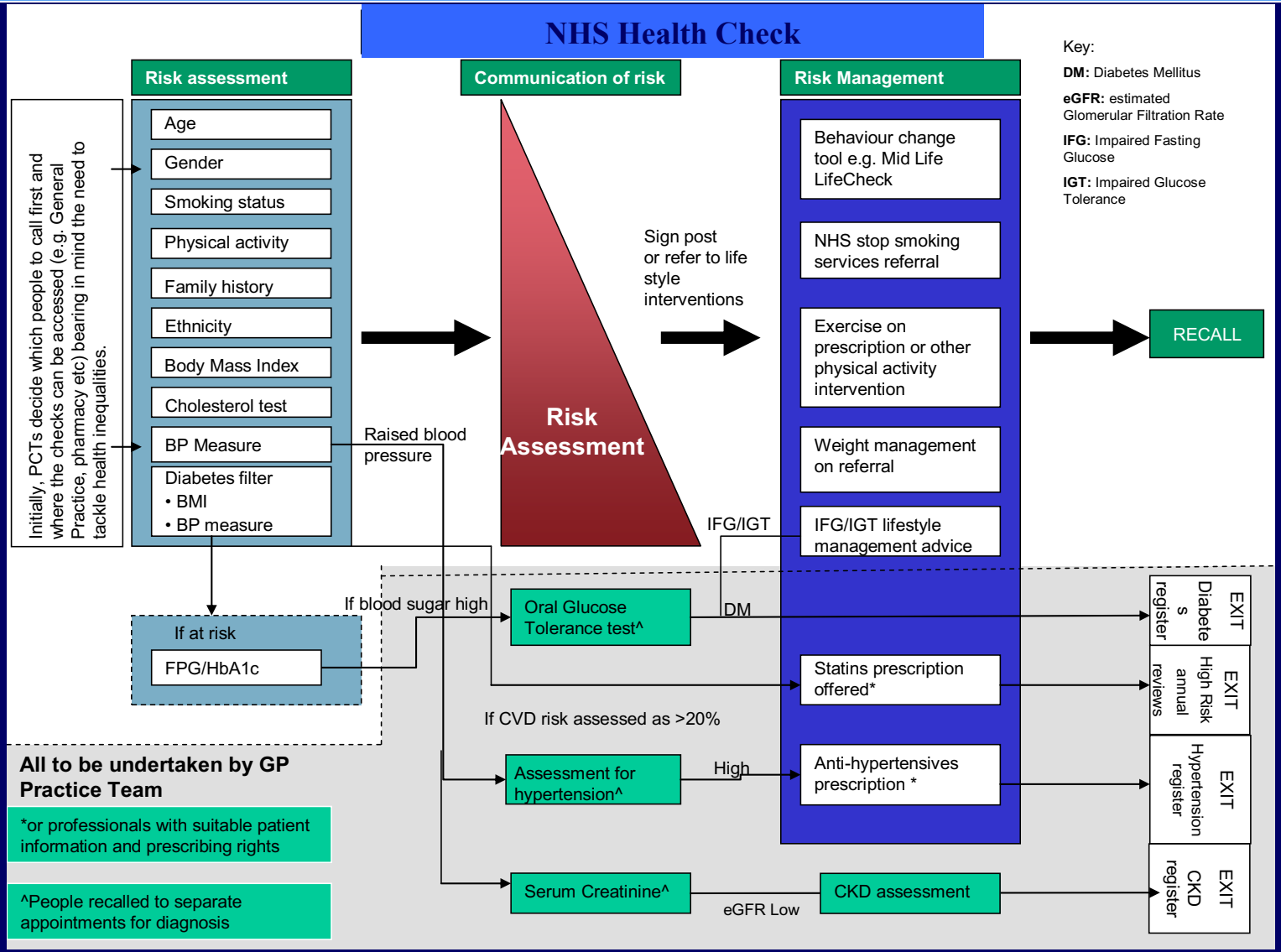

## Women




Berry JD et al. NEJM 2012; 366 : 321

N=257384

# The NHS (Vascular) Health Check




NHS Vascular risk programme briefing packs ; ww.doh.gov.uk

# NICE Key recommendations for Risk Assessment

- Non-fasting samples
  - Measure Total Cholesterol & HDL-C
    - Adds to $HbA_{1c}$ for diagnosis of T2DM
- Use QRISK2/3 calculator
  - Underestimates
    - Recent ex-smoker; ethnicity; mental health problem; obesity
  - Do not use risk calculator in
    - Type 1 DM; CKD 3 or 4; Genetic hyperlipidaemia

# Lipids: screening and the basics

- Initial non-fasting lipid profile
  - TC, TG, HDL-C & nonHDL-C
  - Non-HDL-C = LDL-C + approx 0.8mmol/L
    - i.e. LDL-C 2.00mmol/L = nonHDL-C 2.6 mmol/L
    - i.e. LDL-C 3.00mmol/L – nonHDL-C 3.8mmol/L

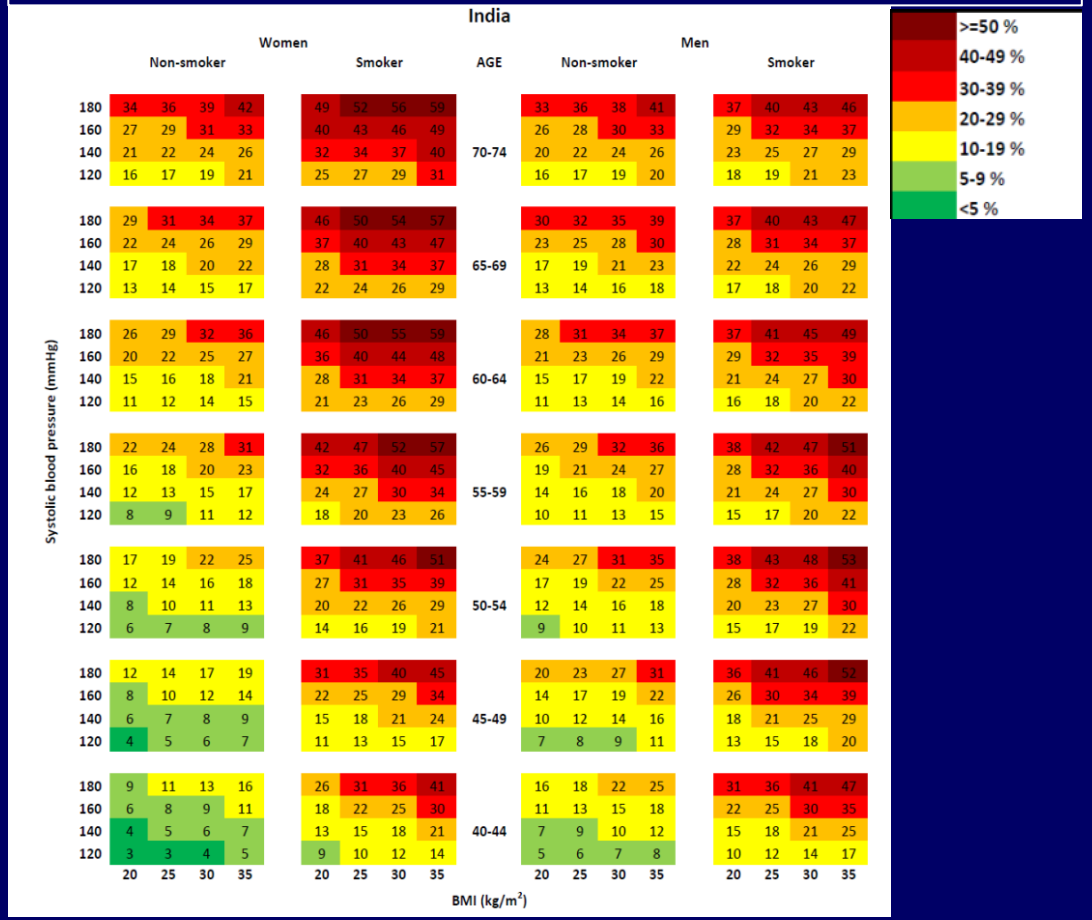
- TC >9mmol/L
  - Consider FH even in no family history of CHD
- TG> 20 mmol/L
  - If not alcohol or new DM- refer to Lipid clinic
- TG 11-20mmol/L
  - Rpt in 7 days; consider referral or advice

# Laboratory vs non-Laboratory based scores (GLOBOrisk)

## Score Components

- Traditional
  - Age & sex,
  - smoking,
  - blood pressure,
  - cholesterol,
  - diabetes
- Non-Laboratory
  - Age & sex,
  - smoking,
  - blood pressure,
  - BMI

## Globorisk: India (BMI)




Ueda P et al. Lancet Diab Endo 2017; 5 : 196

182 countries

# QRISK3 : CVD risk calculator for England

This calculator is only valid if you do not already have a diagnosis of coronary heart disease (including angina or heart attack) or stroke/transient ischaemic attack.

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**About you**

Age (25-84): 42

Sex: Male / Female

Ethnicity: Bangladeshi

UK postcode: leave blank if unknown

Postcode:

**Clinical information**

Smoking status: non-smoker

Diabetes status: none

Angina or heart attack in a 1st degree relative < 60? ☑

Chronic kidney disease (stage 3, 4 or 5)? ☐

Atrial fibrillation? ☐

On blood pressure treatment? ☐

Do you have migraines? ☐

Rheumatoid arthritis? ☐

Systemic lupus erythematosus (SLE)? ☐

Severe mental illness?
(this includes schizophrenia, bipolar disorder and moderate/severe depression) ☐

On atypical antipsychotic medication? ☐

Are you on regular steroid tablets? ☐

A diagnosis of or treatment for erectile disfunction? ☐

**Leave blank if unknown**

Cholesterol/HDL ratio: 4

Systolic blood pressure (mmHg): 150

Standard deviation of at least two most recent systolic blood pressure readings (mmHg): 10

**Body mass index**

Height (cm): 178

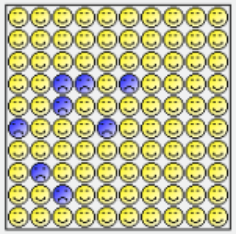
Weight (kg): 95

## Your results

Your risk of having a heart attack or stroke within the next 10 years is:

**8.2%**

In other words, in a crowd of 100 people with the same risk factors as you, 8 are likely to have a heart attack or stroke within the next 10 years.



**Risk of a heart attack or stroke**

Your score has been calculated using estimated data, as some information was left blank.

Your body mass index was calculated as 29.98 kg/m$^2$.

**How does your 10-year score compare?**

**Your score**

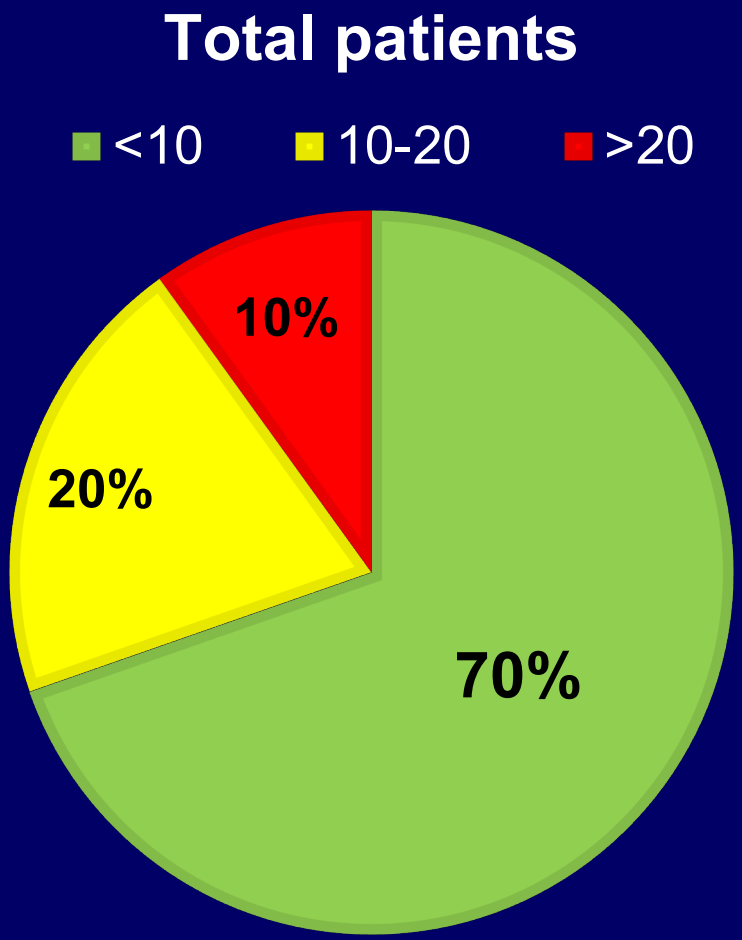
| | |
|---|---|
| Your 10-year QRISK®3 score | 8.2% |
| The score of a healthy person with the same age, sex, and ethnicity* | 2.9% |
| Relative risk** | 2.8 |
| Your QRISK®3 Healthy Heart Age*** | 53 |

