Statin intolerance: definitions, mechanisms & solutions

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Pharmacology of statins

	Increasing lipophilicity						
	Lovastatin	**Simvastatin**	**Atorvastatin**	**Pitavastatin**	**Fluvastatin**	**Rosuvastatin**	**Pravastatin**
IC_{50} HMG-CoA reductase (nM)	2–4	1–2 (active metabolite)	1.16	0.1	3–10	0.16	4
Oral absorption (%)	30	60–85	30	80	98	50	35
Bioavailability (%)	5	<5	12	60	30	20	18
Protein binding (%)	>98	>95	>98	96	>98	90	50
Half life (h)	2–5	2–5	7–20	10–13	1–3	20	1–3
Metabolism by CYP450	3A4 (?2C8)	3A4 (2C8, 2D6)	3A4 (2C8)	(2C9)	2C9	2C9 (2C19)	(3A4)
Cellular transporter	OATP1B1	(MRP2)	OATP1B1	OATP1B1 (MRP2)	OATP1B1	OATP1B1	OATP1B1 (MRP2)
Daily dose (mg)	10–40	10–40	10–80	1–4	80 (retard formulation)	5–40	10–40

Mach F et al. Eur Heart J 2018; 39: 2526

Statin Adverse Events

- **Common side effects**
  - Headache – Myalgia – Fatigue
  - GI intolerance – Flu-like symptoms
- **Increase in liver enzymes**
  - Occurs in 0.5 to 2.5% of cases in dose-dependent manner
  - Serious liver problems are exceedingly rare
  - Manage by reducing statin dose or discontinue until levels return to normal
- **Myopathy**
  - Occurs in 0.2 to 0.4% of patients
  - Rare cases of rhabdomyolysis
  - Reduce by
    - Cautiously using statins in patients with impaired renal function
    - Using the lowest effective dose
    - Cautiously combining statins with fibrates
    - Avoiding drug interactions
    - Careful monitoring of symptoms
  - Presence of muscle toxicity requires the discontinuation of the statin

Statin intolerance

- Statin intolerance is defined as one or more adverse effects associated with statin therapy, which resolves or improves with dose reduction or discontinuation, and can be classified as complete inability to tolerate any dose of a statin or partial intolerance, with inability to tolerate the dose nec- essary to achieve the patient-specific therapeutic objective. To classify a patient as having statin intolerance, a minimum of two statins should have been attempted, including at least one at the lowest approved daily dosage.

Cheeley MK et al. NLA statement J Clin Lipidol 2022; 16 : 361

Statin myopathy

International Definitions

ACC/AHA (4)	CWG (5)	NLA (6)
Myopathy: any muscle symptom (SAMS)	Myopathy: any muscle symptom	Myalgia: aching, stiffness, cramps
Myalgia: SAMS CK = NL	Symptomatic myalgia	Myopathy: weakness
	Myalgia CK ≤ULN	Myositis: inflammation
	Myositis CK >ULN	Myonecrosis CK 3× ULN
	Rhabdomyolysis CK >10× ULN	Mild CK >3, <10× ULN
		Moderate CK >10, <50× ULN
		Severe CK >50× ULN
		Clinical rhabdomyolysis CK >ULN and creatinine >0.5 mg/dl baseline
Myositis: SAMS CK >ULN	HyperCKemia	
	Mild G1 >ULN ≤5× ULN	
	Mild G2 >5, ≤10× ULN	
	Modest >10, ≤50× ULN	
	Severe >50× ULN	
Rhabdomyolysis: CK >10× ULN		

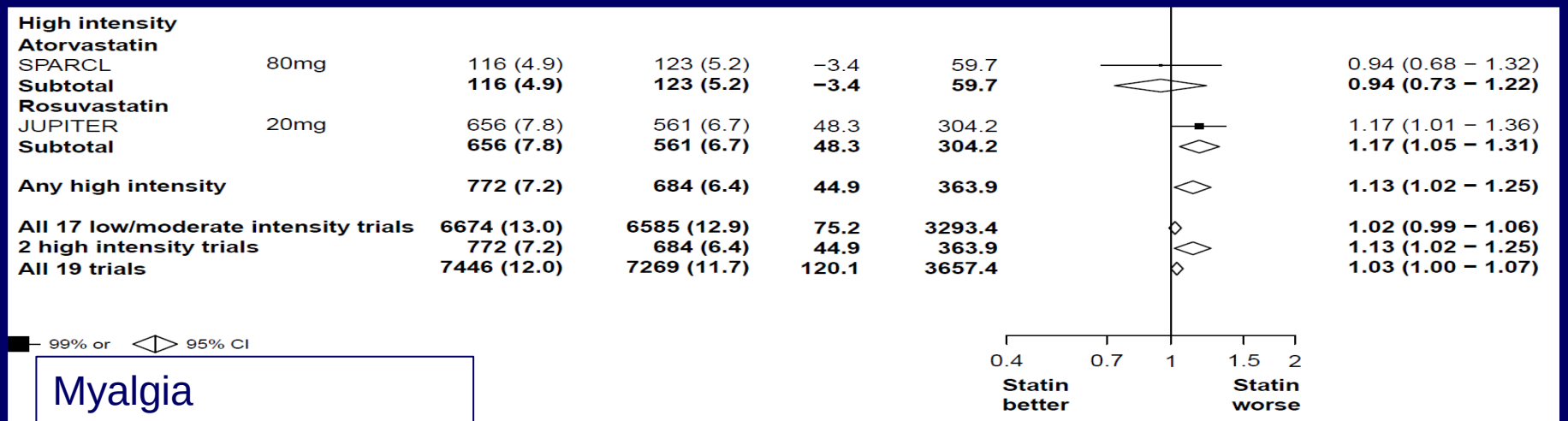
European Statin-associated myotoxicity grading system

SRM Classification	Phenotype	Definition
SRM 0	CK elevation <4× ULN	No muscle symptoms
SRM 1	Myalgia, tolerable	Muscle symptoms without CK elevation
SRM 2	Myalgia, intolerable	Muscle symptoms, CK <4× ULN, complete resolution on dechallenge
SRM 3	Myopathy	CK elevation >4× ULN <10× ULN ± muscle symptoms, complete resolution on dechallenge
SRM 4	Severe myopathy	CK elevation >10× ULN <50× ULN, muscle symptoms, complete resolution on dechallenge
SRM 5	Rhabdomyolysis	CK elevation >10× ULN with evidence of renal Impairment + muscle symptoms or CK <50× ULN
SRM 6	Autoimmune-mediated necrotizing myositis	HMGCR antibodies, HMGCR expression in muscle biopsy, incomplete resolution on dechallenge

Thompson PD et al; JACC 2016; 67: 2395
Alfirevic A et al; Clin Pharm Ther 2014; 96: 470

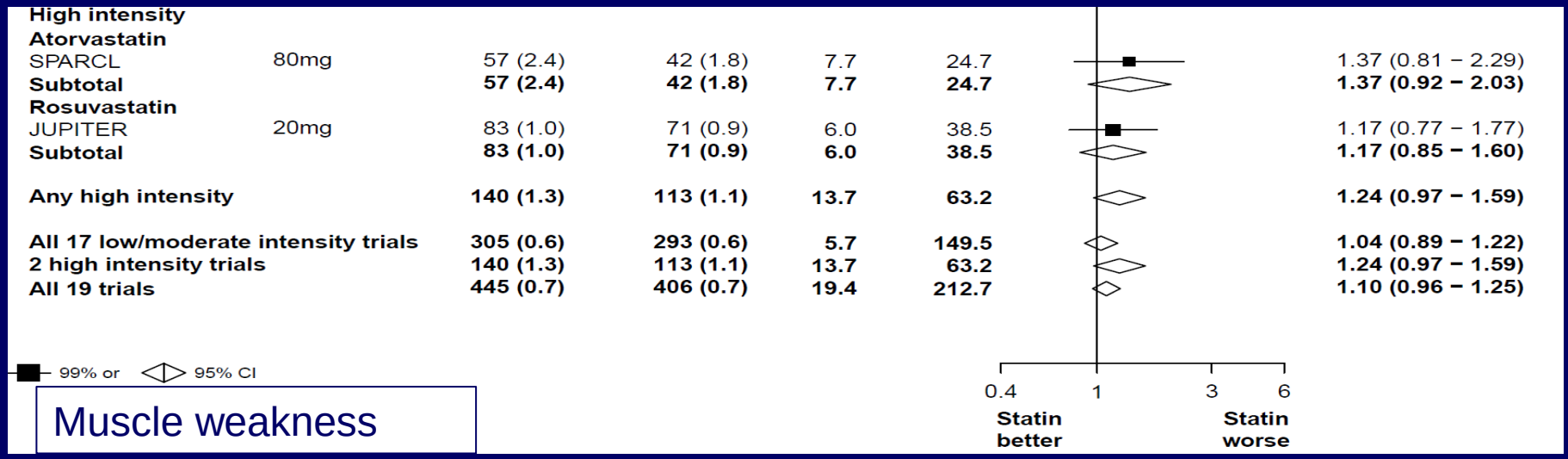
Cholesterol Treatment Trialists: adverse effects

High intensity						
Atorvastatin						
SPARCL	80mg	116 (4.9)	123 (5.2)	−3.4	59.7	0.94 (0.68 – 1.32)
Subtotal		**116 (4.9)**	**123 (5.2)**	**−3.4**	**59.7**	**0.94 (0.73 – 1.22)**
Rosuvastatin						
JUPITER	20mg	656 (7.8)	561 (6.7)	48.3	304.2	1.17 (1.01 – 1.36)
Subtotal		**656 (7.8)**	**561 (6.7)**	**48.3**	**304.2**	**1.17 (1.05 – 1.31)**
Any high intensity		**772 (7.2)**	**684 (6.4)**	**44.9**	**363.9**	**1.13 (1.02 – 1.25)**
All 17 low/moderate intensity trials		**6674 (13.0)**	**6585 (12.9)**	**75.2**	**3293.4**	**1.02 (0.99 – 1.06)**
2 high intensity trials		**772 (7.2)**	**684 (6.4)**	**44.9**	**363.9**	**1.13 (1.02 – 1.25)**
All 19 trials		**7446 (12.0)**	**7269 (11.7)**	**120.1**	**3657.4**	**1.03 (1.00 – 1.07)**



Myalgia

High intensity						
Atorvastatin						
SPARCL	80mg	57 (2.4)	42 (1.8)	7.7	24.7	1.37 (0.81 – 2.29)
Subtotal		**57 (2.4)**	**42 (1.8)**	**7.7**	**24.7**	**1.37 (0.92 – 2.03)**
Rosuvastatin						
JUPITER	20mg	83 (1.0)	71 (0.9)	6.0	38.5	1.17 (0.77 – 1.77)
Subtotal		**83 (1.0)**	**71 (0.9)**	**6.0**	**38.5**	**1.17 (0.85 – 1.60)**
Any high intensity		**140 (1.3)**	**113 (1.1)**	**13.7**	**63.2**	**1.24 (0.97 – 1.59)**
All 17 low/moderate intensity trials		**305 (0.6)**	**293 (0.6)**	**5.7**	**149.5**	**1.04 (0.89 – 1.22)**
2 high intensity trials		**140 (1.3)**	**113 (1.1)**	**13.7**	**63.2**	**1.24 (0.97 – 1.59)**
All 19 trials		**445 (0.7)**	**406 (0.7)**	**19.4**	**212.7**	**1.10 (0.96 – 1.25)**