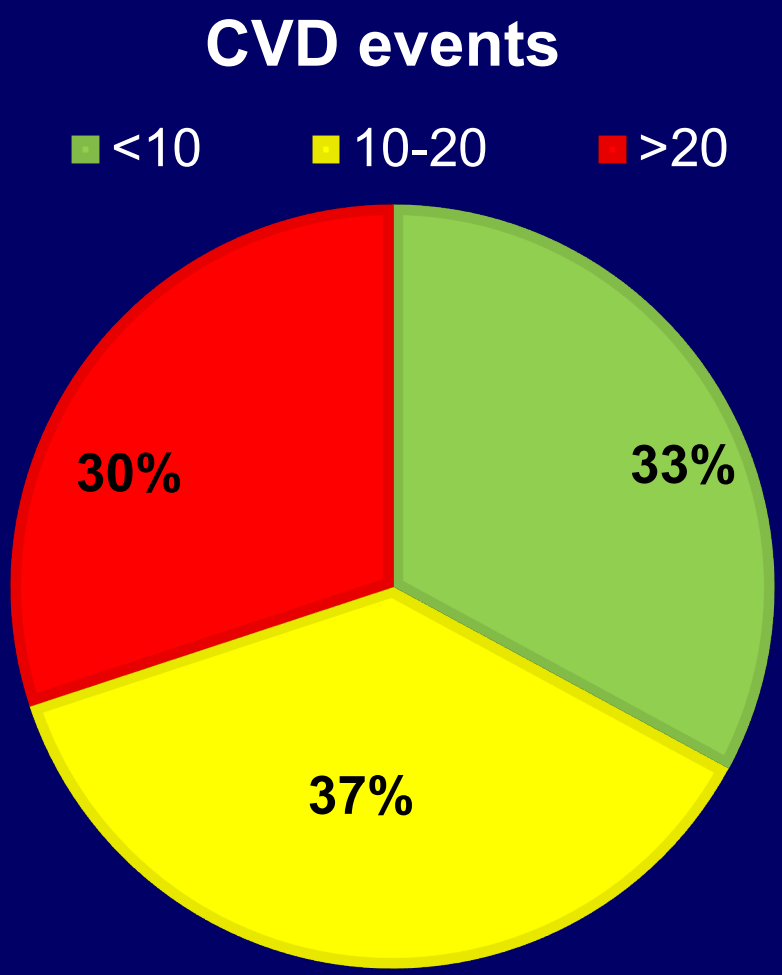
* This is the score of a healthy person of your age, sex and ethnic group, i.e. with no adverse clinical indicators and a cholesterol ratio of 4.0, a stable systolic blood pressure of 125, and BMI of 25.

** Your relative risk is your risk divided by the healthy person's risk.

*** Your QRISK®3 Healthy Heart Age is the age at which a healthy person of your sex and ethnicity has your 10-year QRISK®3 score.

# THIN Cohort: Consequences of changing to 10% risk from 20%



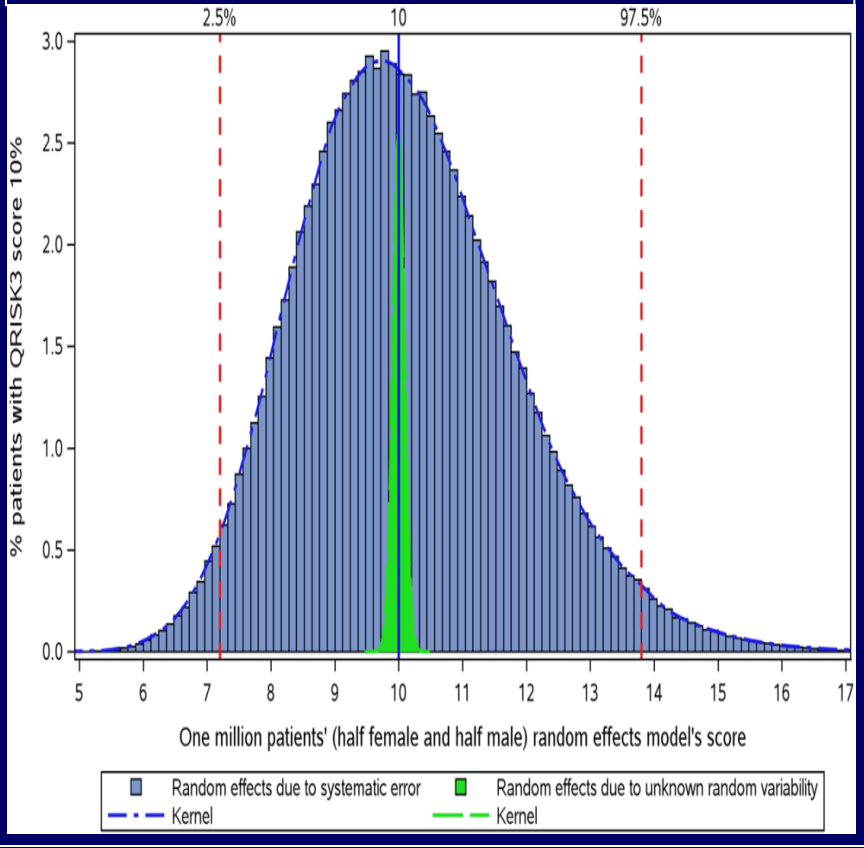




Collins GS et al; BMJ 2009; 339 : b2584

N=1,070,000 age 35-74

# QRISK: NHS data validity

## Systematic vs random effects error




## Corrected for practice recording errors

| QRISK3 predicted CVD risk (over 10 years) | Predicted risk according to random effects model incorporating practice variability | | | | | | |
|---|---|---|---|---|---|---|---|
| | Percentile | | | | | % below/above treatment threshold of 10 year CVD risk (10%) | |
| | 2.5th~97.5th | 5th | 25th | 75th | 95th | ≤10 | >10 |
| <6.5 | 0.1~6.0 | 0.1 | 0.4 | 2.6 | 5.4 | 100.0 | 0.0 |
| 6.5~7.5 | 5.3~9.4 | 5.5 | 6.3 | 7.6 | 8.9 | 99.0 | 1.0 |
| 7.5~8.5 | 6.0~10.7 | 6.3 | 7.2 | 8.7 | 10.2 | 94.0 | 6.0 |
| 8.5~9.5 | 6.8~12.0 | 7.1 | 8.2 | 9.7 | 11.4 | 80.3 | 19.7 |
| 9.5~10.5 | 7.6~13.3 | 7.9 | 9.1 | 10.8 | 12.6 | 54.0 | 46.0 |
| 10.5~11.5 | 8.4~14.6 | 8.8 | 10.0 | 11.9 | 13.9 | 24.4 | 75.6 |
| 11.5~12.5 | 9.2~15.8 | 9.6 | 11.0 | 13.0 | 15.1 | 9.1 | 90.9 |
| 12.5~13.5 | 10.0~17.1 | 10.4 | 11.9 | 14.0 | 16.3 | 2.4 | 97.6 |
| ≥13.5 | 12.7~55.4 | 13.5 | 17.8 | 34.7 | 50.2 | 0.1 | 99.9 |

674 practices (n=4.4M) BMI missing: 19-60%; BP 14-39%; Lipid 48-70% ; Smoking 10-29% CVD endpoint rate: 0.4-1.3/100 pt-yr

Li Y et al; Sci Rep 2019; 9 ; 112222

CI @10% = 7.2-13.7%

# Dietary interventions

- Dated studies
- Poor Evidence
- Modern evidence
  - PREDIMED underpowered
- Conclusions
  - Total fat intake < 30% of energy intake,
  - Saturated fats < 7% of energy intake,
  - Dietary cholesterol < 300 mg/day
  - Saturated fats replaced by MUFA or PUFA fats.

Eat food, not too much; mostly plants.

Michael Pollan (2009)

# MRFIT- the personalised lifestyle intervention trial

| Endpoint | Number of Men With Event (%) | | HR | 95% CI | *P* |
|---|---|---|---|---|---|
| | SI | UC | | | |
| Overall composite CVD endpoint | | | | | |
| Nonfatal or fatal CVD | 581 (9.0) | 652 (10.1) | 0.89 | 0.79–0.99 | 0.04 |
| Nonfatal and fatal composite CVD endpoints | | | | | |
| Nonfatal CVD | 460 (7.2) | 529 (8.2) | 0.87 | 0.76–0.98 | 0.02 |
| Fatal CVD | 139 (2.2) | 146 (2.3) | 0.95 | 0.76–1.20 | 0.68 |
| Components of composite CVD endpoint not shown in lower half of Table 2* | | | | | |
| **Fatal or nonfatal stroke** | **49** | **41** | **1.20** | **0.79–1.81** | **0.40** |
| Nonfatal stroke | 36 | 30 | 1.20 | 0.74–1.95 | 0.46 |
| Fatal stroke | 13 | 11 | 1.18 | 0.53–2.64 | 0.68 |
| **Impaired renal function†** | **9** | **11** | **0.82** | **0.34–1.97** | **0.65** |
| **Other fatal CVD** | **10** | **10** | **1.00** | **0.42–2.40** | **0.99** |

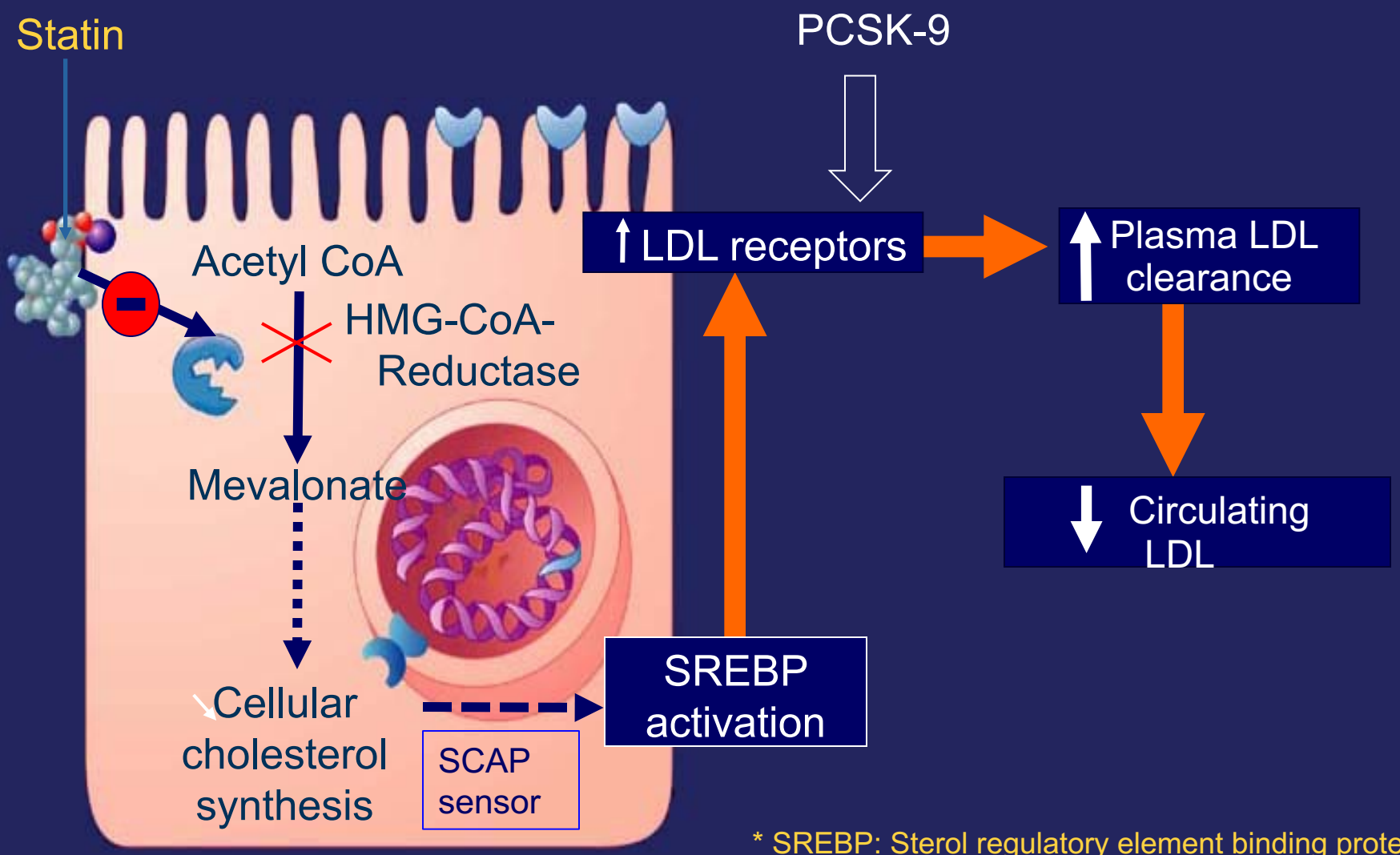
Stamler J et al; JAHA 2012; 1 : e 003640