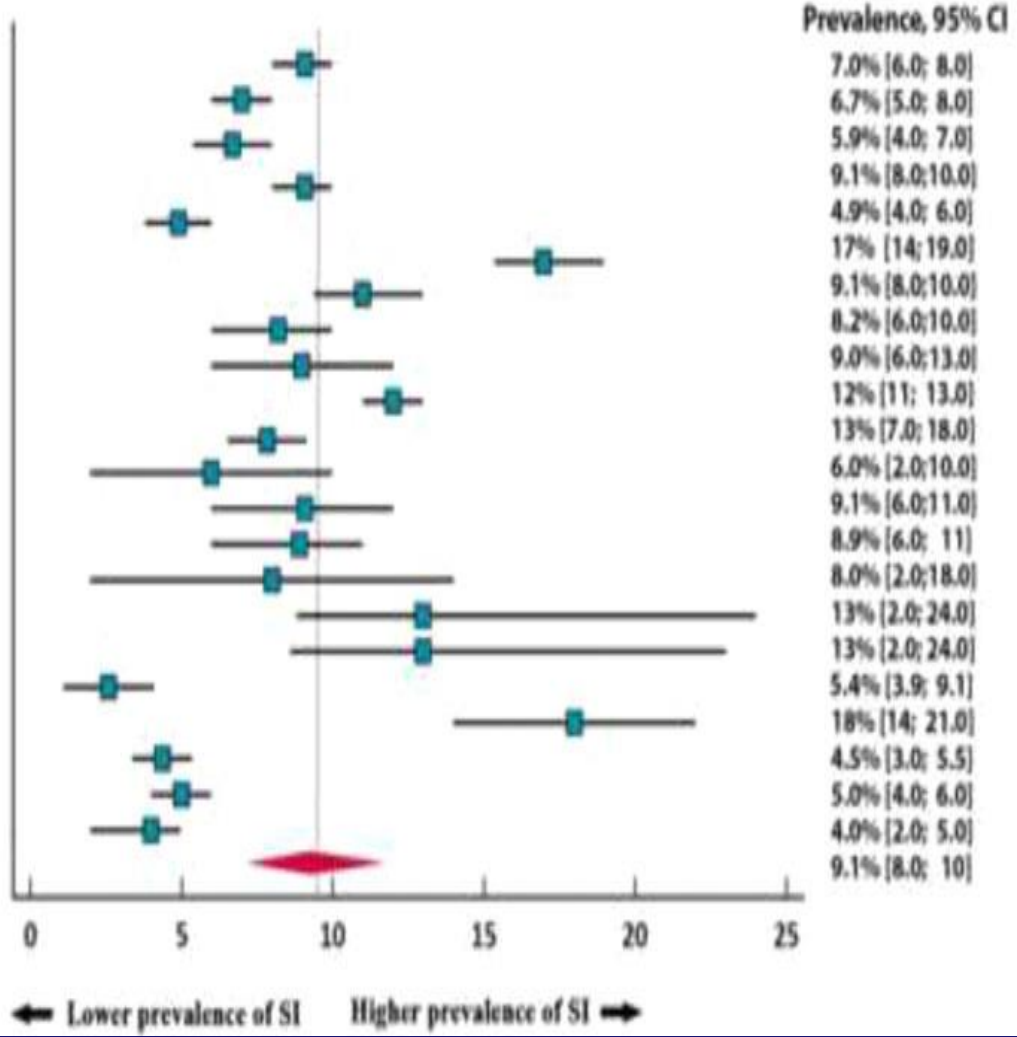
Muscle weakness

CTT group. Lancet 2022; S0140-6736(22)01545-8

Statin intolerance: prevalence

Summary of SI prevalence

SI definition	No. of studies	Population	Prevalence, 95% CI
*NLA	122	1,102,559	7.0% [6.0; 8.0]
*ILEP	109	457,009	6.7% [5.0; 8.0]
*EAS	108	407,509	5.9% [4.0; 7.0]
Type of studies	176	4,143,517	9.1% [8.0;10.0]
*RCTs	112	195,575	4.9% [4.0; 6.0]
*Cohort	62	3,947,942	17% [14; 19.0]
Disease prevention	176	4,143,517	9.1% [8.0;10.0]
*Primary	93	1,726,384	8.2% [6.0;10.0]
**Primary hypercholesterolemia	21	14,663	9.0% [6.0;13.0]
**Hypercholesterolemia	22	114,585	12% [11; 13.0]
**Dyslipidemia	27	744,169	13% [7.0; 18.0]
**DM	14	331,061	6.0% [2.0;10.0]
*Secondary	54	1,166,745	9.1% [6.0;11.0]
**Coronary artery disease	36	1,008,567	8.9% [6.0; 11]
sCAD	13	51,5581	8.0% [2.0;18.0]
ACS	11	146,788	13% [2.0; 24.0]
MI	12	346,198	13% [2.0; 24.0]
**Stroke/TIA	9	158,178	5.4% [3.9; 9.1]
*Combined (Primary and Secondary)	35	1,251,039	18% [14; 21.0]
Liposolubility	126	226,863	4.5% [3.0; 5.5]
*Lipophilic	82	158,924	5.0% [4.0; 6.0]
*Hydrophilic	44	67,939	4.0% [2.0; 5.0]
Overall prevalence	176	4,143,517	9.1% [8.0; 10]



Bytyci I et al. Eur Heart J 2022 – on-line

176 studies; n= 4143517

Risk factors for statin myopathy

Patient-related	Treatment-related
Advanced age	High-dose statin therapy
Female sex	Interactions with concomitant drugs
Small body frame and frailty	Fibrates
Multisystem disease (particularly involvement of liver, kidney, or both)	Cyclosporine
Hypothyroidism	Antifungals
Alcoholism	Macrolide antibiotics
Grapefruit juice consumption (>1 qt/d)	HIV protease inhibitors
Major surgery or perioperative period	Nefazodone
Excessive physical activity	Amiodarone
History of myopathy while receiving another lipid-lowering therapy	Verapamil
History of creatine kinase elevation	
Unexplained cramps	
Family history of myopathy	
Family history of myopathy while receiving lipid-lowering therapy	

Joy TR & Hegele RA. Ann Intern Med 2009; 150 : 858

Statin-induced myalgia or myopathy?

Myalgia/Myositis

Muscle symptoms

- Physical exertion (particularly in unaccustomed individuals)
- Viral illness
- Vitamin D deficiency
- Hypo- or hyperthyroidism
- The Cushing syndrome or adrenal insufficiency
- Hypoparathyroidism
- Fibromyalgia
- Polymyalgia rheumatica
- Polymyositis
- Systemic lupus erythematosus
- Tendon or joint disorder
- Trauma
- Seizures or severe chills
- Peripheral arterial disease†
- Medications
  - Glucocorticoids
  - Antipsychotics
  - Antiretroviral drugs
  - Illicit drugs (cocaine or amphetamines)

Creatine kinase elevation

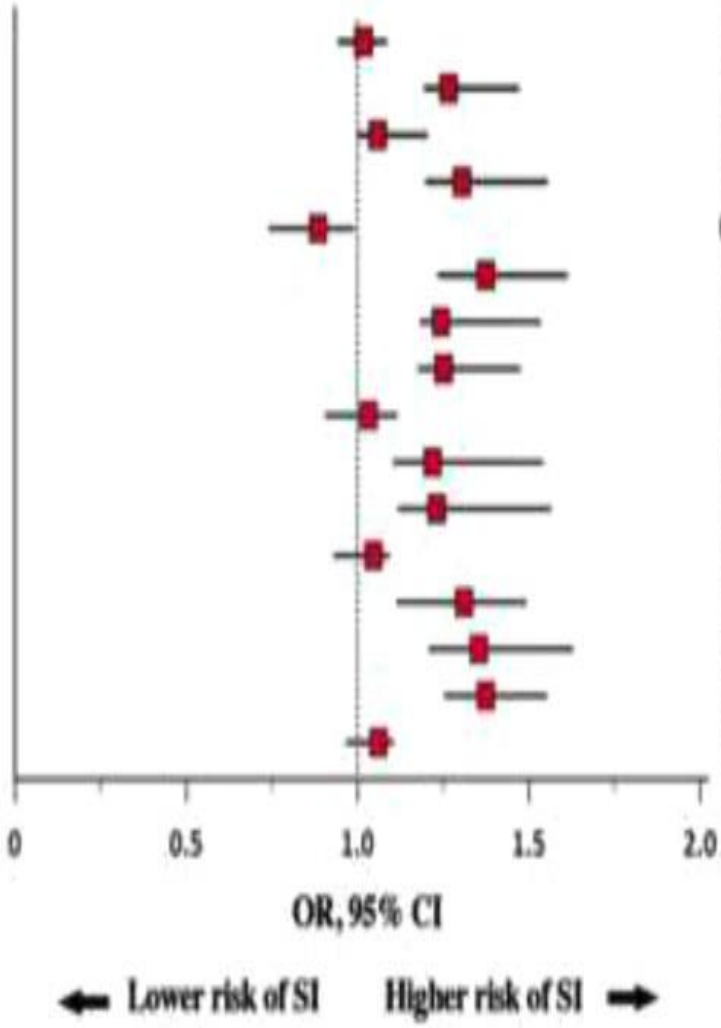
Creatine kinase elevations

- Physical exertion
- Hypothyroidism
- Metabolic or inflammatory myopathies
- Alcoholism
- Neuropathy or radiculopathy
- Ethnicity (black Americans may have elevated baseline creatine kinase levels)
- Idiopathic hyperCKemia‡
- Seizure or severe chills
- Trauma
- Medications
  - Illicit drugs (cocaine or amphetamines)
  - Antipsychotics

Joy TR & Hegele RA. Ann Intern Med 2009; 150 : 858
Kim E & Wierzbicki AS. BMJ. 2021; 373 : n1486

Statin intolerance: risk factors

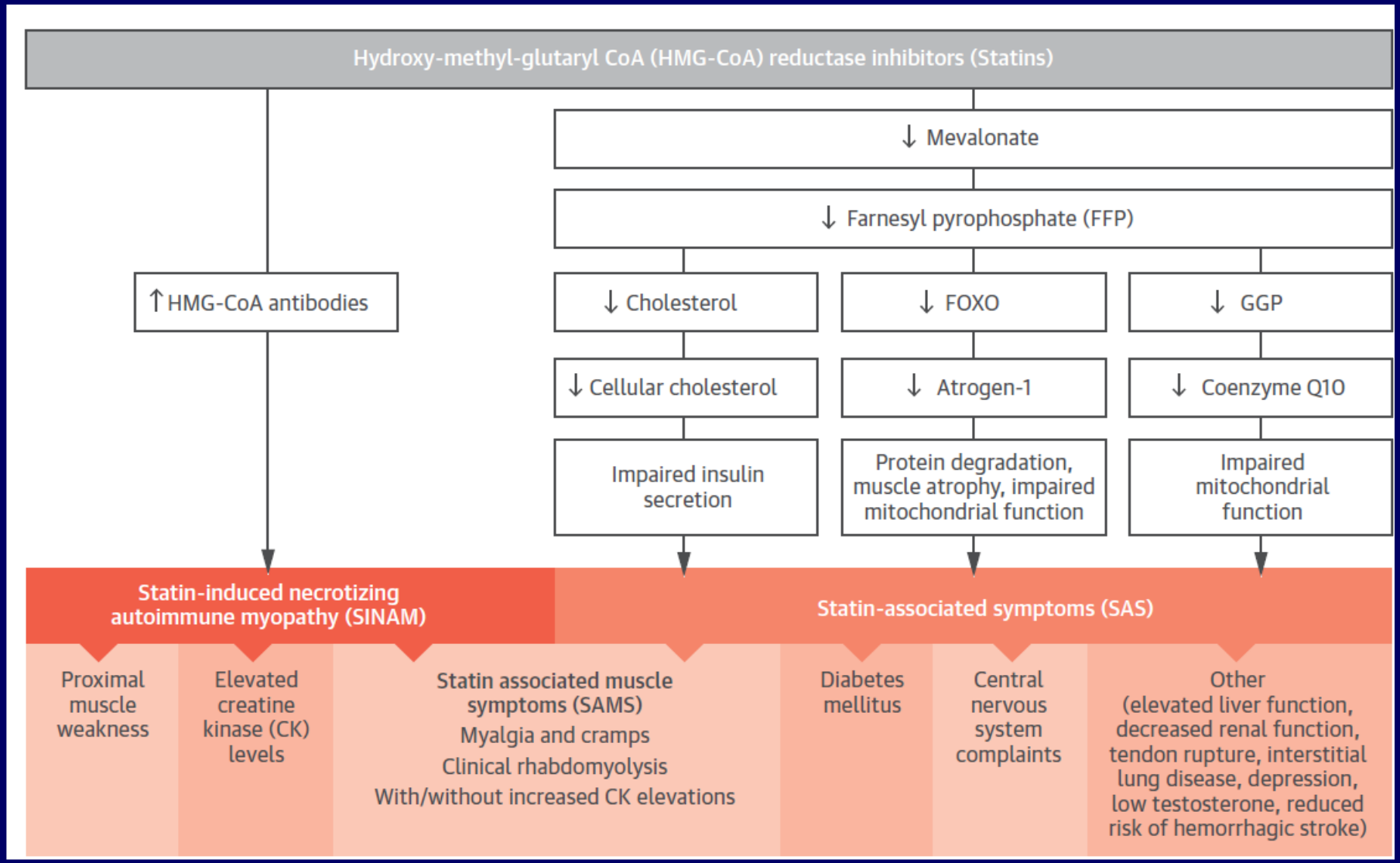
Risk factors and drugs	No. of studies	Population	OR, 95% CI, p value
Arterial hypertension	65	1,802,149	1.018 (0.943, 1.086), p=0.398
Diabetes mellitus	64	1,002,992	1.266 (1.194, 1.474), p=0.022
BMI	36	982,783	1.059 (1.002, 1.205), p=0.092
Obesity	15	98,448	1.306 (1.199, 1.556), p=0.023
Depression	10	85,309	0.885 (0.742, 0.989), p=0.042
Hypothyroidism	16	110,987	1.376 (1.235, 1.612), p=0.013
CLD	8	78,301	1.243 (1.182, 1.535), p=0.037
CRF	22	209,853	1.252 (1.176, 1.478), p=0.032
Smoking	60	1,754,300	1.033 (0.905, 1.117), p=0.601
Alcohol	8	77,309	1.220 (1.104, 1.542), p=0.031
Exercise	11	89,805	1.232 (1.118, 1.565), p=0.032
Warfarin	10	66,803	1.048 (0.930, 1.095), p=0.156
Aniarrhythmic	8	70,902	1.355 (1.210, 1.630), p=0.036
CCB	21	108,906	1.312 (1.115, 1.494), p=0.032
Statin dose	131	2,810,789	1.375 (1.254, 1.554), p=0.013
Follow-up duration	158	3,900,789	1.061 (0.967, 1.107), p=0.488



Bytyci I et al. Eur Heart J 2022 – on-line

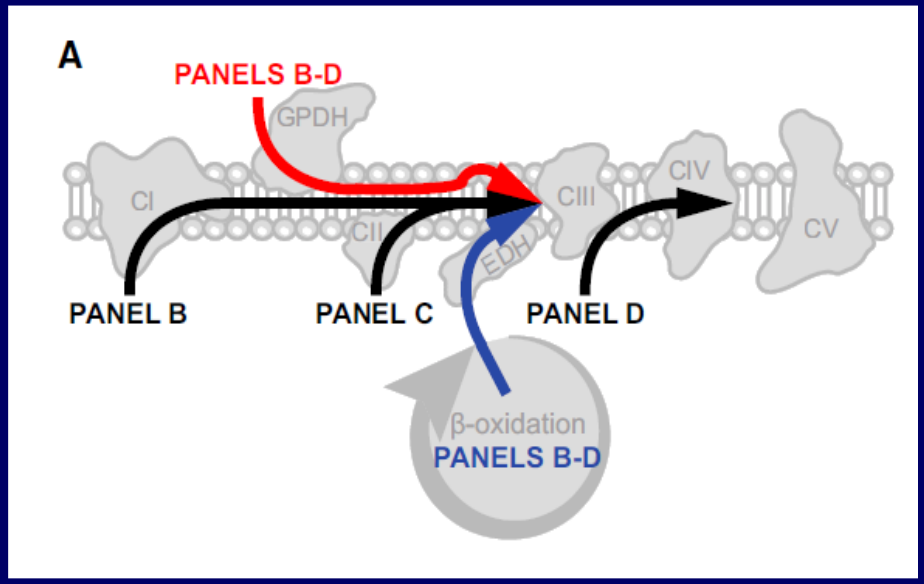
176 studies; n= 4143517

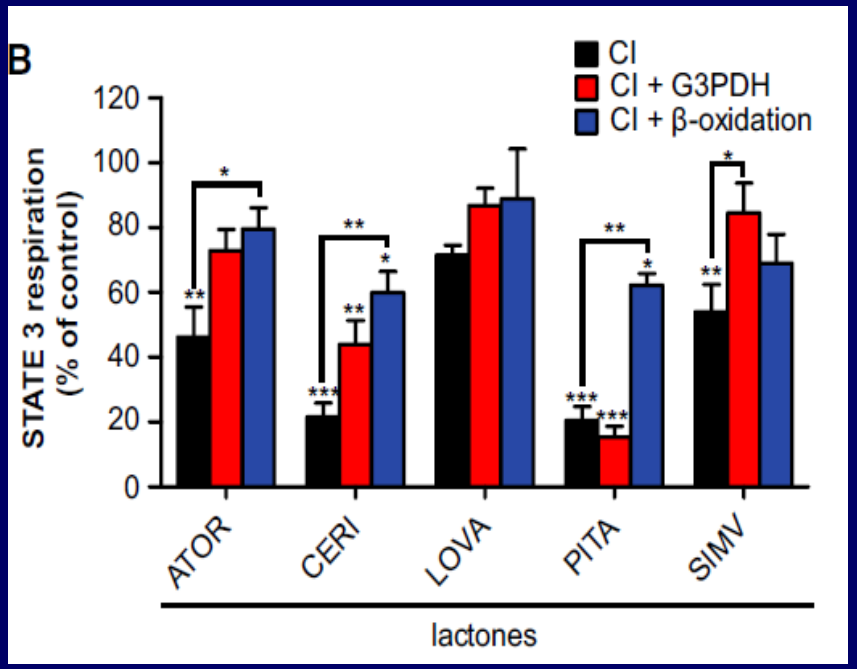
Mechanisms of statin myopathy

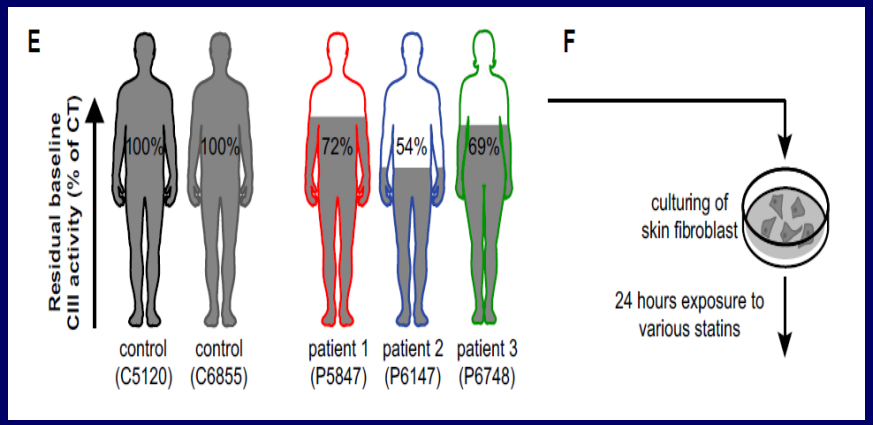


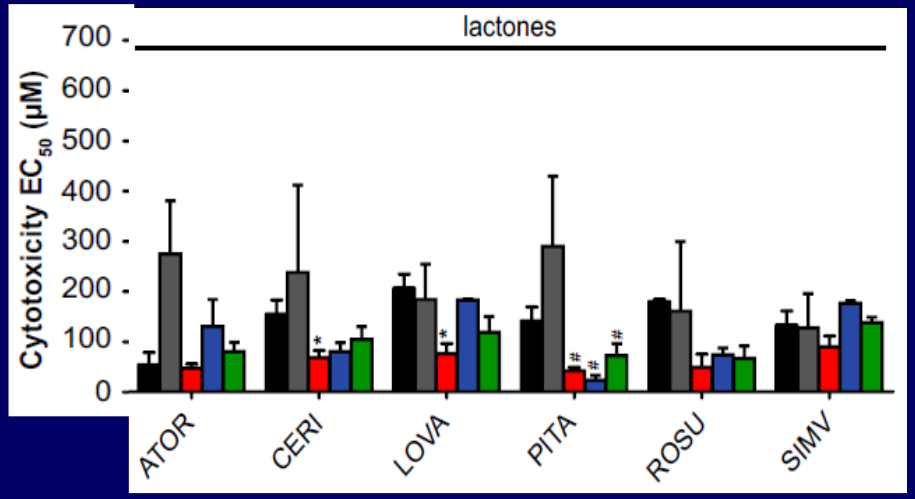
Thompson PD et al; JACC 2016; 67: 2395

Statin myopathy- a mitochondrial complex 3 problem



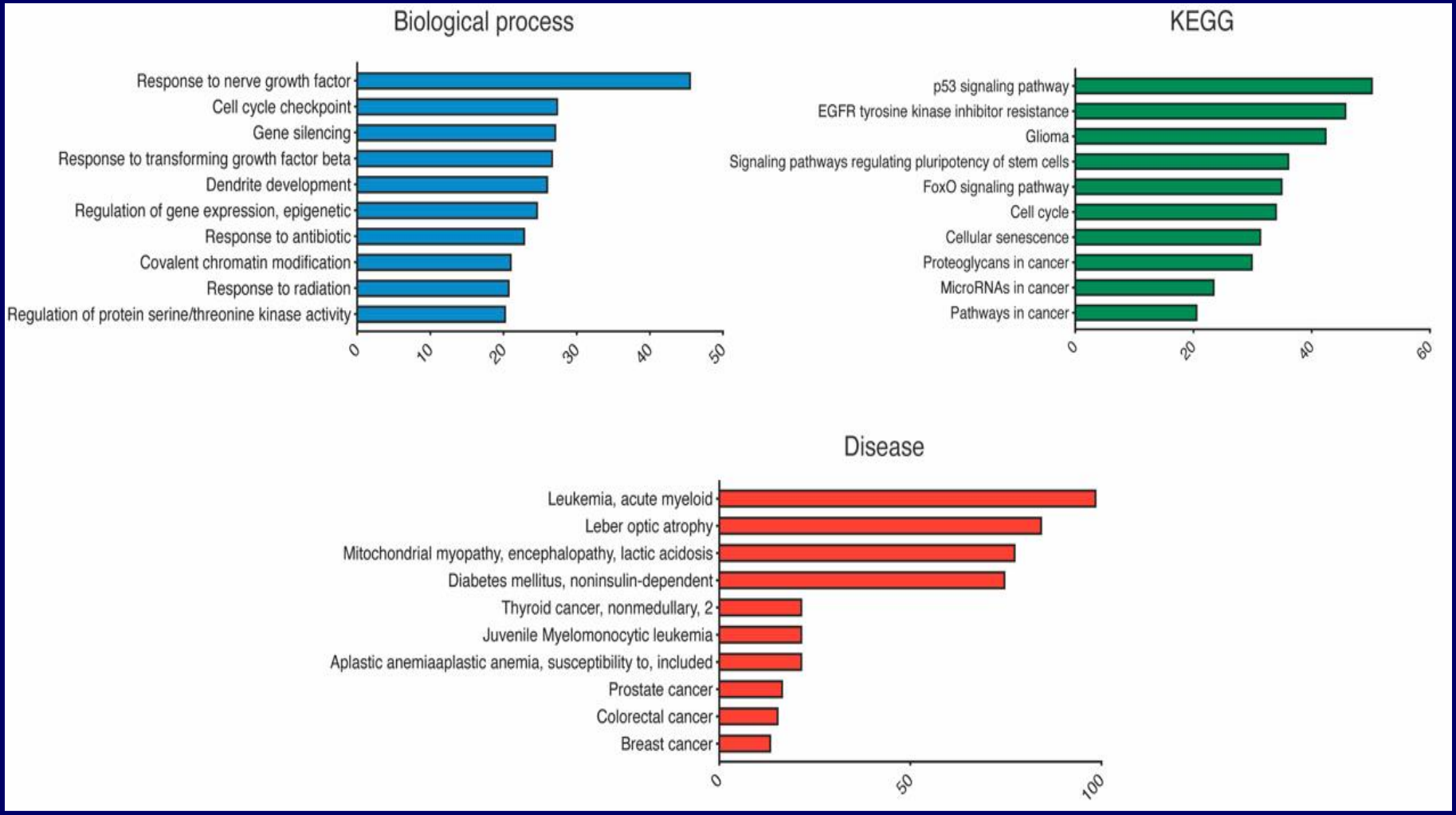






Schirris TJJ et al. Cell Metab 2015; 22: 399

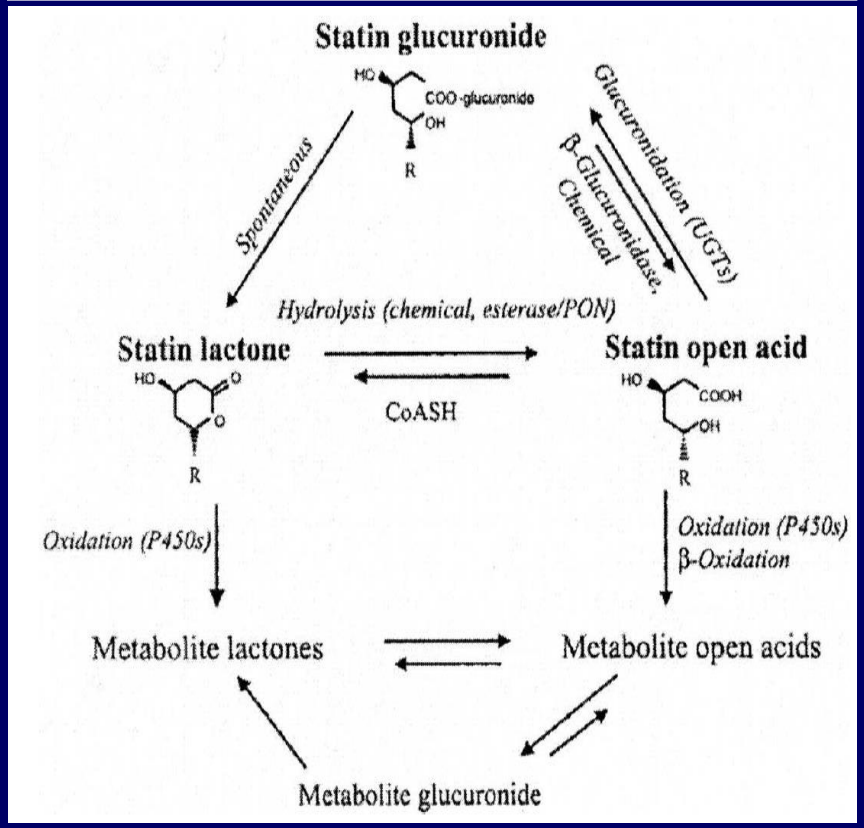
Statin intolerance: microRNA signature profiles