NNT = 95

N=12866

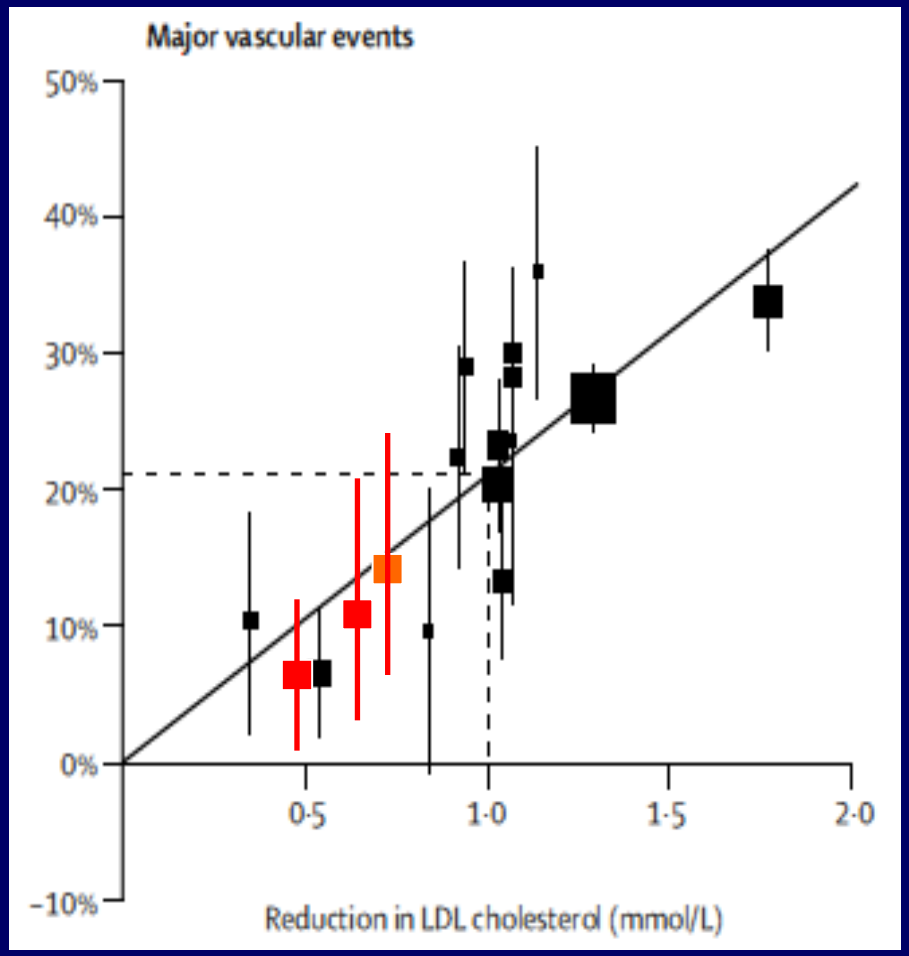
# Statins: Mechanisms of action

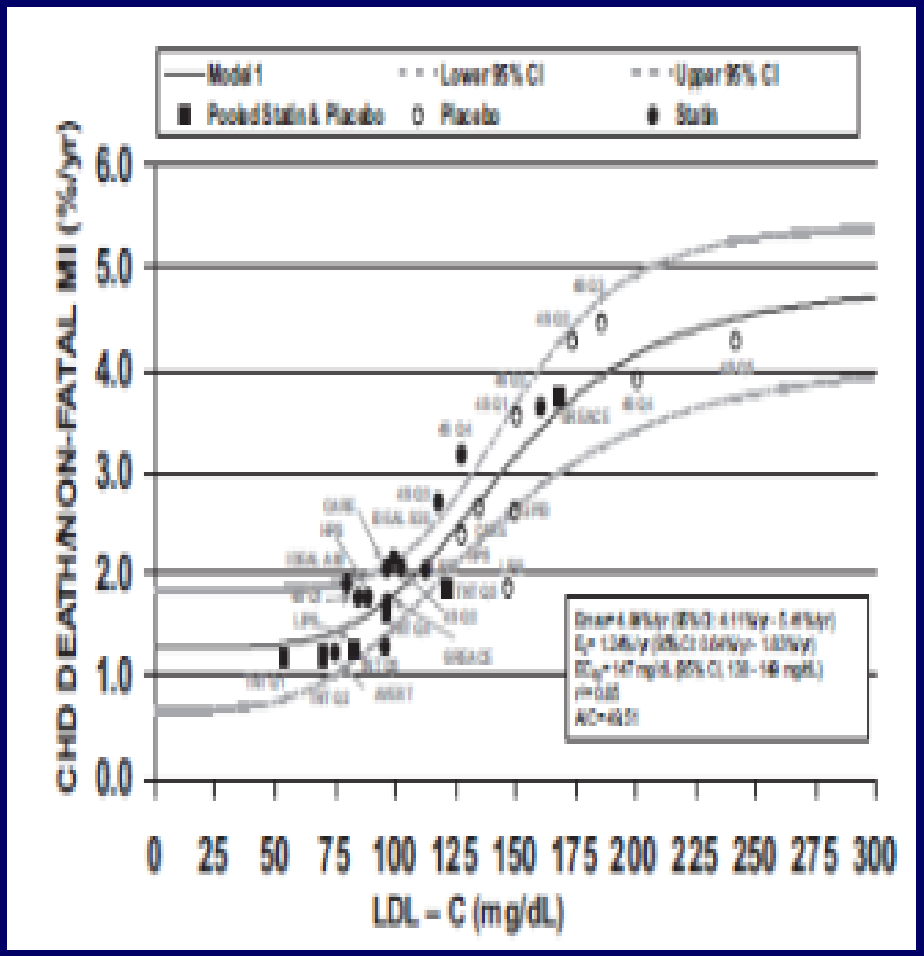
## SREBP* feedback control




* SREBP: Sterol regulatory element binding protein

# Meta-analyses of CHD vs LDL-C and Incremental effects of lipid drugs




Cholesterol Treatment Trialists; Lancet 2010; 376: 1670

Charland SL & Stanek EJ; Pharmacother 2014; 34 : 452

# Statin interventions

| | Active treatment | Control | Relative risk | Absolute Effect (per thousand) |
|---|---|---|---|---|
| **Statin vs placebo** | | | | |
| **CVD mortality** | 2347/59459 (3.9%) | 2882/59459 (4.8%) | 0.81 (0.77-0.86) | **-9** (-7 to -11) |
| **Non-fatal MI** | 1593/45915 (3.5%) | 2318/45567 (5.1%) | 0.69 (0.65-0.73) | **-16** (-14 to -18) |
| **Stroke** | 1456/54602 (2.7%) | 1867/54642 (3.4%) | 0.78 (0.73-0.83) | **-8** (-6 to -9) |
| | | | | |
| **Statin : High intensity vs. moderate intensity** | | | | |
| **CVD mortality** | 972/17730 (5.5%) | 1026/17720 (7.0%) | 0.95 (0.87-1.03) | -3 (-8 to +2) |
| **Non-fatal MI** | 1058/17730 (6.0%) | 41247/17720 (2.8%) | 0.79 (0.67-0.93) | **-13** (-4 to -20) |
| **Stroke** | 388/12735 (3.0%) | 439/12714 (3.5%) | 0.88 (0.77-1.01) | -4 (0 to -8) |

Rabar S et al; BMJ 2014; 349 :g4356

# Comparing statin intensity

## US comparison

| Statin Therapy | Daily Dose | | |
|---|---|---|---|
| | High-Intensity† | Moderate-Intensity‡ | Low-Intensity§ |
| Atorvastatin | 40‖–80 mg | 10 (20) mg | – |
| Rosuvastatin | 20 (40) mg | (5) 10 mg | – |
| Simvastatin | – | 20–40 mg¶ | 10 mg |
| Pravastatin | – | 40 (80) mg | 10–20 mg |
| Lovastatin | – | 40 mg | 20 mg |
| Fluvastatin | – | 80 mg (Fluvastatin XL) | 20–40 mg |
| Fluvastatin | – | 40 mg** | – |
| Pitavastatin | – | 2–4 mg | 1 mg |

>50% 30-50% <30%

Stone NJ et al; Circ 2014; 129 : S1-S45;

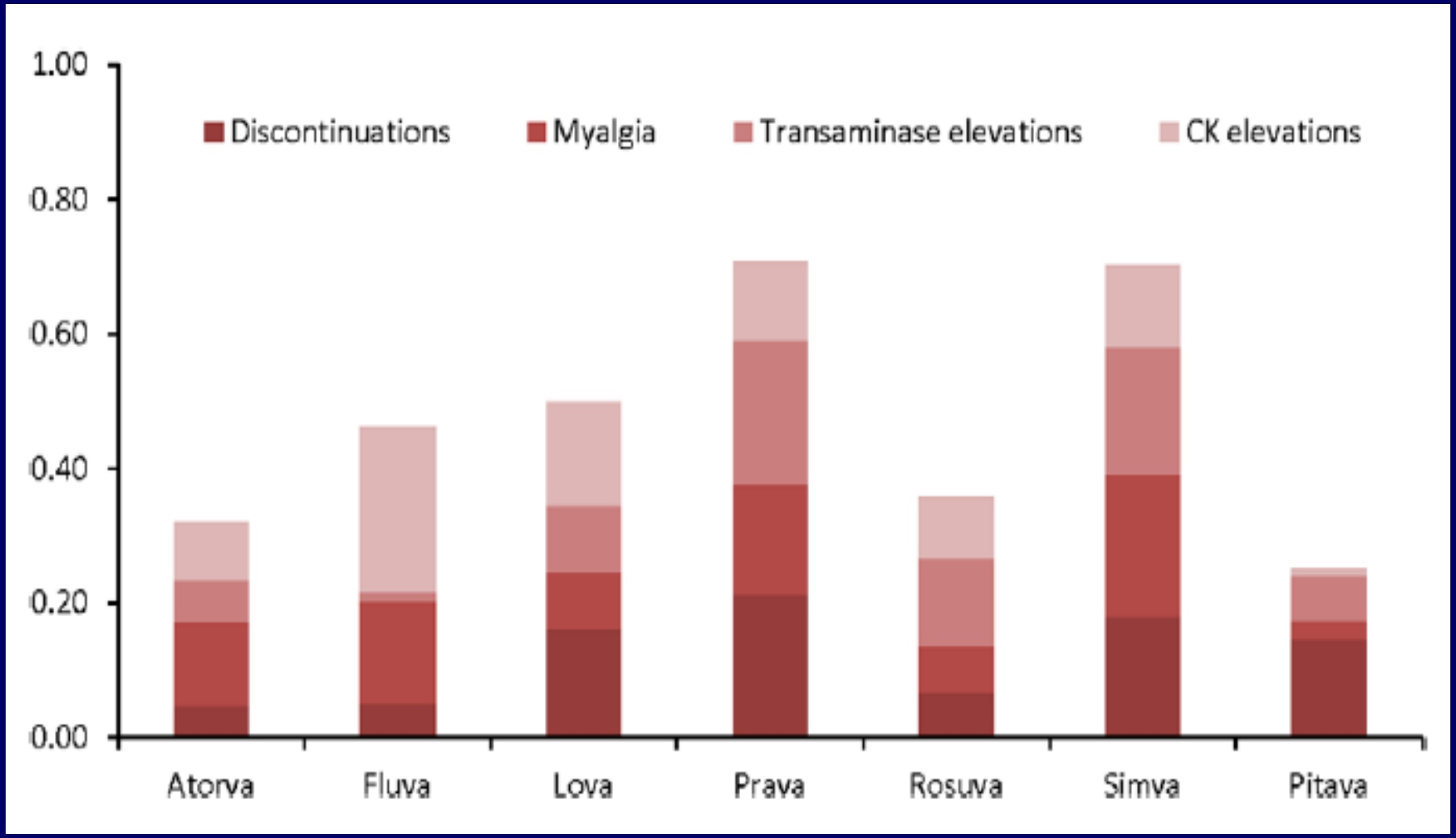
## NICE lipids comparison

| Low intensity | Medium intensity | High intensity |
|---|---|---|
| Fluvastatin 20 mg | Atorvastatin 10mg | Atorvastatin 20mg |
| Fluvastatin 40 mg | Fluvastatin 80 mg | Atorvastatin 40 mg |
| Pravastatin 5 mg | Rosuvastatin 5 mg | Atorvastatin 80 mg |
| Pravastatin 10 mg | Simvastatin 20 mg | Rosuvastatin 10 mg |
| Pravastatin 20 mg | Simvastatin 40 mg | Rosuvastatin 20 mg |
| Pravastatin 40 mg | | Rosuvastatin 40 mg |
| Simvastatin 10 mg | | ~~Simvastatin 80 mg~~ |