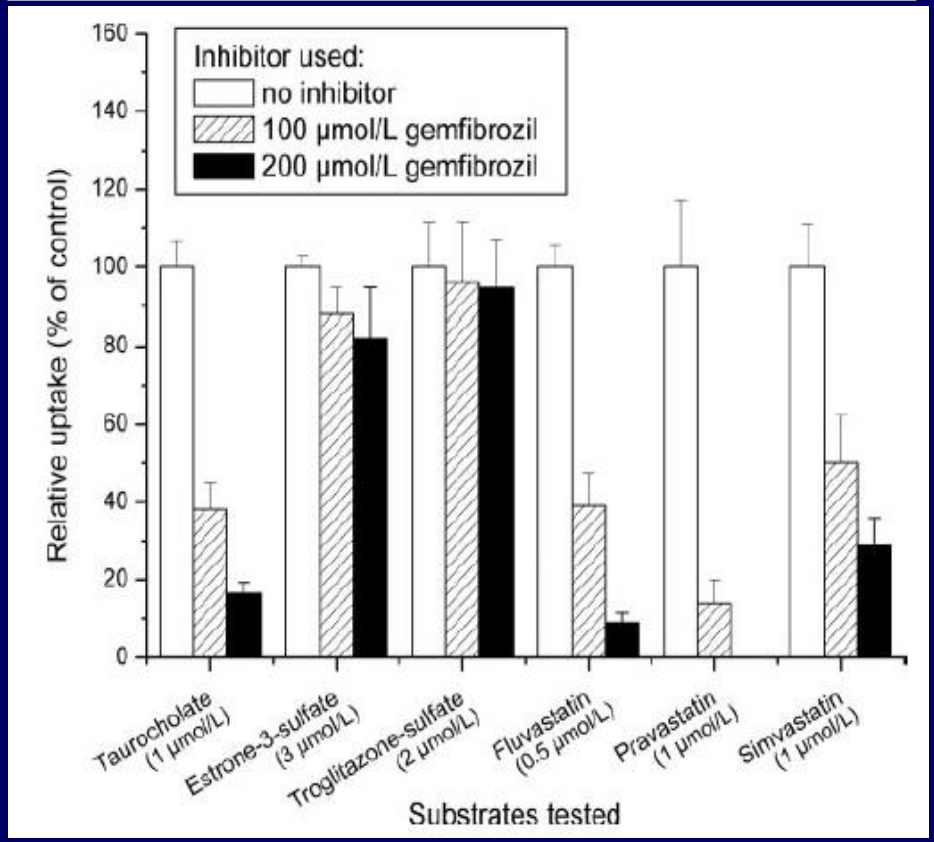
Mangas A et al. Int J Mol Sci 2022; 23: 8146

Statin interaction mechanisms

Statin metabolic pathway



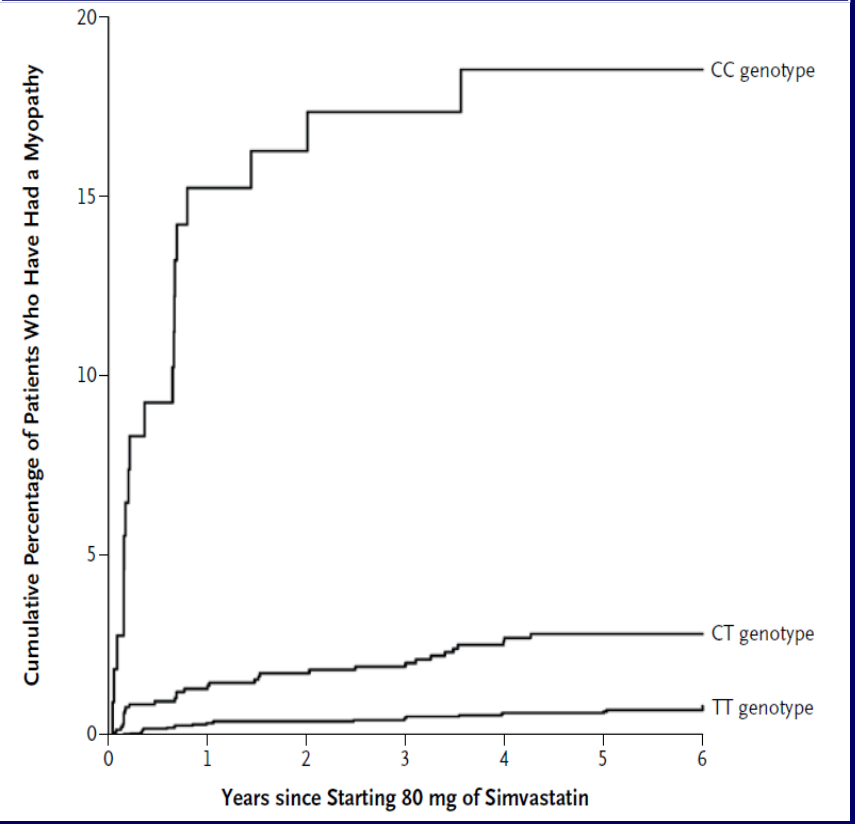
OAT1B1 transporter interactions



Noe J et al; Drug Disp Metab 2007; 35 : 1308

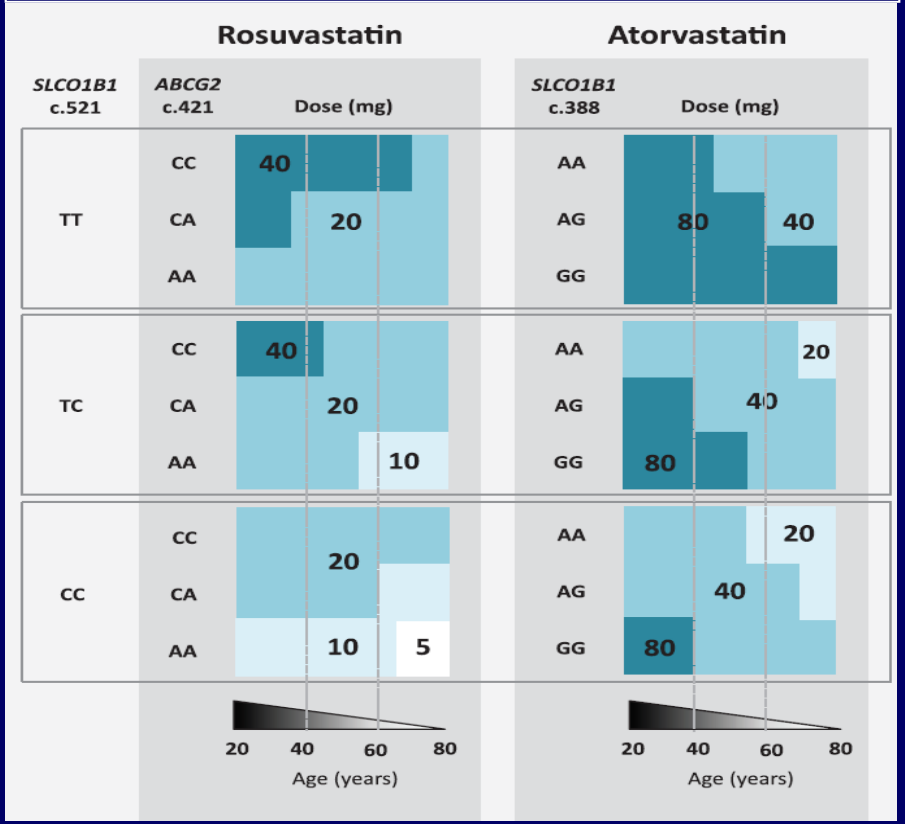
Statin pharmacogenetics: SLCO1B1

Simvastatin 80mg (diltiazem/CCB)-risk



N=12455

SLCO1B1 algorithm: Rosuva- & Atorva-statin



N=299; 45-fold variation in statin concentration. 50% @90th centile

SEARCH group; NEJM 2008; 359 : 789

De Gorter MK et al. Circ CV Genet 2013: 6: 400

Managing statin intolerance

Statin intolerance score

Regarding this statin regimen:

		Enter score:
A. Location and pattern of muscle symptoms (If more than one category applies, record the highest number.)		
Symmetric, hip flexors or thighs	3	
Symmetric, calves	2	
Symmetric, proximal upper extremity	2	
Asymmetric, intermittent, or not specific to any area	1	
B. Timing of muscle symptom onset in relation to starting statin regimen		
<4 weeks	3	
4–12 weeks	2	
>12 weeks	1	
C. Timing of muscle symptom improvement after withdrawal of statin (If patient is still taking statin, stop regimen and monitor symptoms.)		
<2 weeks	2	
2–4 weeks	1	
No improvement after 4 weeks	0	

Rechallenge the patient with a statin regimen, (even if same statin compound or regimen as above) **then complete final question:**

D. Timing of recurrence of similar muscle symptoms in relation to starting second regimen		
<4 weeks	3	
4–12 weeks	1	
>12 weeks or similar symptoms did not reoccur	0	
Total: All four scores above must be entered before totaling		

Regarding this statin regimen *before* the most recent regimen:

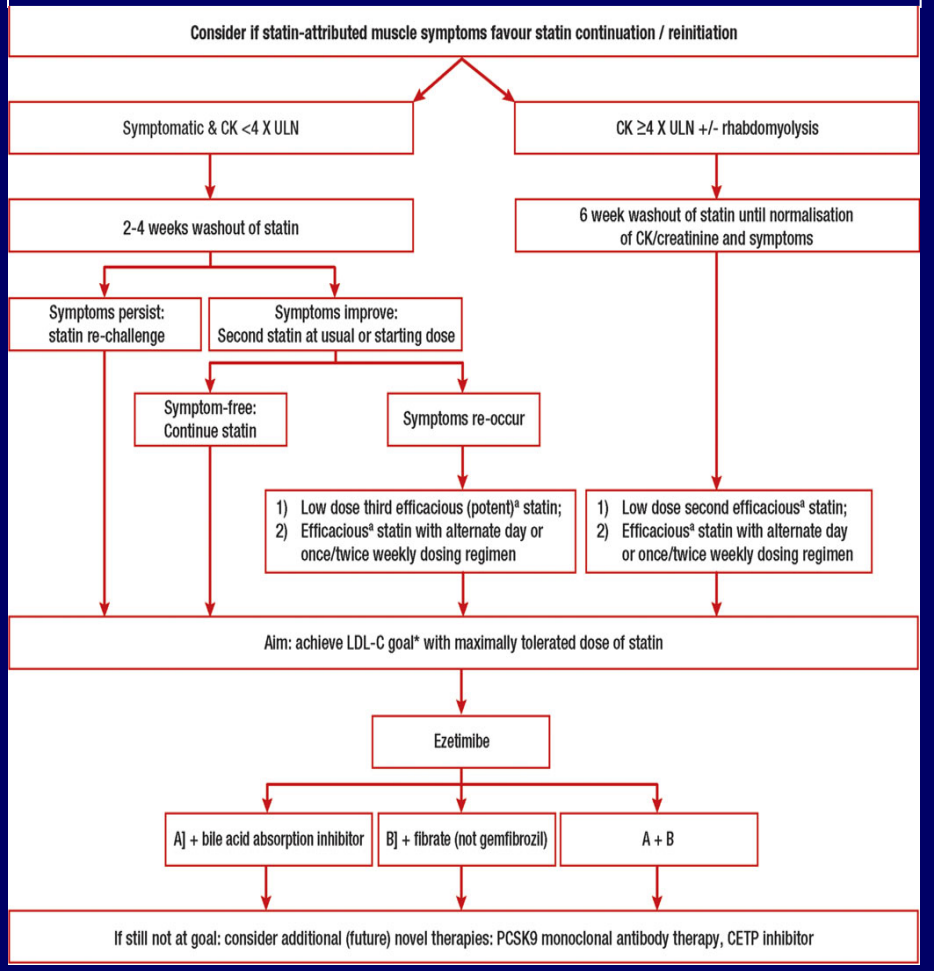
		Enter score:
A. Location and pattern of muscle symptoms (If more than one category applies, record the highest number.)		
Symmetric, hip flexors or thighs	3	
Symmetric, calves	2	
Symmetric, proximal upper extremity	2	
Asymmetric, intermittent, or not specific to any area	1	
B. Timing of muscle symptom onset in relation to starting statin regimen		
<4 weeks	3	
4–12 weeks	2	
>12 weeks	1	
C. Timing of muscle symptom improvement after withdrawal of statin		
<2 weeks	2	
2–4 weeks	1	
No improvement after 4 weeks	0	

Regarding the *most recent* statin regimen: (even if same statin compound as above)

D. Timing of recurrence of similar muscle symptoms in relation to starting regimen		
<4 weeks	3	
4–12 weeks	1	
>12 weeks or similar symptoms did not reoccur	0	
Total: All four scores above must be entered before totaling		