<30% 31 - 40% >40%

Rabar S et al; BMJ 2014; 349 :g4356

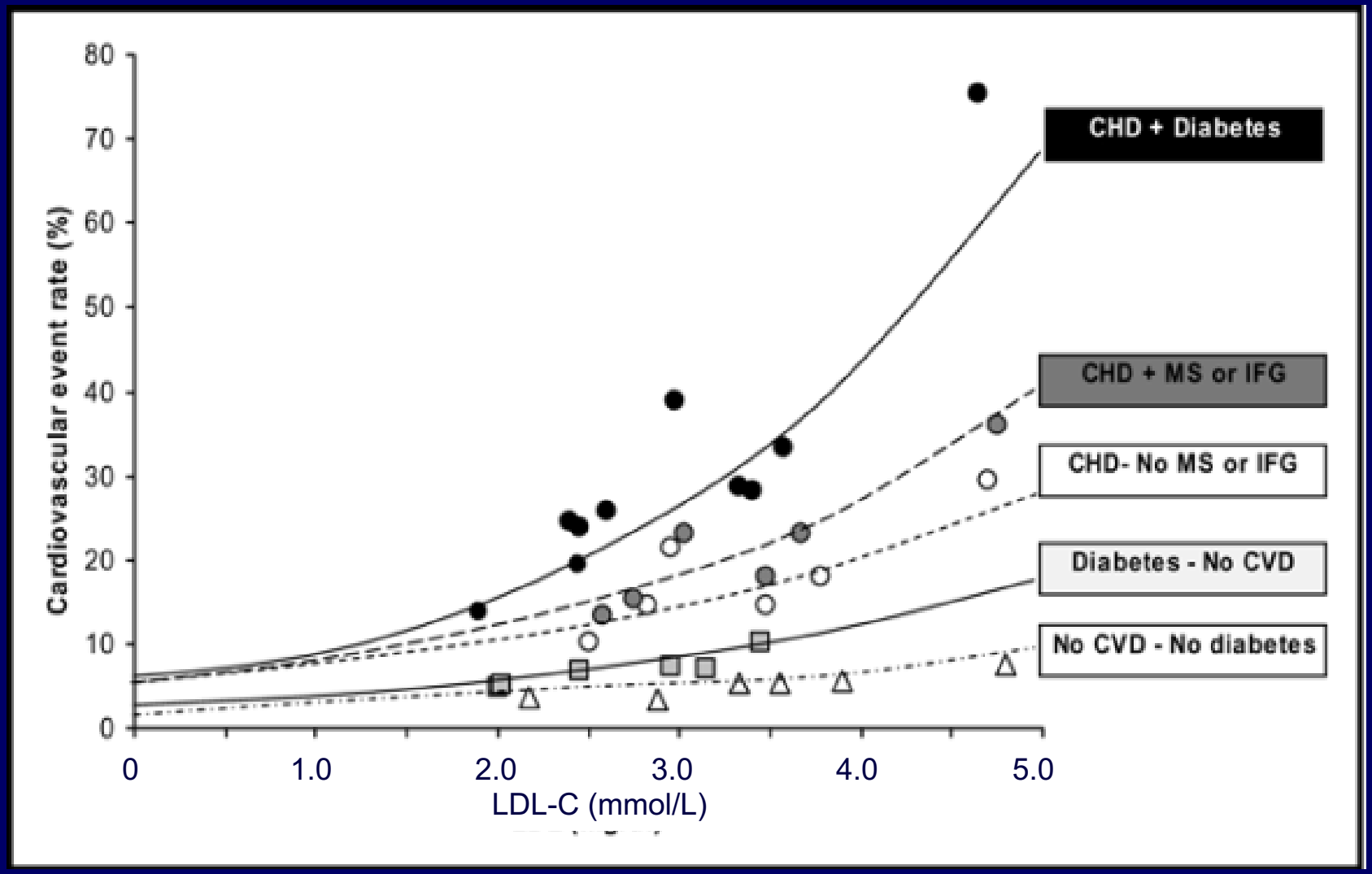
# Predicting the best statin to use




Trials =135; n=246955

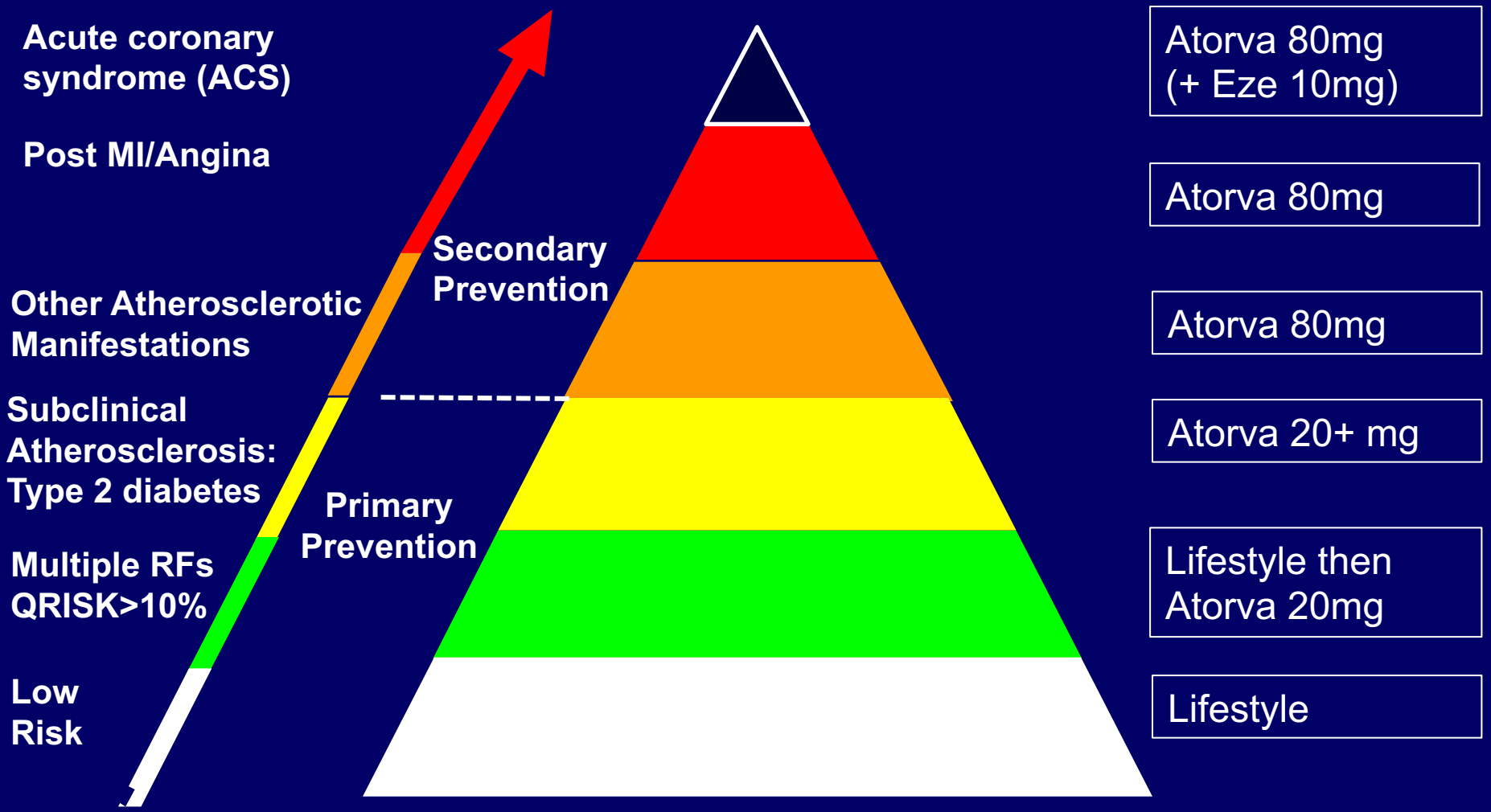
Naci H et al; Circ CV Qual Outcome 2013; 6: 390

# CVD risk for different groups




Robinson JG & Stone N. Am J Cardiol 2006; 98 : 1405

# NICE –CG 181 Continuum of CVD Risk and its treatment




Courtesy of CD Furberg.; modified to include NICE CG181

# Efficacy and NNT of QRISK 10% risk assessment with atorvastatin 20mg

| | | |
|---|---|---|
| Male 60 years old, non-smoker, systolic BP 138 mmHg, serum cholesterol 4.7 mmol/L, HDL cholesterol 1.2 mmol/L, non-HDL cholesterol 3.5 mmol/L, serum : HDL cholesterol ratio 3.92. | 10% | 36 |
| Male 58 years old, non-smoker, systolic 143 mmHg, serum cholesterol 7.0 mmol/L, HDL cholesterol 1.5 mmol/L, non-HDL cholesterol 5.5 mmol/L, serum: HDL cholesterol ratio 4.67. | 10% | 24 |

| 10-year cardiovascular disease risk, % | Pretreatment LDL cholesterol (change on treatment), mmol/L | | | | | |
|---|---|---|---|---|---|---|
| | 2 (−0.86) | 3 (−1.29) | 4 (−1.72) | 5 (−2.15) | 6 (−2.58) | 7 (−3.01) |
| | NNT* with atorvastatin 20 mg daily | | | | | |
| 5 | 103 | 73 | 57 | 48 | 42 | 38 |
| 7.5 | 69 | 49 | 38 | 32 | 28 | 25 |
| 10 | 52 | 36 | 29 | 24 | 21 | 19 |
| 20 | 26 | 18 | 14 | 12 | 11 | 9 |
| 30 | 17 | 12 | 10 | 8 | 7 | 6 |

Soran H et al; Eur Heart J 2015; 36 : 2975

# Statin Side effects

| | Active treatment | Control | Relative risk | Absolute Effect (per thousand) |
|---|---|---|---|---|
| **Statin** | | | | |
| **Myalgia** | 348/14960 (2.3%) | 288/14520 (2.0%) | 1.02 (0.88-1.19) | +1 (-1 to +5) |
| **Rhabdomyolysis** | 138/2454 (5.6%) | 158/2446 (6.5%) | 0.87 (0.70-1.08) | -8 (-19 to +5) |
| **Elevated transaminase** | 282/42702 (0.66%) | 142/42667 (0.35%) | 1.90 (1.56-2.32) | +3 (+2 to +5) |
| **New onset diabetes** | 1829/38996 (4.7%) | 1675/39021 (4.3%) | 1.09 (1.03-1.17) | +4 (+1 to +7) |

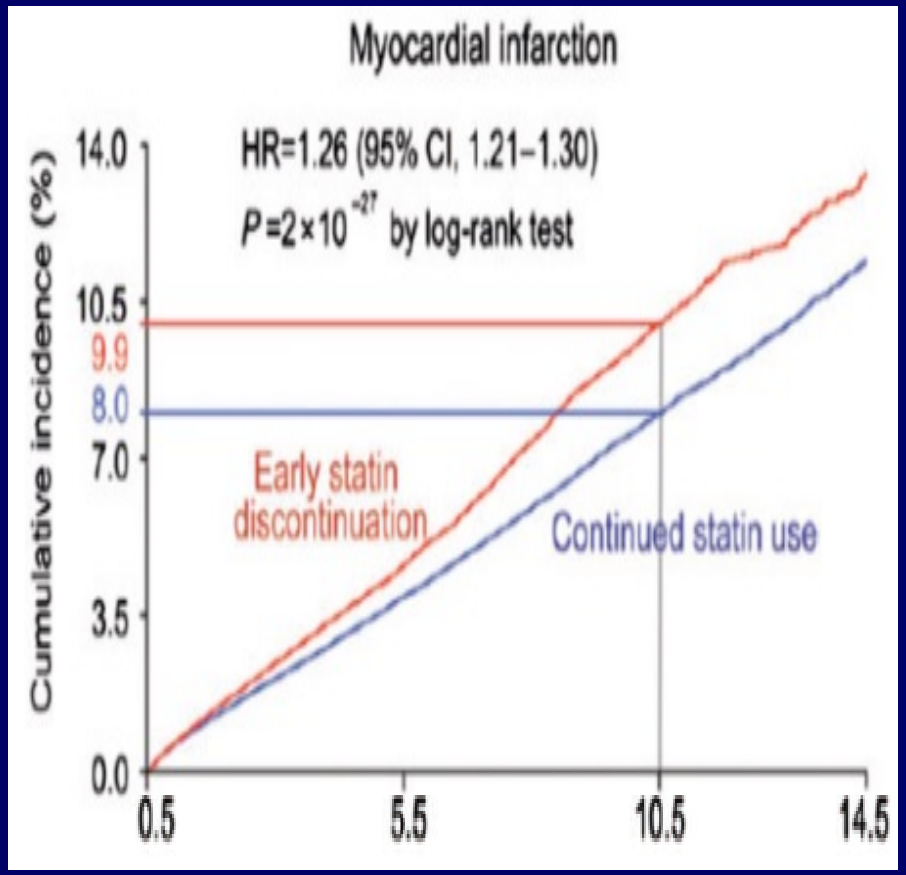
Rabar S et al; BMJ 2014; 349 :g4356

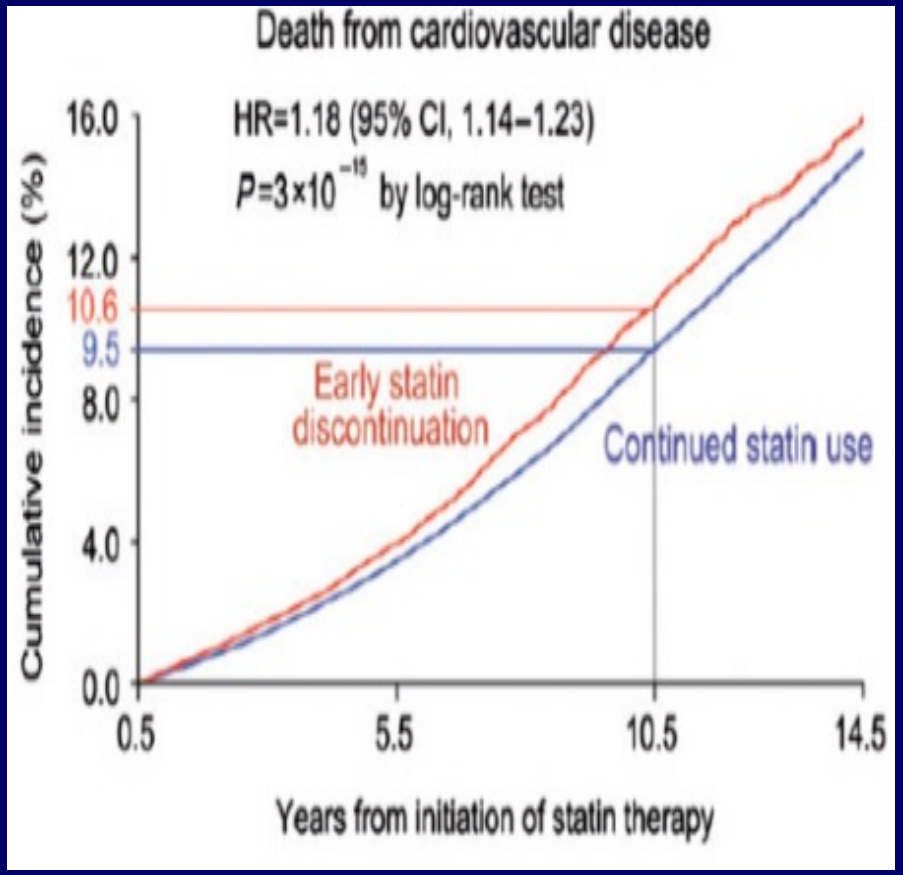
# New onset diabetes with statins

| Risk factors | Study | Hazard ratio (95% CI) for new-onset diabetes | P value |
|---|---|---|---|
| **Fasting glucose per 10 mg/dl increase** | TNT | 2.53 [2.34, 2.73] | <0.0001 |
| | IDEAL | 2.49 [2.26, 2.74] | <0.0001 |
| **BMI per 3 kg/m$^2$increase** | TNT | 1.21 [1.16, 1.26] | <0.0001 |
| | IDEAL | 1.29 [1.20, 1.38] | <0.0001 |
| **Natural log [WBC] per 0.25 log (103/mm$^3$) increase** | TNT | 1.15 [1.06, 1.24] | 0.0012 |
| **Natural log [triglyceride] per 1.0 log (mg/dl) increase** | TNT | 1.85 [1.53, 2.22] | <0.0001 |
| | IDEAL | 1.48 [1.19, 1.83] | 0.0004 |
| **Hypertension** | TNT | 1.24 [1.05, 1.46] | 0.0098 |
| | IDEAL | 1.32 [1.09, 1.60] | 0.005 |
| **Effect of atorvastatin 80 mg** | TNT | 1.10 [0.94, 1.29] | 0.226 |
| | IDEAL | 1.19 [0.98, 1.43] | 0.075 |