Interpretation	Total score:	2-6	7-8	9-11
	Likelihood that the patient's muscle symptoms are due to statin use:	Unlikely	Possible	Probable

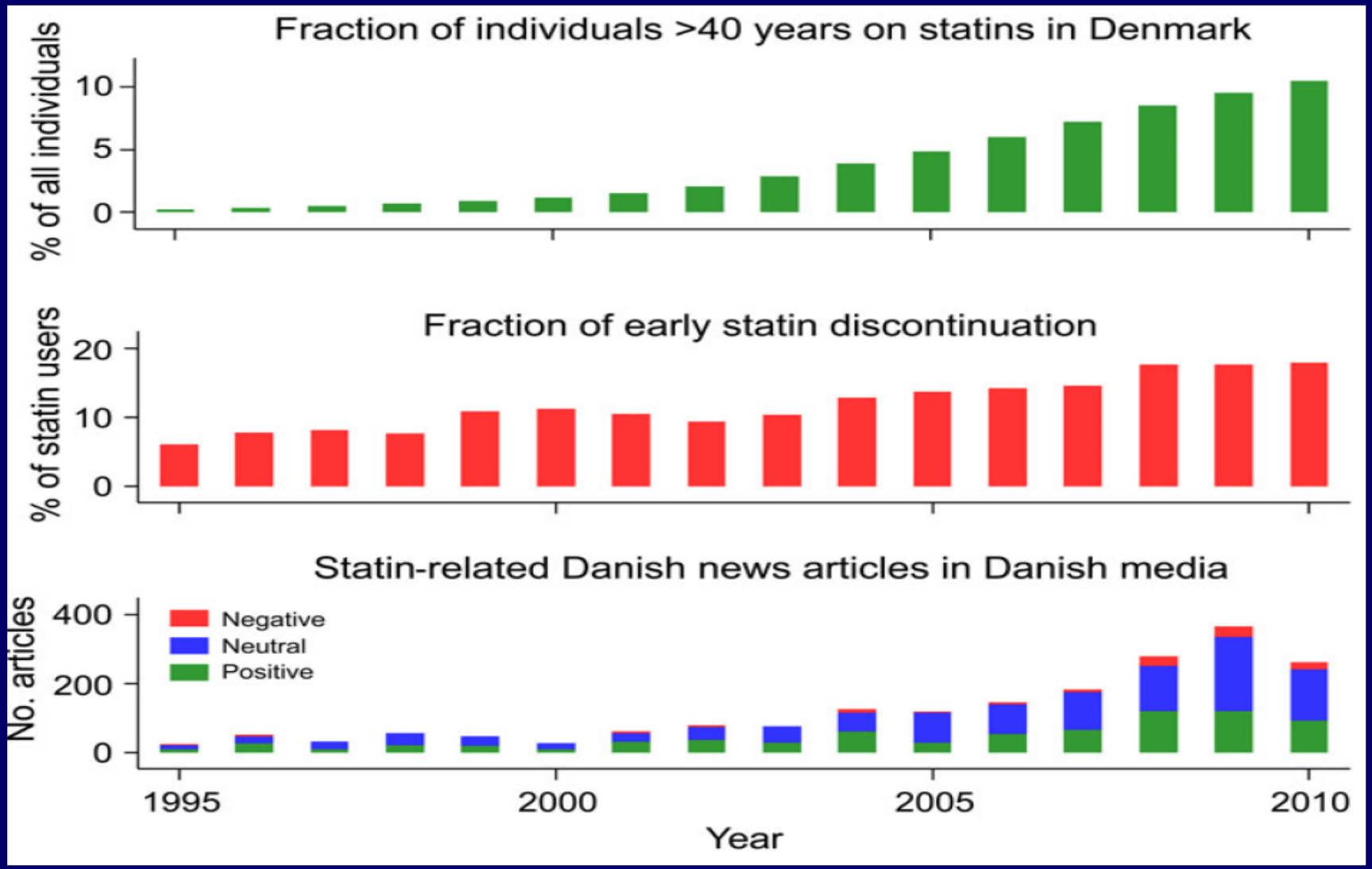
Intolerance treatment



Rosenson RB et al. JACC 2017; 70 : 1290

Stroes ES et al. Eur Heart J 2015; 36 : 1012

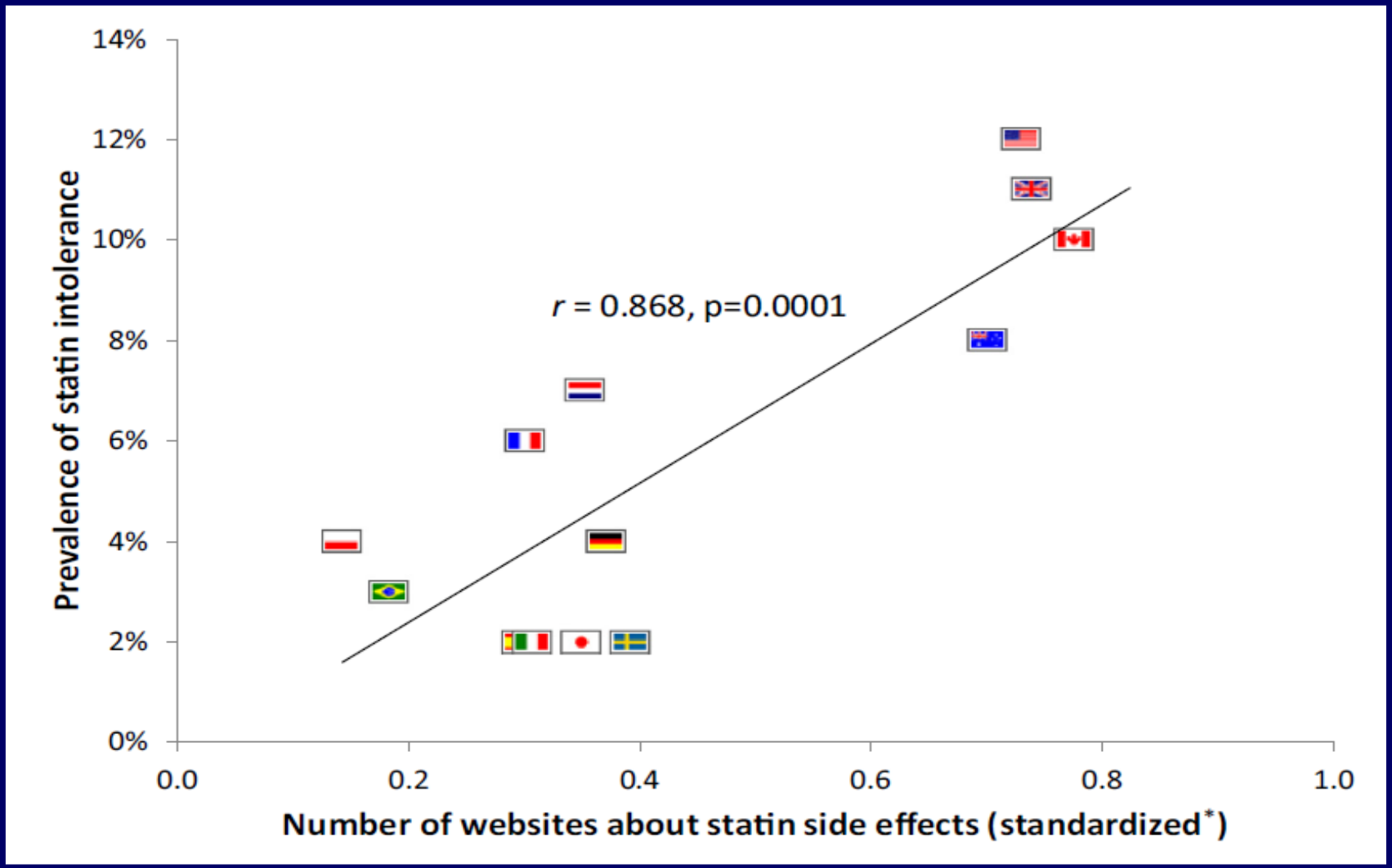
Statins & the media



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

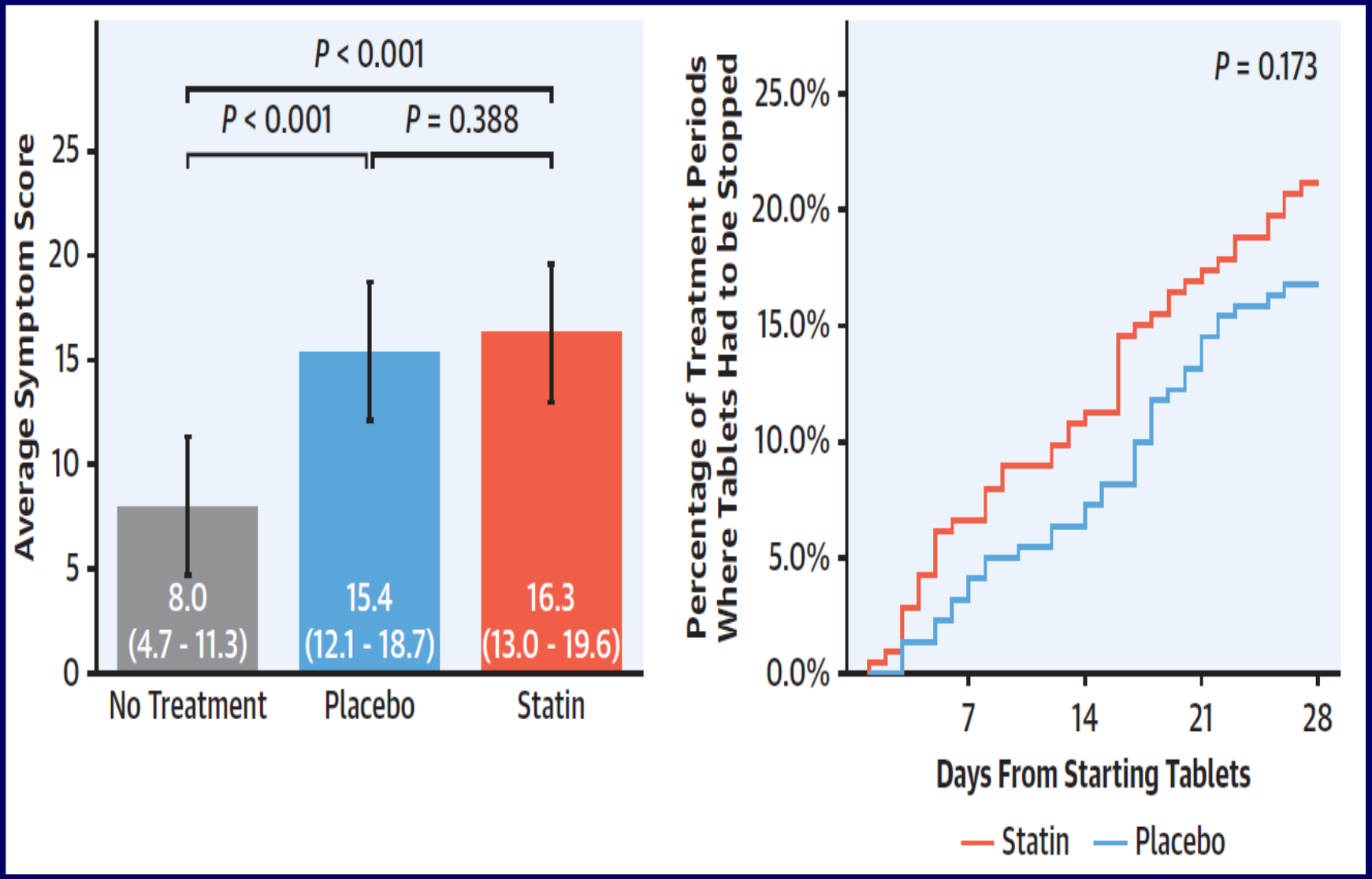
N= 508800

Statins & the internet



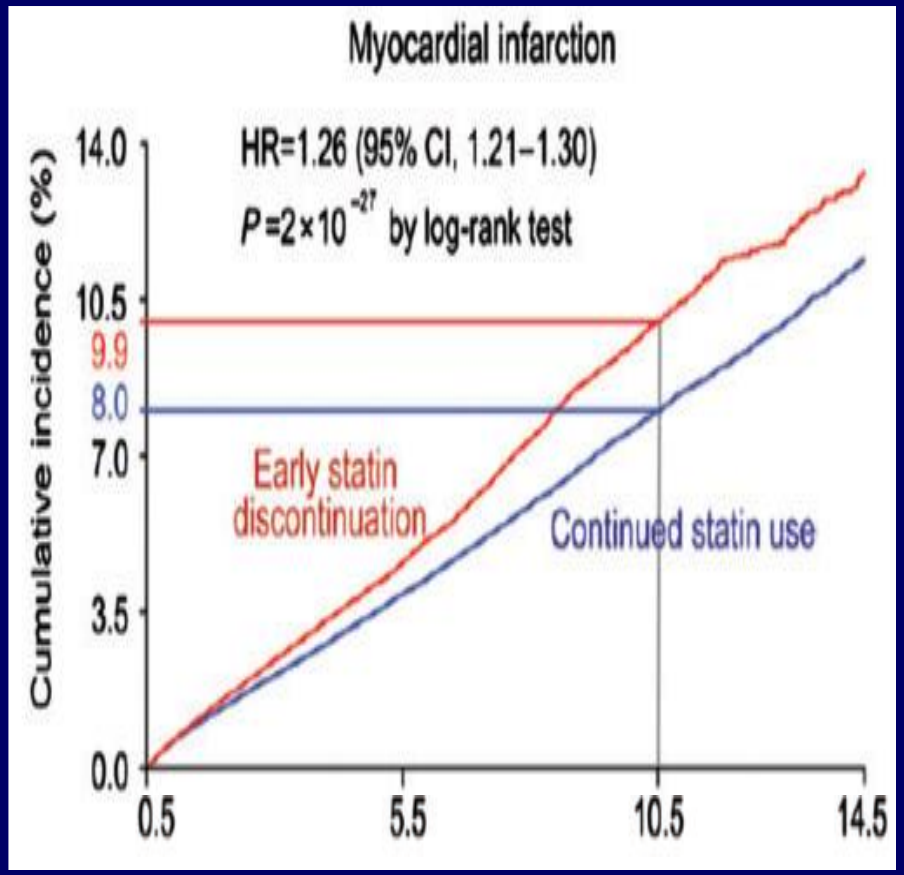
Khan S et al; Int J Cardiol 2018; 25 : 25