Rabar S et al; BMJ 2014 & Waters DD et al. J Am Coll Cardiol. 2011; 57 :1535

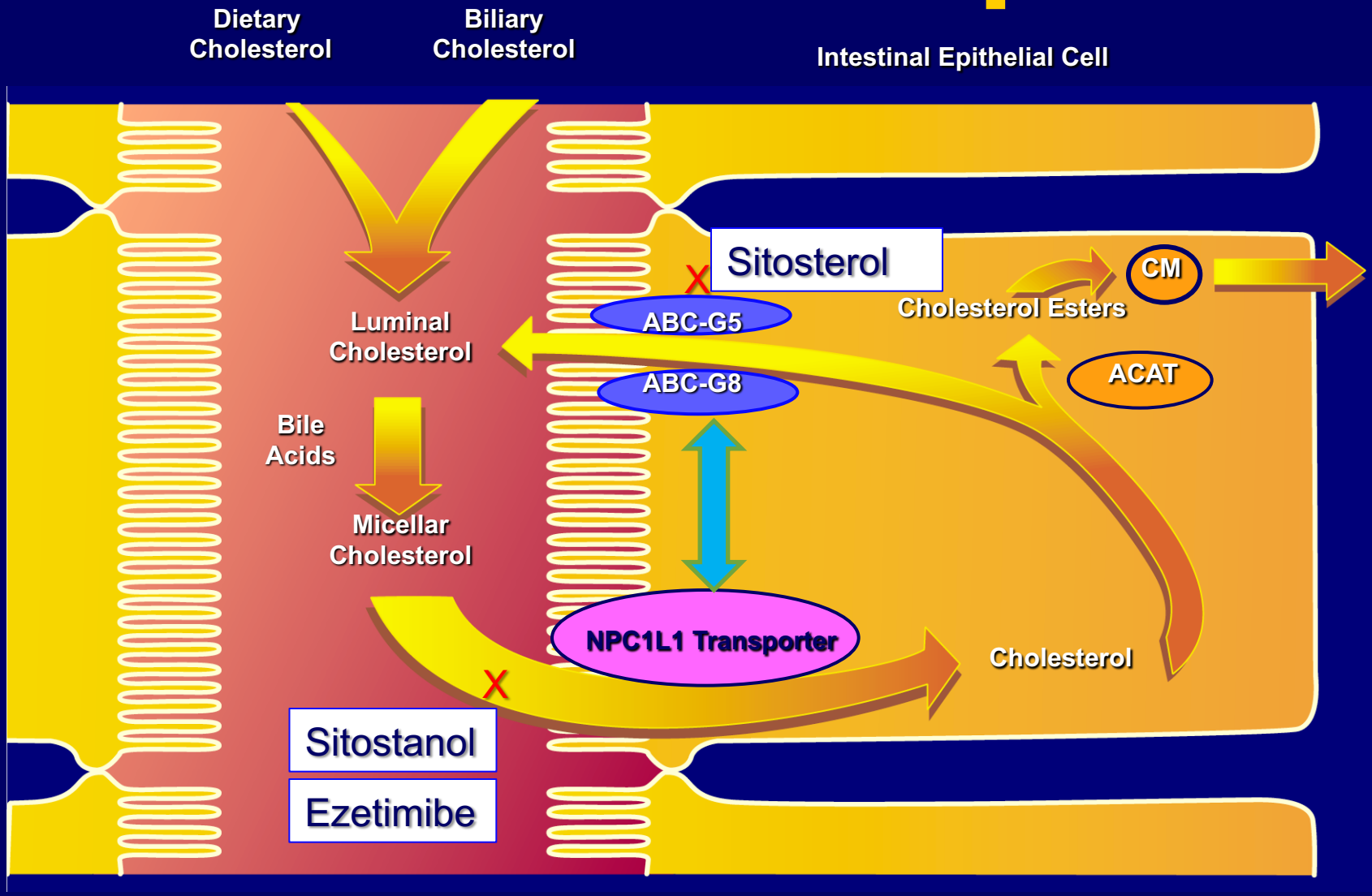
# Statin discontinuation - consequences



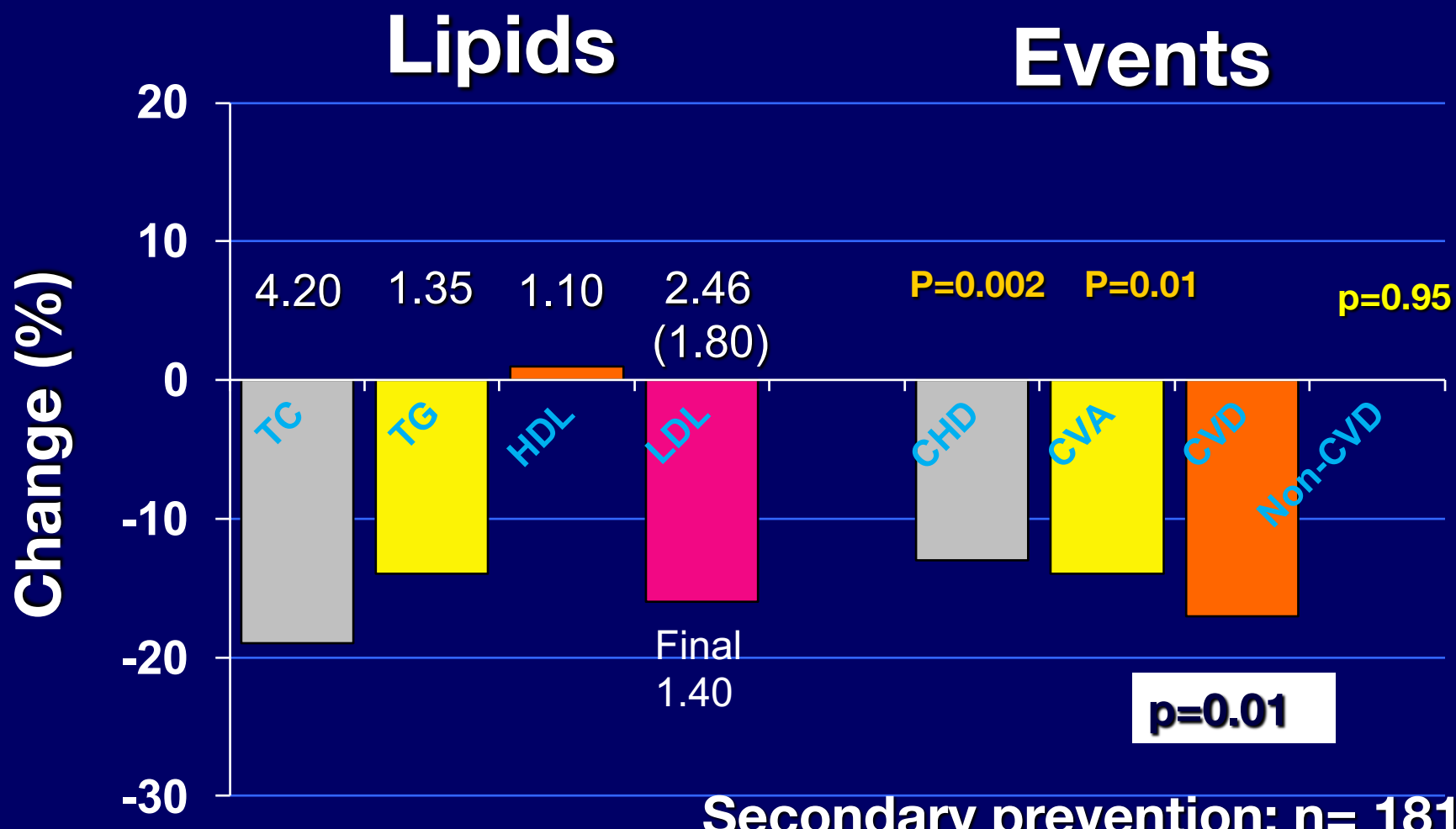




Neilsen SF & Nordestgaard BG. Eur Heart J 2016; 37 : 908

# Steps Involved in Cholesterol Absorption



# IMPROVE –IT : Ezetimibe in statin-treated ACS



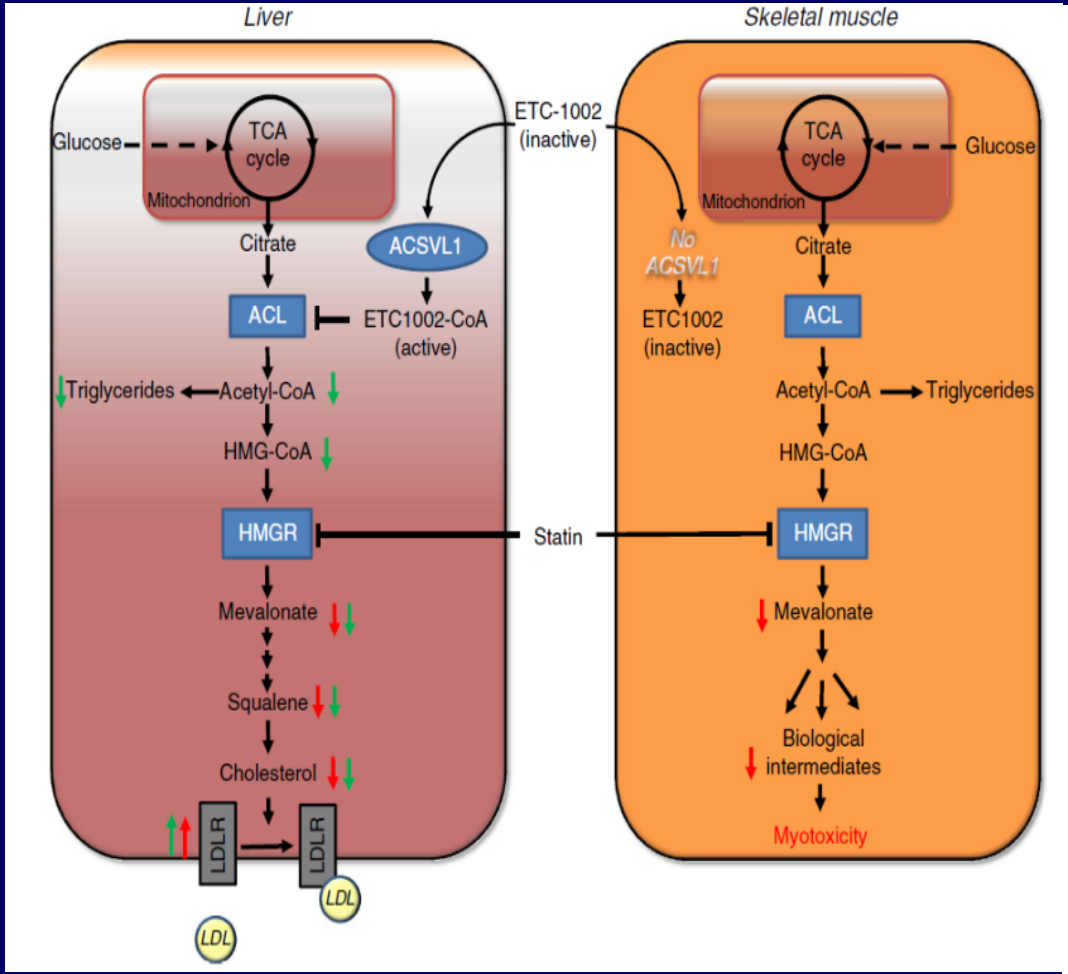

**Secondary prevention; n= 18144**

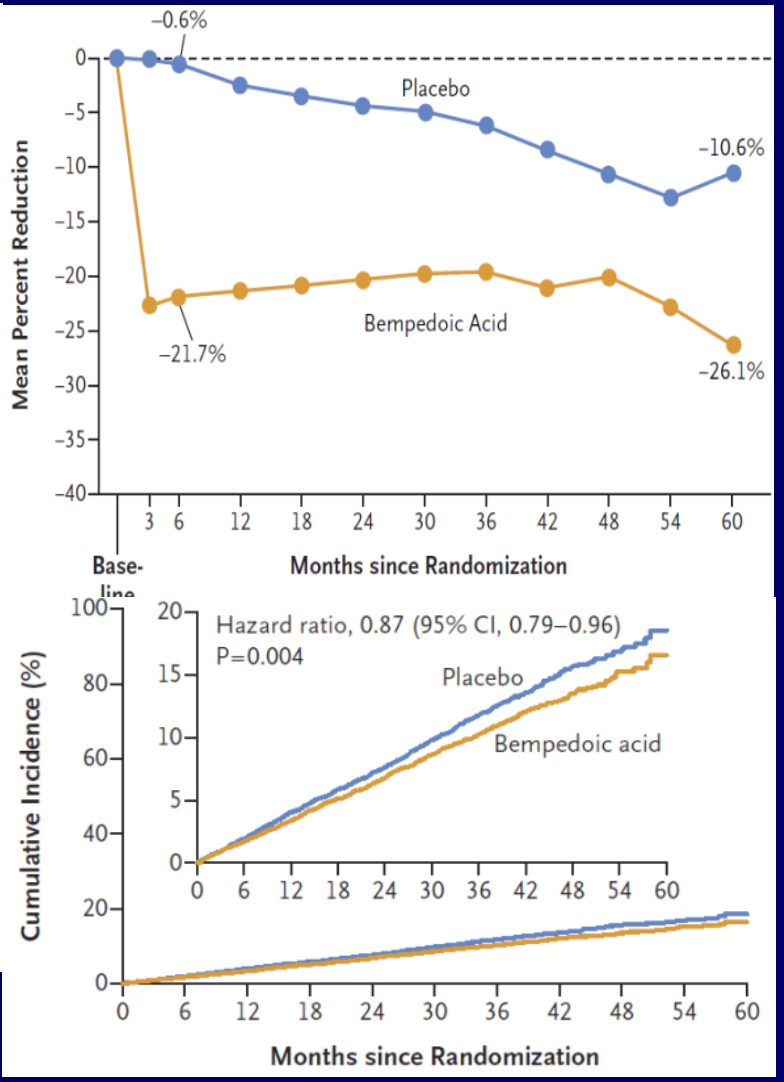
**NNT including PCI = 50**

Cannon CP et al ; NEJM 2015; 372 : 2387

Effects larger in elderly & Type 2 DM

# Hepatic ATP-citrate lyase & bempedoic acid in CVD

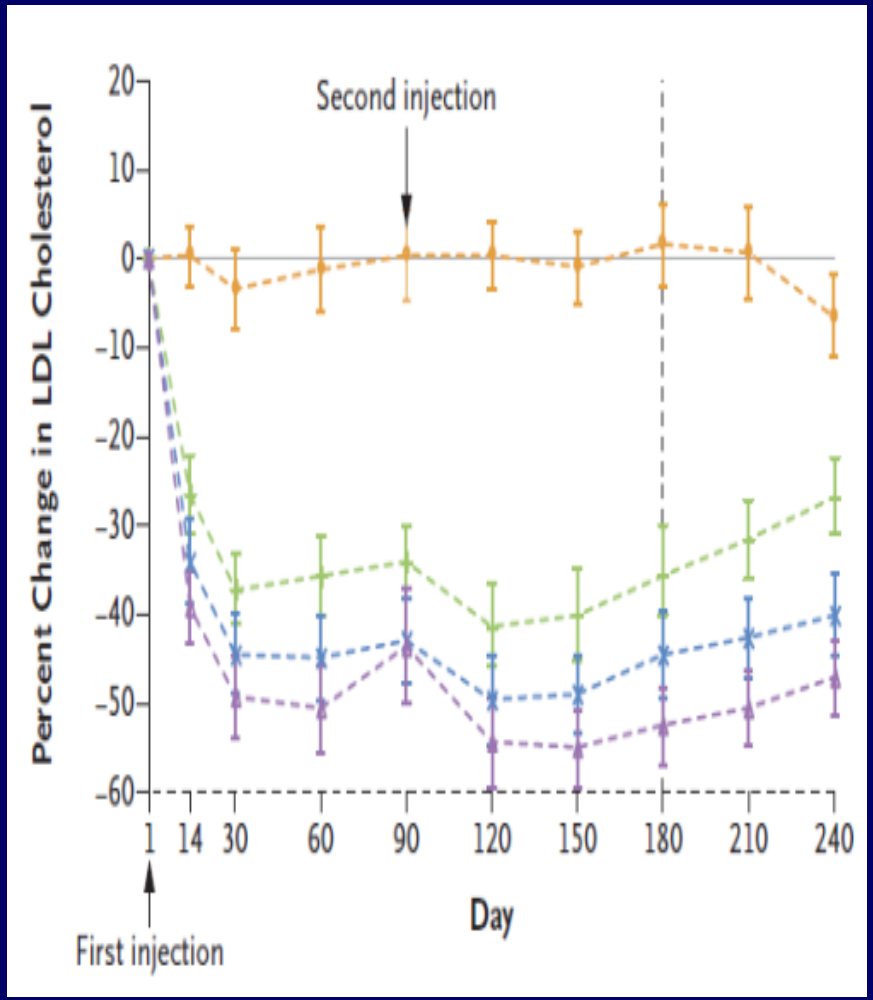



Pinkosky SL et al. Nature Comm 2016; 7: 13457
Nissen SE et al. NEJM 2023; 388: 1353

# Effects of PSCK-9 inhibition on LDL-C & apoB

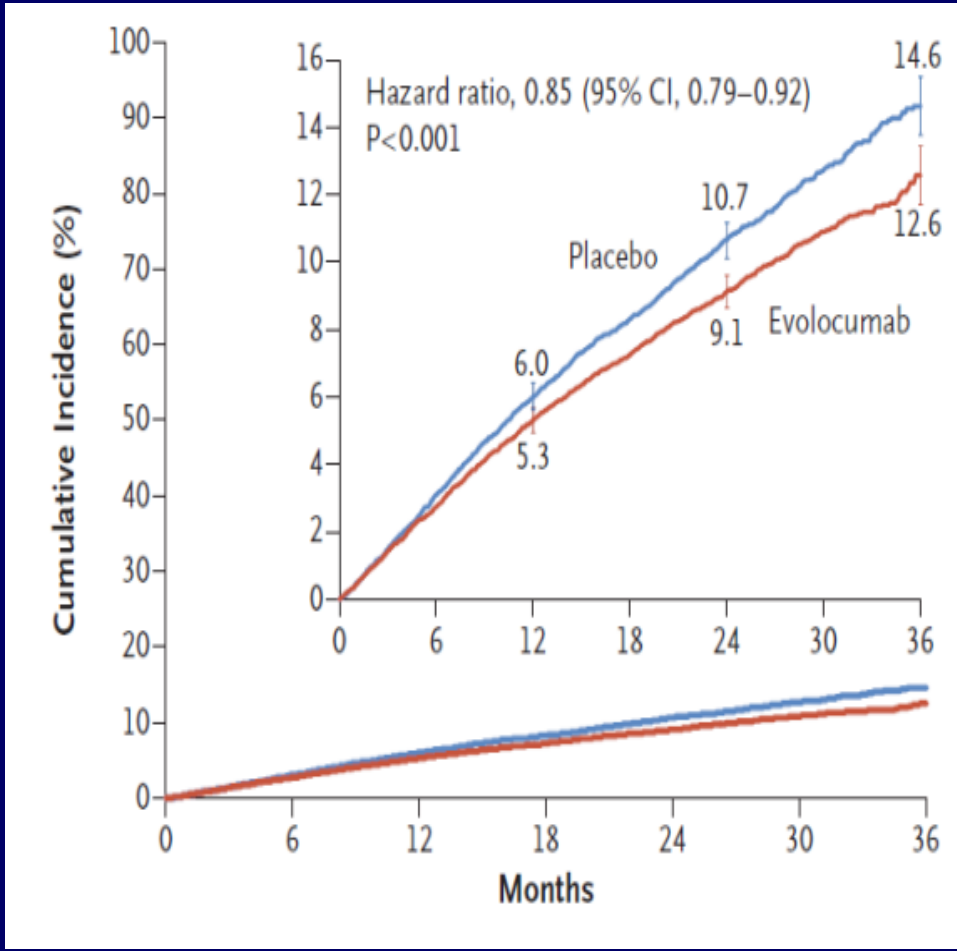
- PSCK-9 inhibitors
  - Small molecule
    - Pre-clinical only
  - Antibody
    - Alirocumab;
    - Evolocumab:
    - Bococizumab- discontinued
  - Antisense oligonucleotide
    - SPC-5001- discontinued
  - Targeted siRNA
    - inclisiran

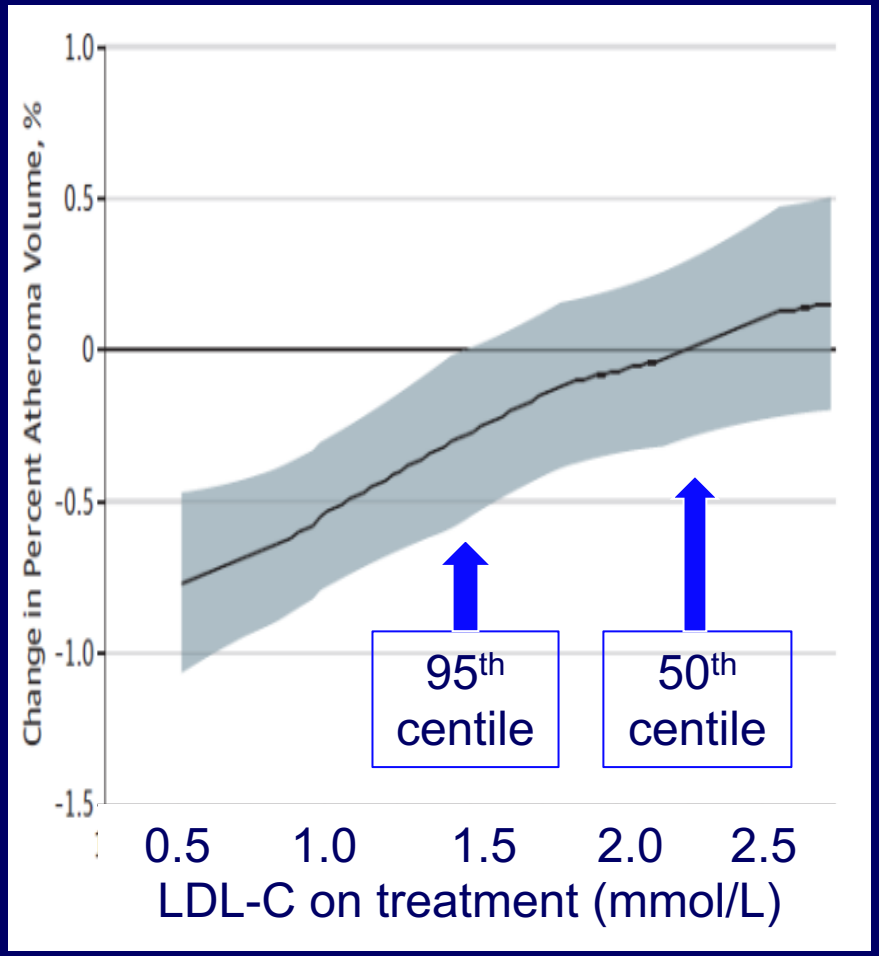



Inclisiran- 2 injections

Stein EA et al; Lancet 2012; 380 : 29
Ray KK et al; NEJM 2017: 376: 1430

# PCSK-9 inhibition-Evolocumab: FOURIER-ACS & GLAGOV-IVUS




Sabatine M et al; NEJM 2017; 376: 1713
Nicholls SJ et al. JAMA 2016; 316: 2373

# Other LDL-C lowering drugs: ezetimibe & PCSK9 inhibitors

| | Active Treatment | Control | Relative Risk | Absolute Effect (Events/1000) |
|---|---|---|---|---|
| **Ezetimibe (IMPROVE-IT)** | (7 years) | | | |
| **CVD Mortality** | 617/9424 (6.5%) | 627/9440 (6.7%) | 0.99 (0.89-1.10) | Nil -7 to +7 |
| **Non-Fatal MI** | 1191/9424 (12.6%) | 1345/9440 (14.8%) | 0.90 (0.84-0.97) | **-15 (-4 to -24)** |
| **Stroke** | 383/9424 (4.1%) | 437/9440 (4.8%) | 0.88 (0.77-1.01) | -6 (-11 to Zero) |
| **PCSK-9** | (1.1-2.2 years) | | | |
| **CVD Mortality** | 555/36968 (1.5%) | 576/36964 (1.6%) | 0.96 (0.80-1.20) | Nil (-2 to +4) |
| **Non-Fatal MI** | 1256/36968 (3.4%) | 1571/36964 (4.3%) | 0.80 (0.62-0.88) | **-9 (-8 to -16)** |
| **Stroke** | 363/36968 (1.0%) | 489/36964 (1.3%) | 0.74 (0.34-1.04) | -3 (-6 to +1) |