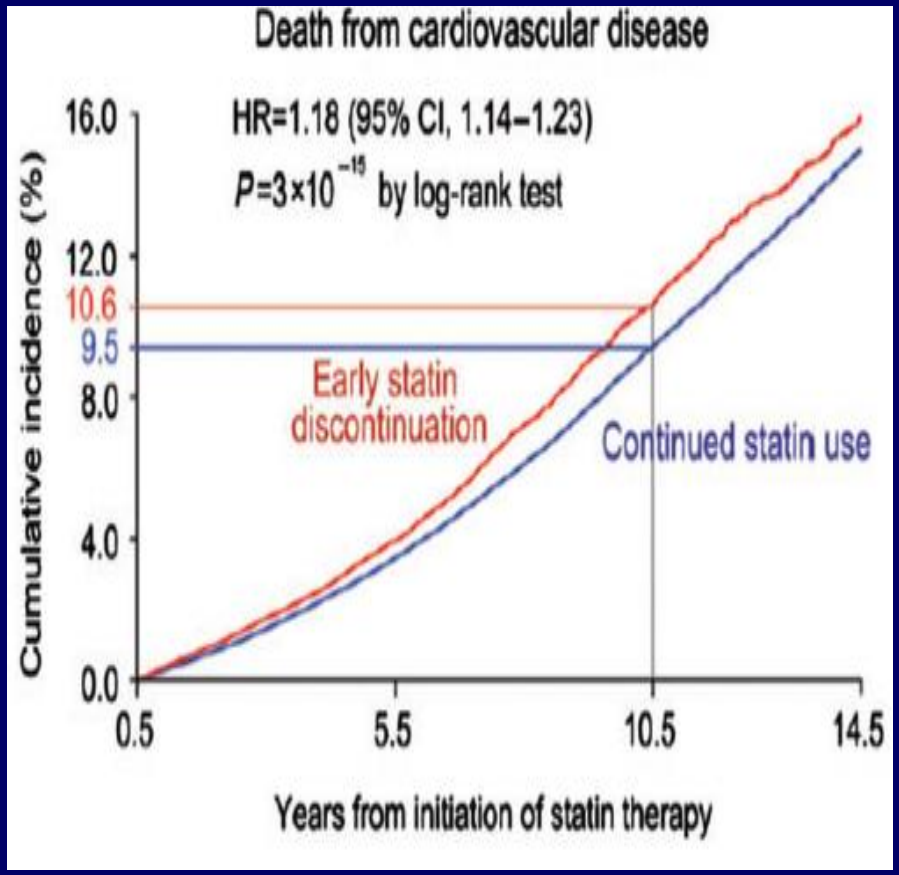
Statin nocebo effect



Howard JP et al. JACC 2022; 78: 1210

Statin discontinuation - consequences





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

MEGA study

Characteristics (n=7832)

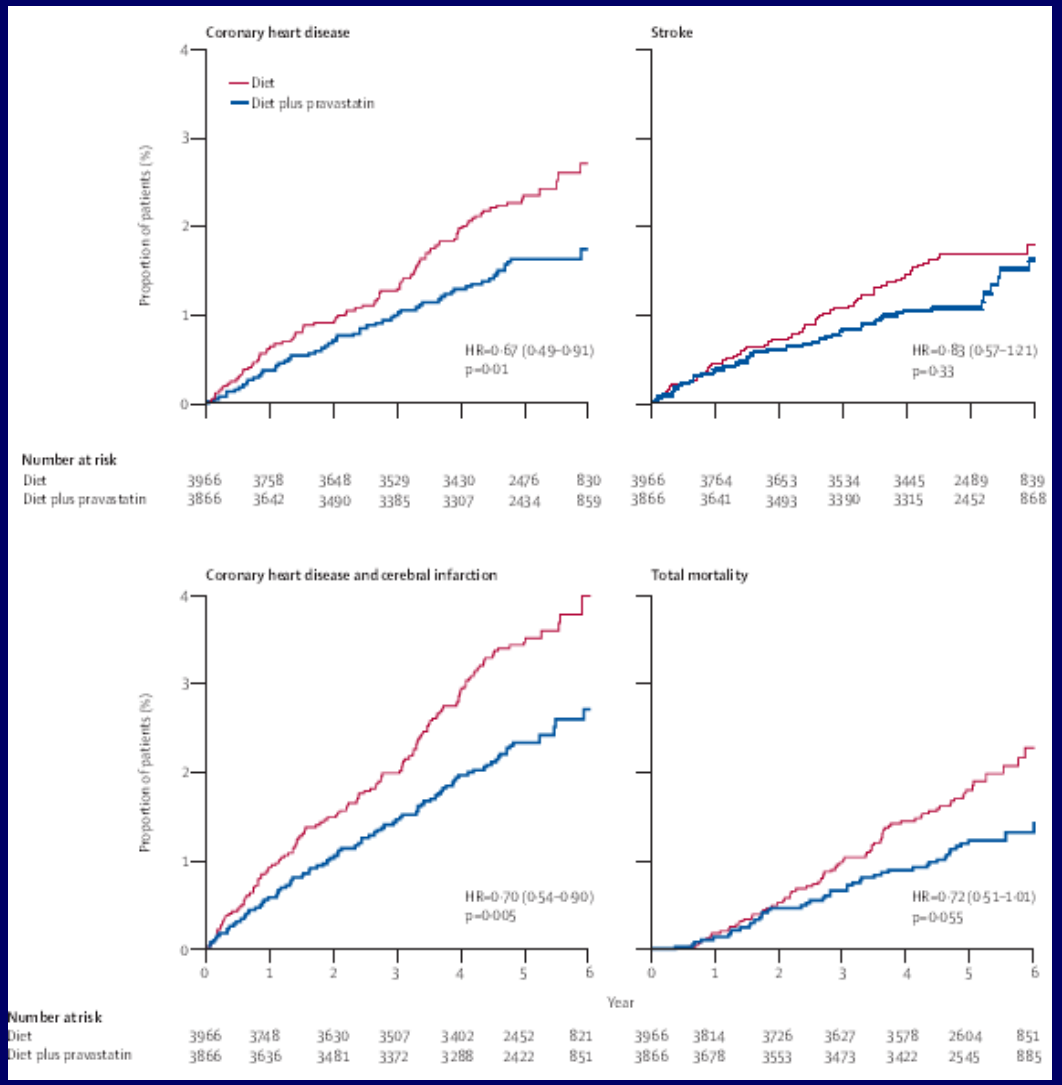
- Age 58±7
- Male 31%
- BP 132±17/79±10mmHg
- DM 21%