Wierzbicki AS et al; Curr Op Cardiol 2018; 33 : 416

# Guidelines for PCSK-9 inhibitors

| | Alirocumab (TA393) (2016) | Evolocumab (TA394) (2016) | Inclisiran (TA733) (2021) |
|---|---|---|---|
| **Surrogate (lipid) outcomes** | FH, T2DM, CVD, statin intolerance (ODYSSEY programme) | FH, T2DM, CVD. Statin intolerance (Scientists' names programme) | FH, T2DM, CVD (Orion programme) |
| **CVD outcomes study** | ODYSSEY-Outcomes | FOURIER | Under way |
| | | | |
| **NICE recommendations** | **Add-on to maximal tolerated therapy** | | |
| **Coronary artery disease/single vascular bed** | LDL-C >4mmol/L | LDL-C >4mmol/L | CVD event & LDL-C > 2.6mmol/L |
| **Dual vascular bed** | LDL-C >3.5mmol/L | LDL-C >3.5mmol/L | CVD event & LDL-C > 2.6mmol/L |
| **Familial hypercholesterolaemia (primary prevention)** | LDL-C >5.0mmol/L | LDL-C >5.0mmol/L | Not recommended |
| **Primary prevention (common causes)** | Not recommended | Not recommended | Not recommended |

www. NICE.org.uk

# Other secondary Drug Interventions

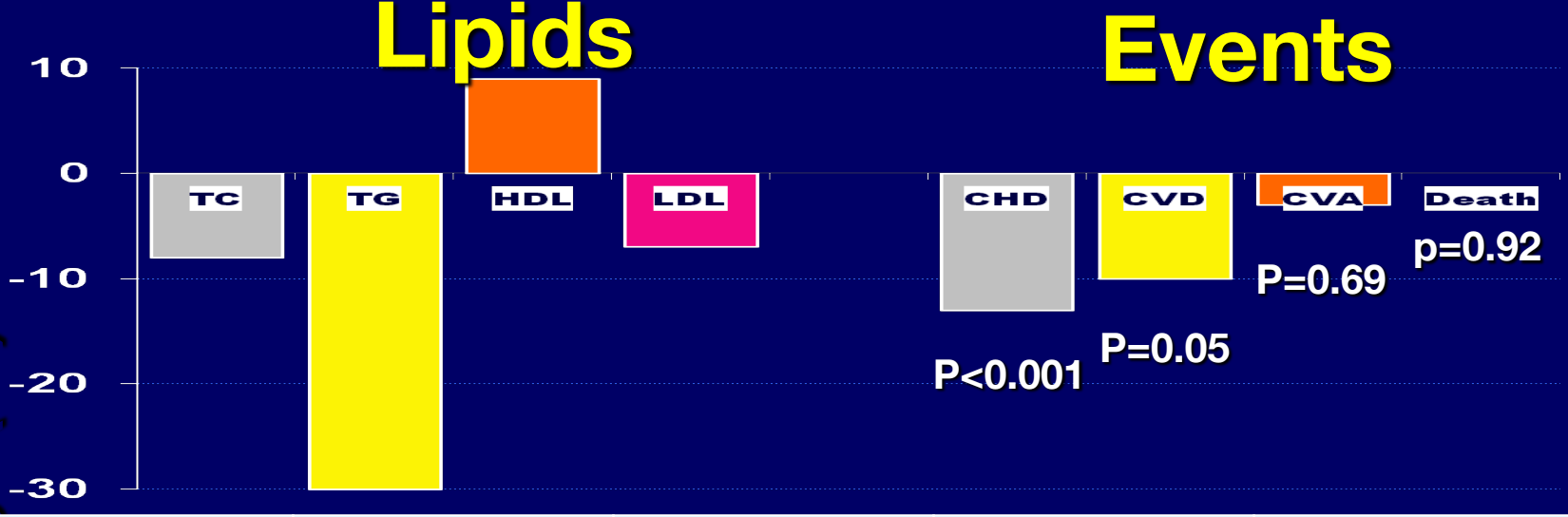
- Bile acid sequestrants
  - Weak monotherapy evidence on CVD
  - No combination evidence with statins
  - Do not use

- Fibrates
  - Meta-analysis:  moderate monotherapy benefit
  - Meta-analysis: No combination therapy benefit
  - No routine use ( i.e. 2nd/3rd line)

- Omega-3 Fatty acids
  - Mixed diet and supplement trials. Multiple supplement trials used
  - Meta-analysis: no combination therapy benefit (low dose)
  - Under NICE HTA review  (REDUCE-IT vs STRENGTH)

# Fibrates : meta-analyses

**Secondary& primary prevention; 10 &18 studies; n= 36489 & 45,058**



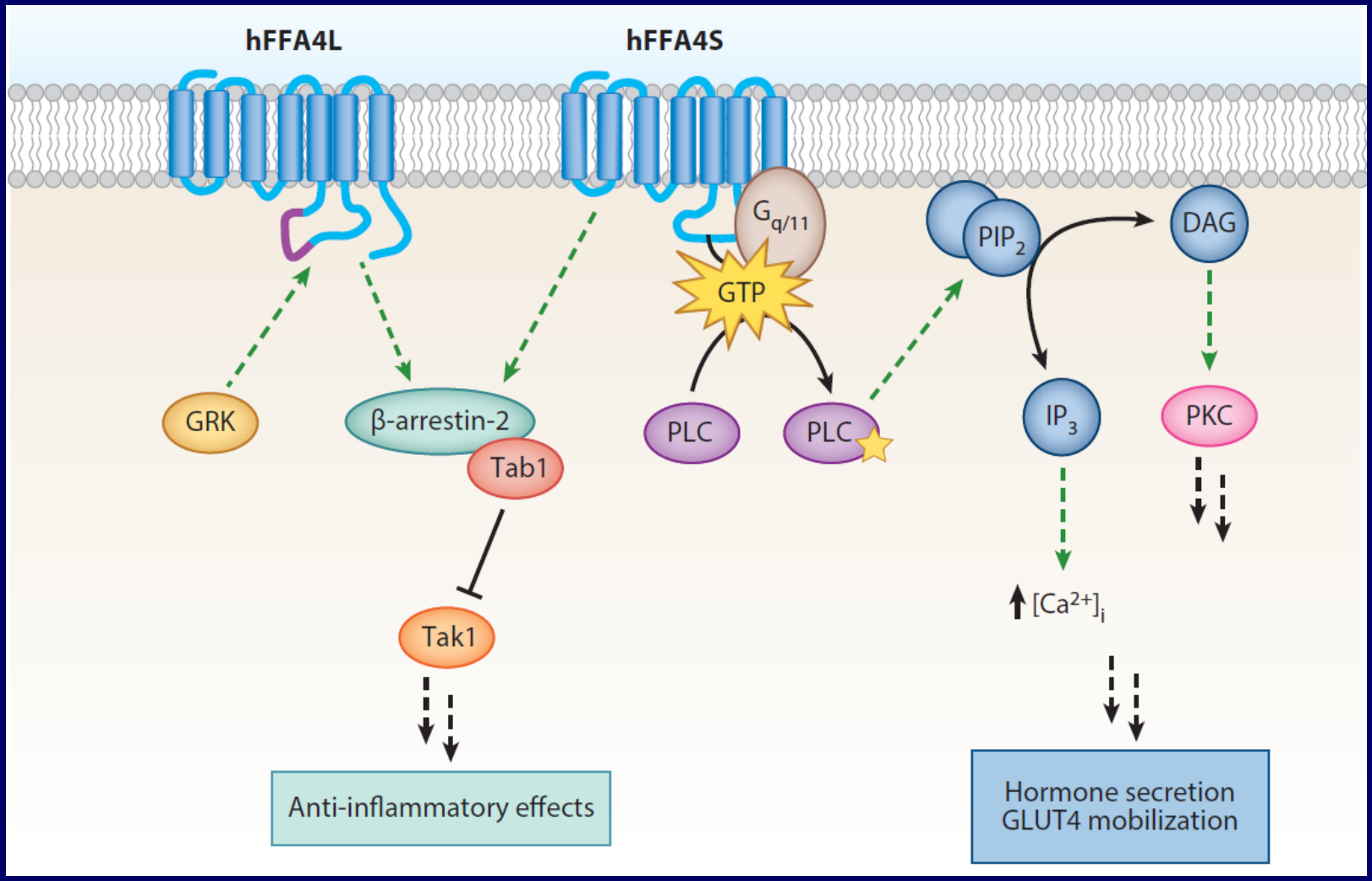

| | Active treatment | Control | Relative risk | Absolute Effect |
|---|---|---|---|---|
| **Fibrates** | | | | |
| **CVD mortality** | 704/21886 (3.2%) | 1032/23536 (4.4%) | 0.92 (0.81-1.04) | -4 (-8 to +2) |
| **Non-fatal MI** | 1104/21896 (5.0%) | 1574/23549 (6.7%) | 0.80 (0.74-0.87) | **-13** (-9 to -17) |
| **Stroke** | 610/20784 (2.9%) | 772/22404 (3.5%) | 1.01 (0.90-1.13) | Zero (-4 to +5) |

Saha S et al; Am Heart J 2007; 154: 943 Jun M et al; Lancet 2010 ; 375 : 1875

# Drugs affecting inflammation & CVD

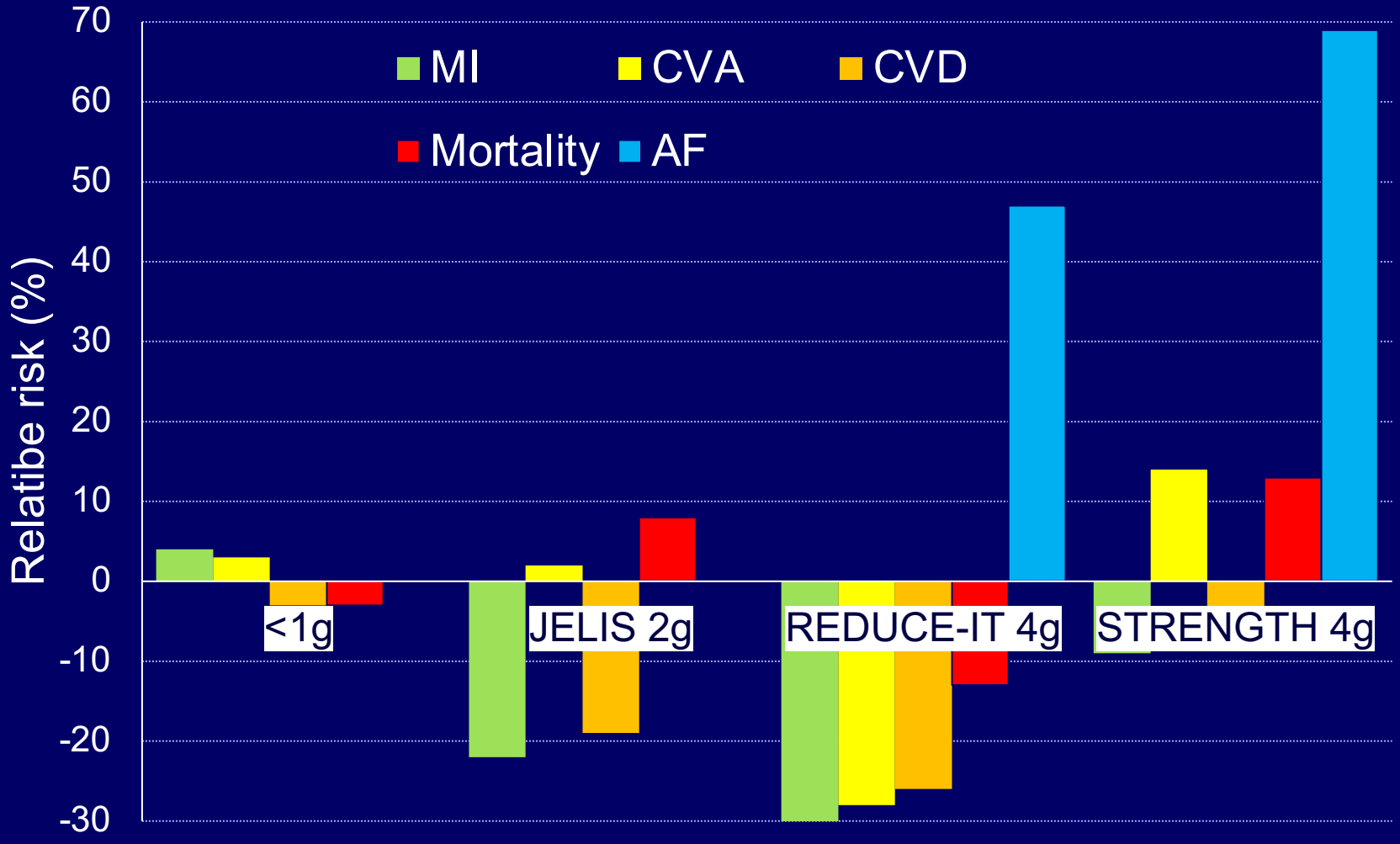
| Indirect effects | Direct effects |
| --- | --- |
| • Statin<br>  • Rho kinase activity<br>• Fibrate<br>  • PPAR effects<br>• Omega-3 fatty acid<br>  • FFAR-4 (GPR120)<br>• Thiazolidinedione<br>  • 2º Fibrate effect<br>• BET inhibitors<br>  • Apabetalone | • ACAT inhibitors (macrophage)<br>  • Avasimibe ; Pactimibe<br>• VCAM-1 uncouplers<br>  • Probucol; AGI-1067<br>• PLA2 inhibitors<br>  • Daraplabib (LpPLA2) ; Varespladib (sPLA2)<br>• IL-1β inhibitors<br>  • Canakinumab<br>• Microtubule inhibitors<br>  • Colchicine |

# Mechanism of omega-3 FA receptor- FFA-4/GP120




Ulven T & Christiansen E; Ann Rev Nutr 2015; 35 : 239

# Omega-3 fatty acid trials




Aung T et al. JAMA Cardiol 2018; 3 : 225
Bhatt D et al. NEJM 2019; 390 : 12
Nicholls SJ et al; JAMA 2020;

# Lipid monitoring

- LFTs
  - Check transaminase after 3 months then yearly

- No need for CK unless symptomatic
  - Do not offer statin if CK >1000iu/L (5 x ULN)
- Check glucose if new on statin and high risk for DM. Do not stop statin therapy if glucose increases.