TC 6.27±0.31mM
TG 1.44 (1.07-2.02) mM
HDL 1.49±0.39mM
LDL 4.05±0.45mM

- Aspirin 1%
- BP drug 39%

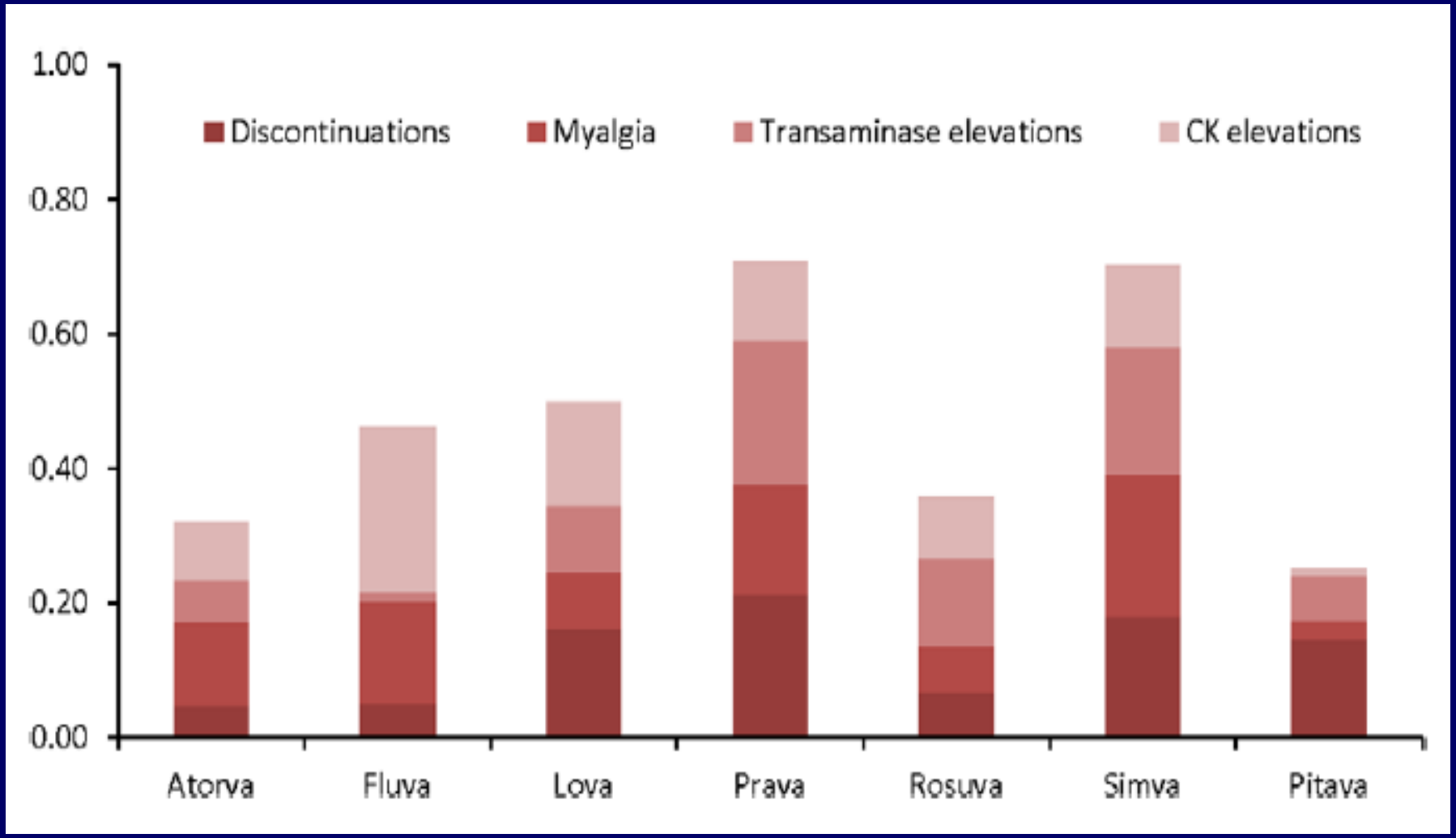
CHD risk 5% @ 10 years

- Randomised pravastatin 10-20mg vs. placebo
  - Average dose 10.6mg for 10 yrs



Nakamura H et al; Lancet 2006; 368: 1153-63

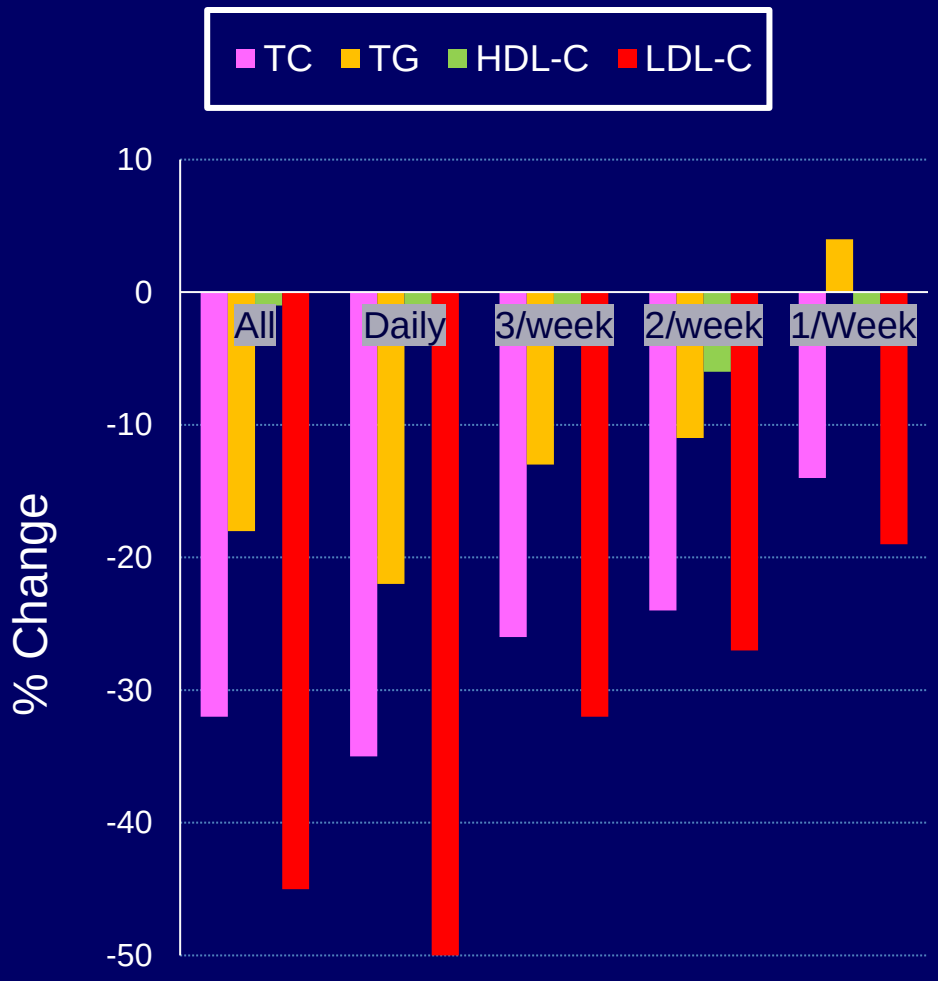
Predicting the best statin to use

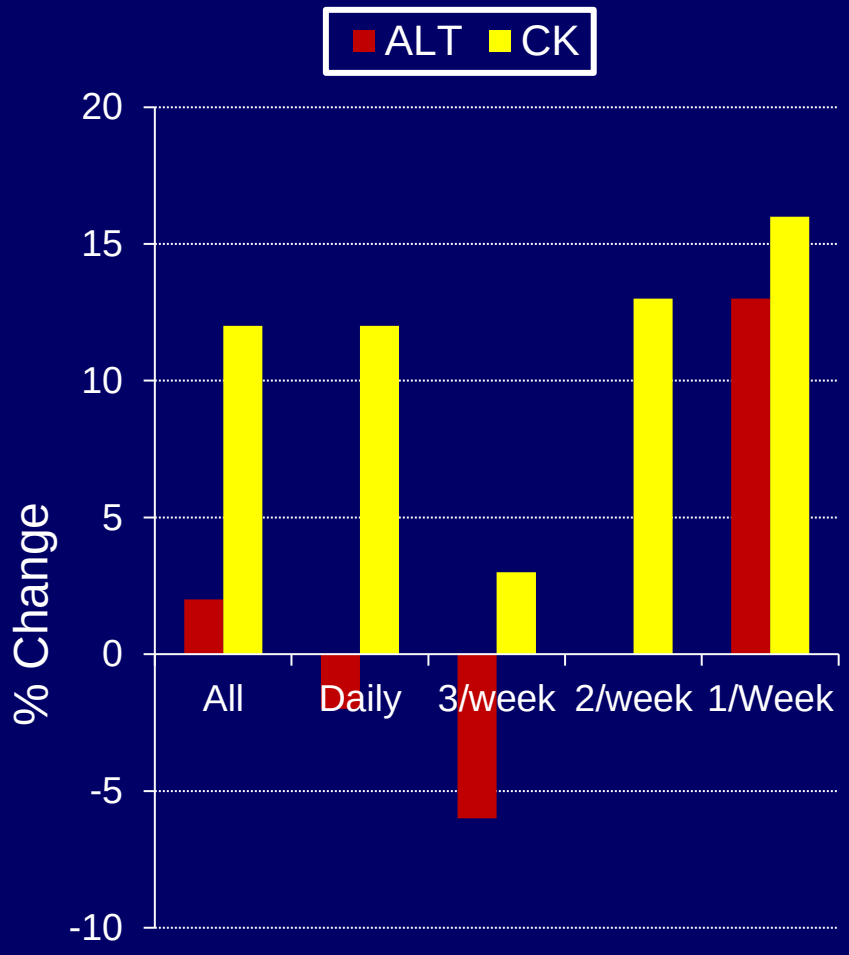


Trials =135; n=246955

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

Intermittent dosing of rosuvastatin 5mg in previously intolerant patients

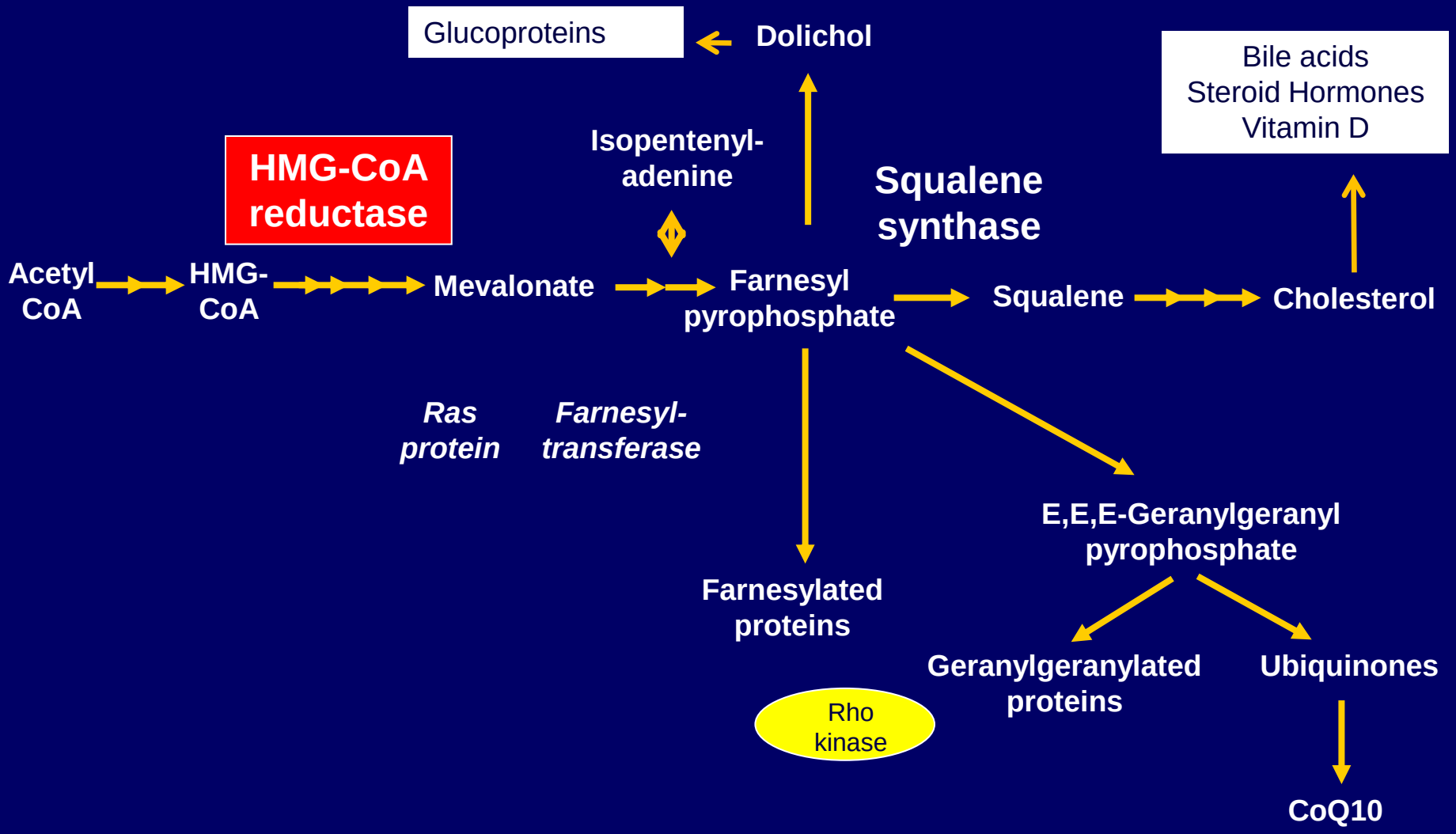




N=325

Meek C et al; Curr Med Res Opin 2012; 28 : 371

Cholesterol Biosynthetic Pathway



Statins & CoQ_{10} Supplementation

First author (reference)	CoQ10 dose, duration	Statin type/dose	SAMS assessment	Muscle outcome
Caso [33]	100 mg/day, 30 d	Variety	Self-report	↓ Muscle pain
Young [34]	200 mg/d, 12 wk	S 10–40 mg	Self-report	↔ Pain, statin tolerance
Bookstaver [35]	60 mg/2 × d, 3 mo	Variety	Self-report	↔ Pain at 1 month
Bogsrud [36]	400 mg/d, 12 wk[a]	A 10 mg	Self-report	↔ Symptoms or function
Fedacko [3]	200 mg/d, 3 mo	Variety	Self-report	↓ Muscle pain, SAMS cases
Skarlovnik [39]	50 mg/2 × d, 30 d	Variety	Dechallenge/rechallenge	↓ Muscle pain, symptoms
Taylor [40]	600 mg/d, 8 wk	S 20 mg	Placebo/statin trial	↔ Muscle pain, SAMS cases
Buettner [41]	300 mg/2 × d, 4 wk	Variety	Dechallenge/rechallenge	↔ SAMS cases, mitochondrial function

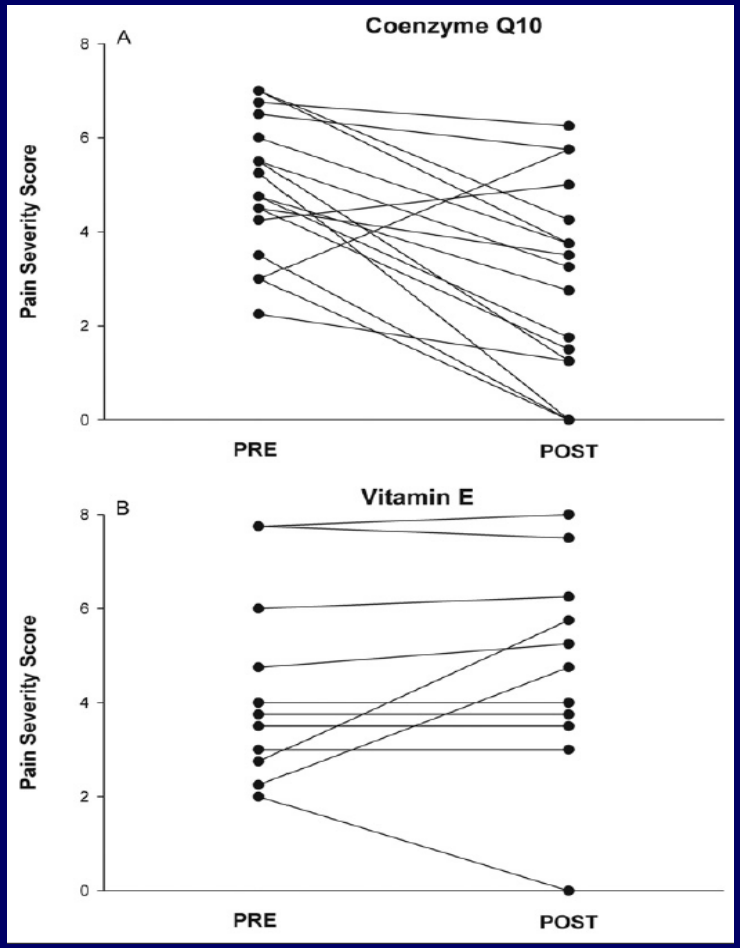
Taylor BA. Am J Cardiovasc Drugs 2018; 18: 75

Statin myopathy and CoQ10 supplementation

Characteristics, plasma lipid profile, and creatine kinase (CK) concentration of subjects in the coenzyme Q10 and vitamin E groups

Variable	Coenzyme Q10 (n = 18)	Vitamin E (n = 14)
Women/men	6/12	9/5
Age (yrs)	58 ± 3	64 ± 2
Height (m)	1.70 ± 0.03	1.65 ± 0.03
Weight (kg)	84.0 ± 3.5	86.1 ± 5.8
Body mass index (kg/m^2)	28.1 ± 1.0	29.8 ± 1.7
Triglycerides (mg/dl)	196 ± 30	155 ± 18
Cholesterol (mg/dl)	183 ± 10	189 ± 14
LDL cholesterol (mg/dl)	96 ± 3	115 ± 13
CK (U/L)	129 ± 15	133 ± 37

Data expressed as mean ± SEM.