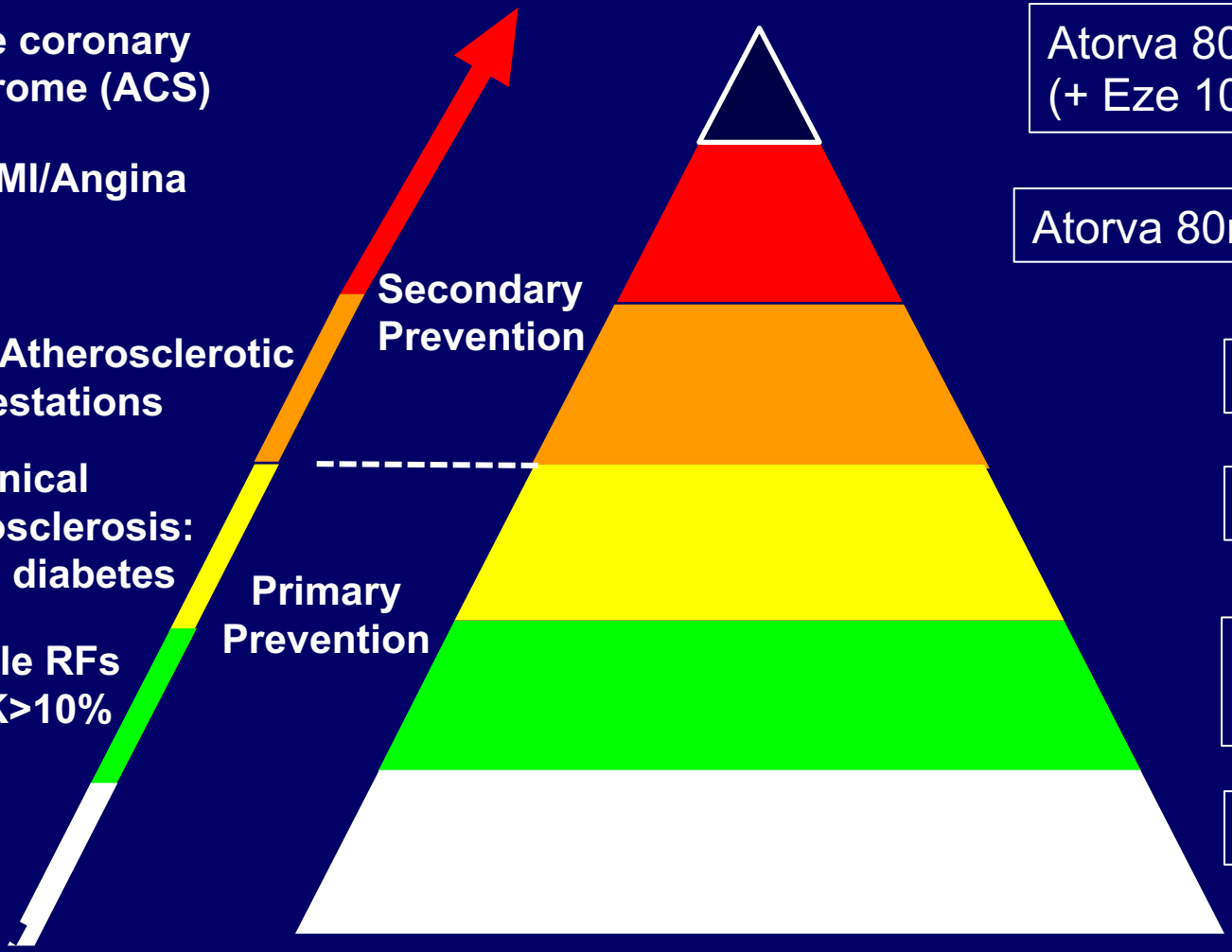
- Check adherence etc if non-HDL-C response <40%

- Statin intolerance
  - Any dose statin reduces CVD
  - Reduce dose; switch intensity class; consult specialist

# Guidelines: Defining recommendations

| Targets | Drug-based |
| --- | --- |
| • Consistent with epidemiology<br>• Rare in clinical trials<br>• Traditional output<br>• Focused on single risk factor<br>• Set on 50$^{th}$ centile<br>• Requires multiple monitoring | • Consistent with trials<br>  • Exception limits defined<br>• Common trial design<br>• Novel output<br>• Focused on overall risk<br>• Centile-independent<br>• Minimal monitoring required |

# NICE –CG 181 Continuum of CVD Risk and its treatment




Courtesy of CD Furberg.; modified to include NICE CG181

# Primary Prevention: Medicines Optimisation for Lipid Management

**Lifestyle change and dietary measures** are key to CVD event reduction together with drug therapy

**In primary care check:** non-fasting lipid profile: TC, TG, HDL-C, LDL-C, non-HDL-C; liver function (LFTs), HbA1c, TSH & renal function, blood pressure (BP), weight, smoking status and calculate QRisk2 score (www.qrisk.org)

**QRisk3 does not apply in** : FH, type 1 diabetes (T1DM)
CKD 3- **high CVD risk and need a high intensity statin.**
**Offer** HI statin to patients with **Type 1 DM** and **age >40 years** or **DM >10 years** or **nephropathy** or **other CVD risk factors** *NI*

**Other CVD risk factors, if present**,:
Severe obesity (BMI >40kg/$m^2$), socio-economic status, human immunodeficiency virus (HIV) treatment, severe mental illness, autoimmune disease (RA or SLE) medications that may cause dyslipidaemia, impaired fasting glycaemia

**Consider options** with shared decision making , education and lifestyle interventions to **modify CVD risk.**
Consider the risk:benefit of therapy holistically: e.g. patients aged ≥ 85years consider frailty, life expectancy and co-morbidities

**Optimise** management of BP and other co-morbidities. **Support** lifestyle

**If QRisk ≥10%:** consider **moderate dose** of a **high intensity drug** atorvastatin 20mg (or rosuvastatin 10mg) daily

**Step 1 in primary care:** Consider up-titration to maximum dose atorvastatin 80mg (alternative is rosuvastatin 20-40mg

**After 3 months, has non-HDL cholesterol fallen by ≥ 40% from baseline?**
Check adherence to medication, timing of dose, statin adverse effects/intolerance/hesitancy & diet/lifestyle

**Step 2:** If intolerant to higher dose of statin, consider adding ezetimibe 10mg daily

**After 3 months, has non-HDL cholesterol fallen by ≥ 40% from baseline?** Check adherence , adverse effects

**Step 3 :** If intolerant to any statin, start ezetimibe 10mg daily, consider adding bempedoic acid 180mg daily

**Review annually** for adherence to medications, diet and lifestyle, check required bloods eg lipids. Refer for support as required from specialist teams.

Refer to lipid clinic

# Secondary Prevention: Medicines optimisation for Lipid Management

1) **Check baseline bloods** (non-fasting lipid profile, LFTs, HbA1c, thyroid and renal function)

2) **Offer high dose high intensity statin:** atorvastatin 40-80mg (or rosuvastatin 20-40mg) to adults with CVD: acute coronary syndromes (ACS), angina, myocardial infarction (MI), revascularisation, stroke or TIA, peripheral arterial disease or abdominal aortic aneurysm (AAA)

3) **Support self-management** e.g. smoking, diet, obesity, alcohol intake, activity, blood pressure & glycaemic control (HbA1c)

In primary care check: **Is patient on high dose, high intensity statin?** atorvastatin 40-80mg (alternative is rosuvastatin 20mg-40mg)

**Has non-HDL-C reduced> 40% from baseline at 3 months?** if no baseline : target nHDL-C <2.5mmol/L or LDL-C <2.0mmo/L

Discuss statin choice: check adherence- After 3 months check non-fasting lipid profile (TC, TG, HDL, LDL-C); LFTs

**Has non-HDL-C reduced >40% from baseline at 3 months?** If no baseline: target nHDL-C < 2.5mmol/L or LDL-C <2.0mmol/L). Check adherence

Consider adding Ezetimibe 10mg daily S

After 3 months, check non-fasting lipid profile (TC, TG, HDL, LDL-C); LFTs

**Has non-HDL-C reduced >40% from baseline at 3 months?** (if no baseline: target nonHDL-C <2.5mmol/L or LDL-C <2.0mmo/L

Following a review of adherence/adverse effects/intolerance/hesitancy and lifestyle interventions

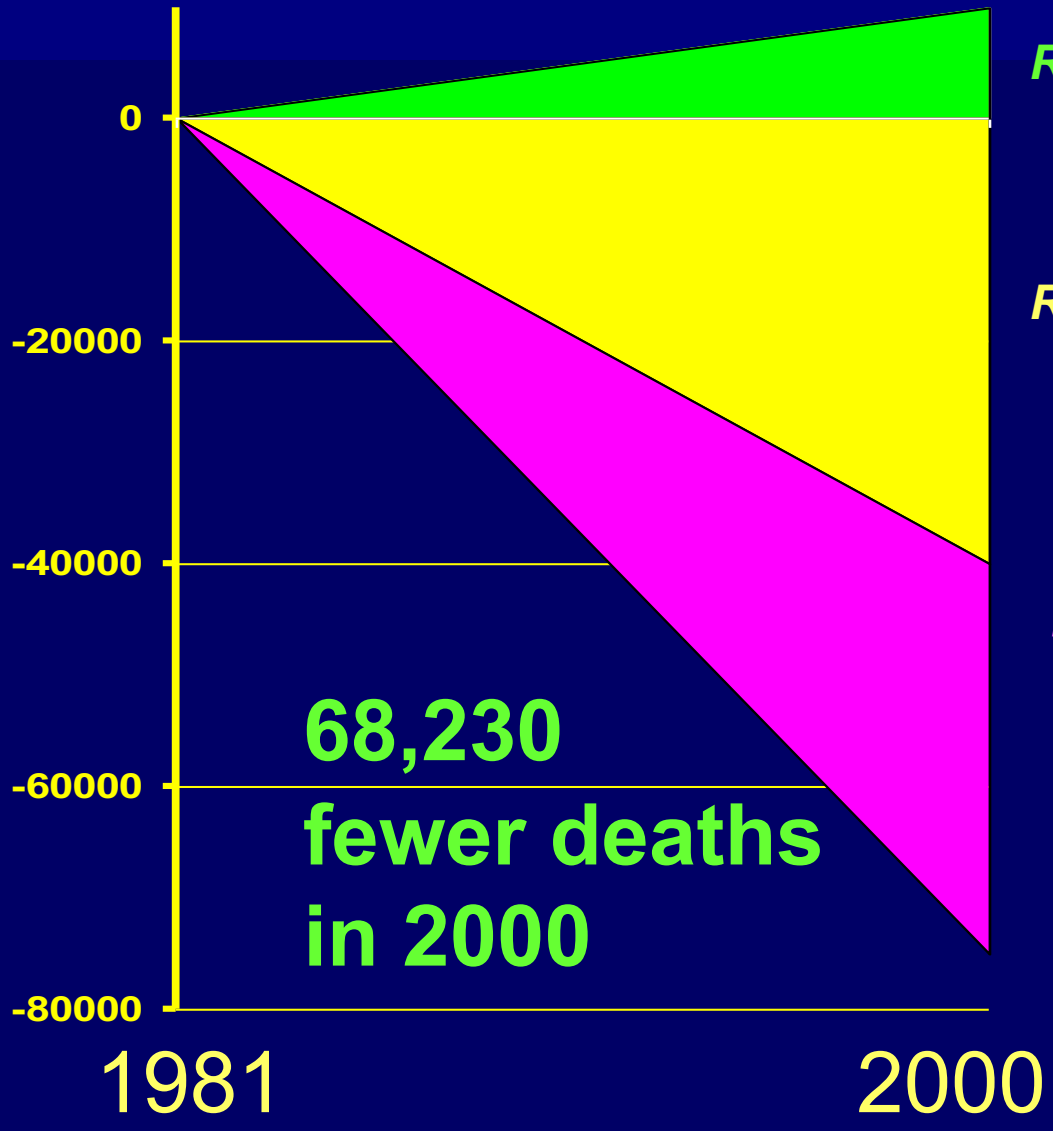
Consider inclisiran initiation in primary care if LDL ≥2.6 mmol/L following advice from a specialist

**Refer to lipid clinic if** LDL-C >4mmol/L (or LDL-C >3.5mmol/L with recurrent CVD event or multivascular disease) to consider PCSK9 antibody

**Refer to lipid clinic** if statin intolerance: lipid clinic will consider addition of bempedoic acid to ezetimibe or inclisiran

**Review annually** for adherence to medications, support diet and lifestyle, and check required bloods eg lipid profile, LFTs

# Explaining the fall in coronary heart disease deaths in England & Wales 1981-2000




*Risk Factors worse +13%*

- Obesity (increase) +3.5%
- Diabetes (increase) +4.8%
- Physical activity (less) +4.4%

*Risk Factors better -71%*

- Smoking -41%
- Cholesterol -9%
- Population BP fall -9%
- Deprivation -3%
- Other factors -8%

*Treatments -42%*

- AMI treatments -8%
- Secondary prevention -11%
- Heart failure -12%
- Angina:CABG & PTCA -4%
- Angina: Aspirin etc -5%
- Hypertension therapies -3%

Unal, Critchley & Capewell
Circulation 2004 109(9) 1101