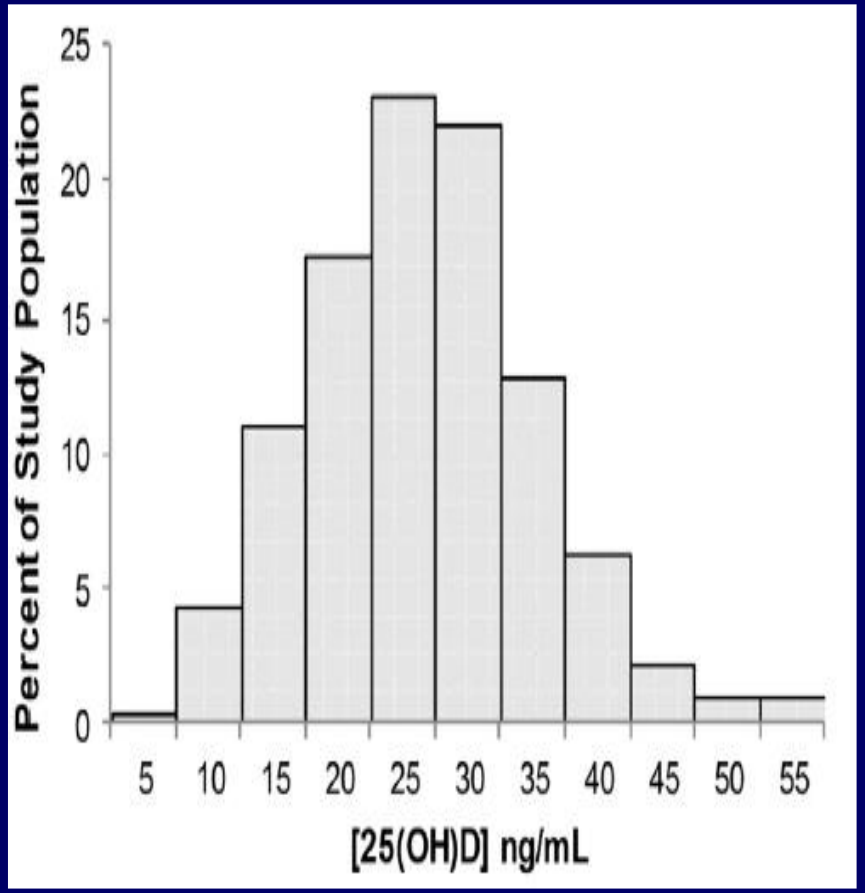


Pain severity ↓40% p<0.001

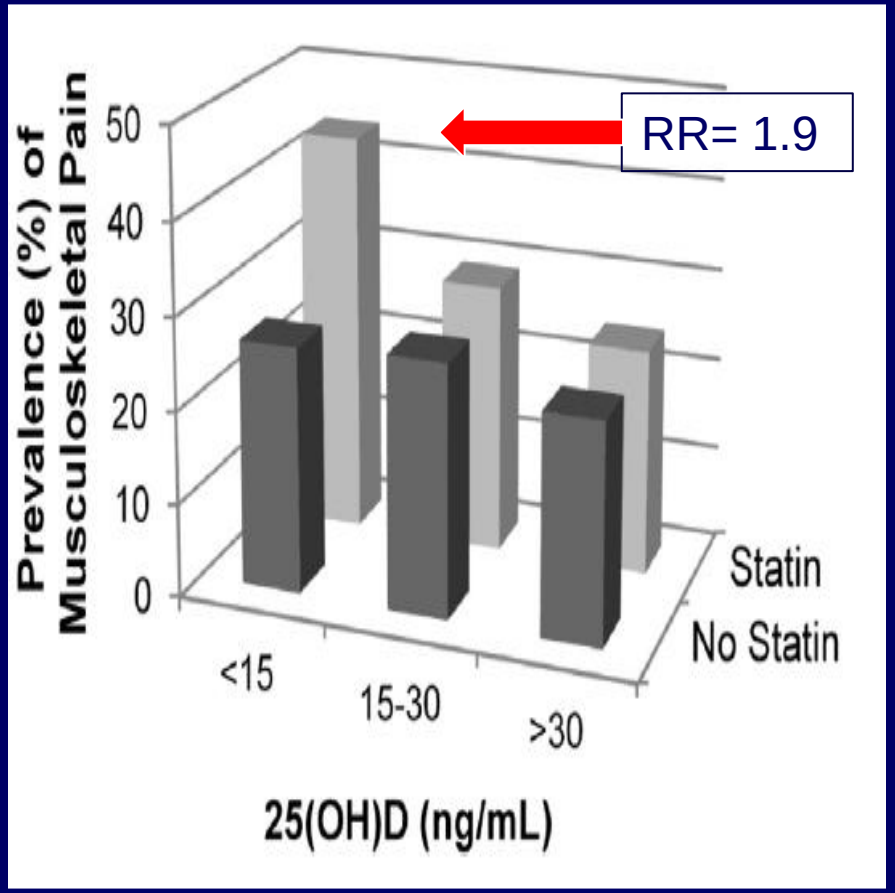
Caso G et al. Am J Cardiol 2007; 99 : 1049

Statins & vitamin D

Vitamin D distribution



NHANES



N=6233

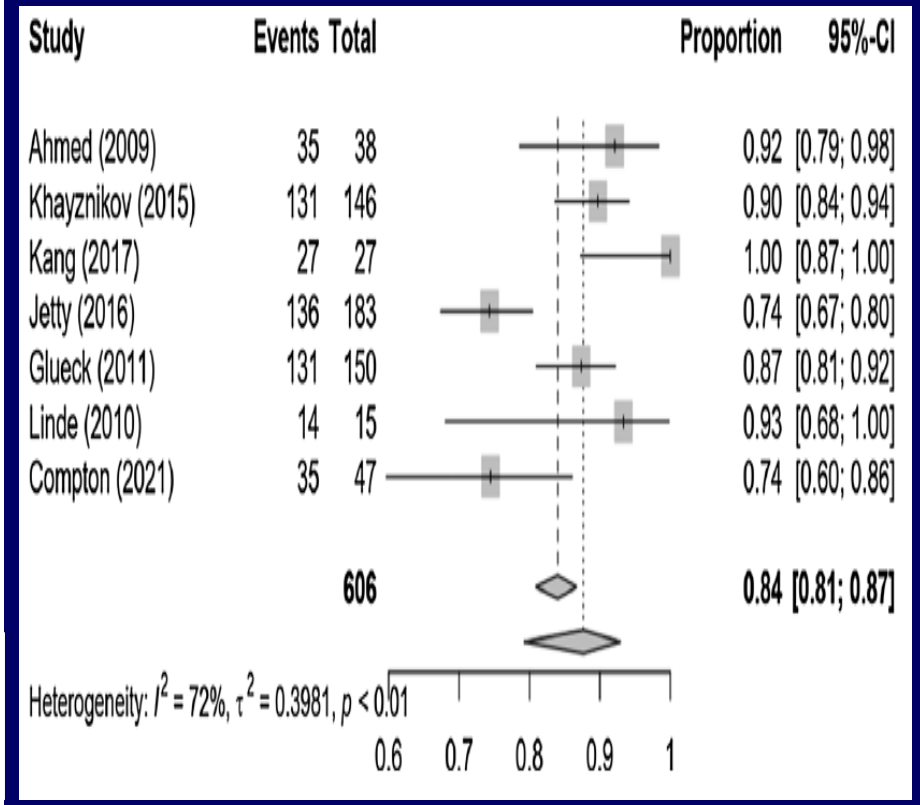
Morioka TY et al; Athero 2015; 238: 77

High dose vitamin D supplements and statin therapy

Follow- up duration and Baseline vitamin D

Duration of treatment Months mean (SD), median	*n*	/D normalized g/ml/≥79.9 nmol/L) follow-up *n* (%)	Myositis–myalgia free on follow-up *n* (%)
<3 months 1.4 (0.6), 1.2	34	25 (74%)	33 (97%)
3–<5 months 3.8 (0.6), 3.8	20	16 (80%)	17 (85%)
5–<8 months 6.5 (1.0), 6.8	21	18 (86%)	18 (86%)
8–<14 months 11.0 (1.8), 11.4	31	23 (74%)	25 (81%)
14–<20 months 16.6 (1.7), 16.9	10	7 (70%)	7 (70%)
20–<25 months 22.4 (1.0), 22.2	12	11 (92%)	11 (92%)
≥25 months 31.1 (4.4), 30.8	22	17 (77%)	20 (91%)
Total cohort 11.5 (10.3), 8.1	150		

Myalgia results

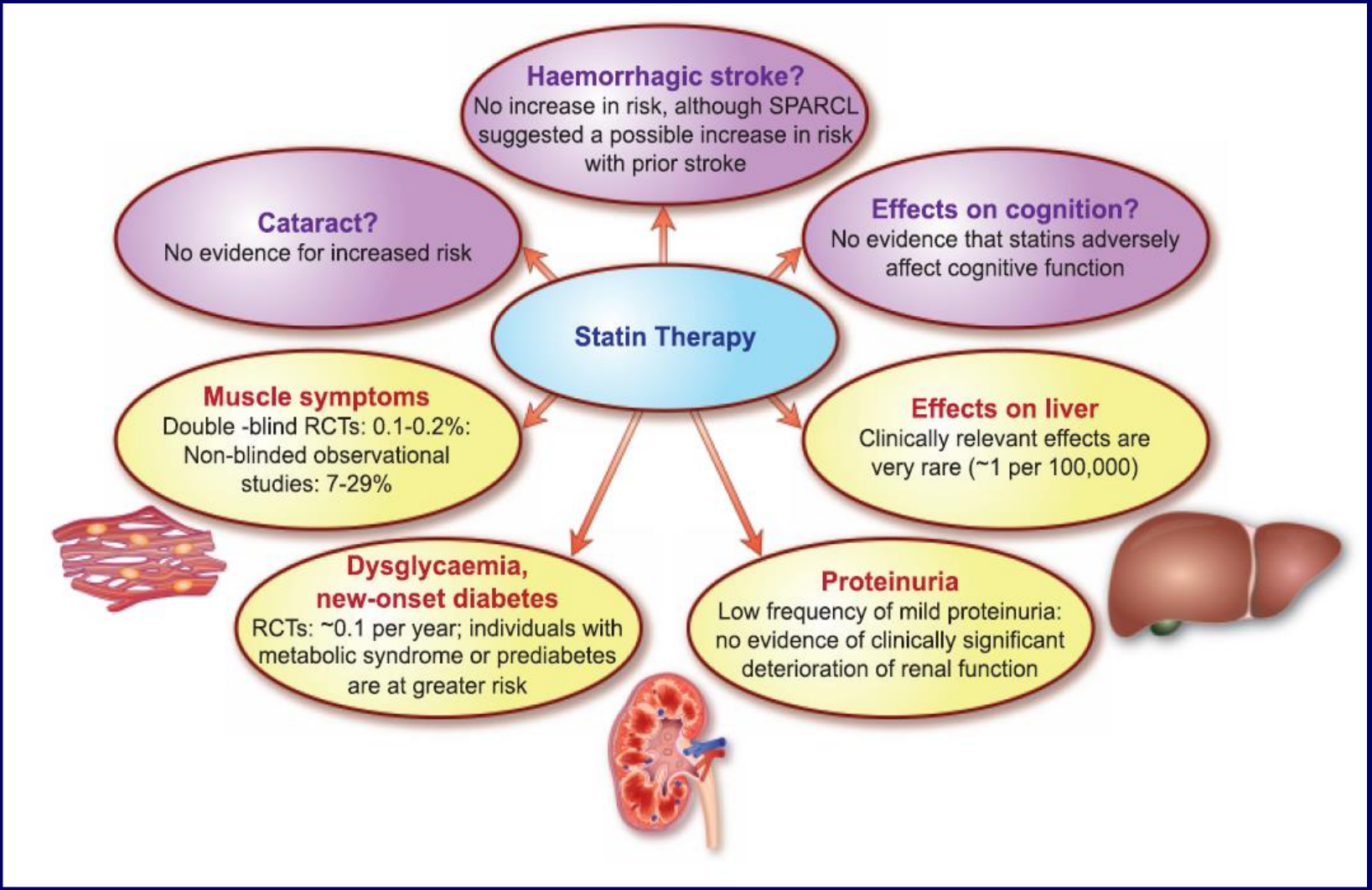


Glueck C et al; CMRO 2011; 27: 1673

Teo CB et al; Hi BP & CVD Res 2022; 29 : 337

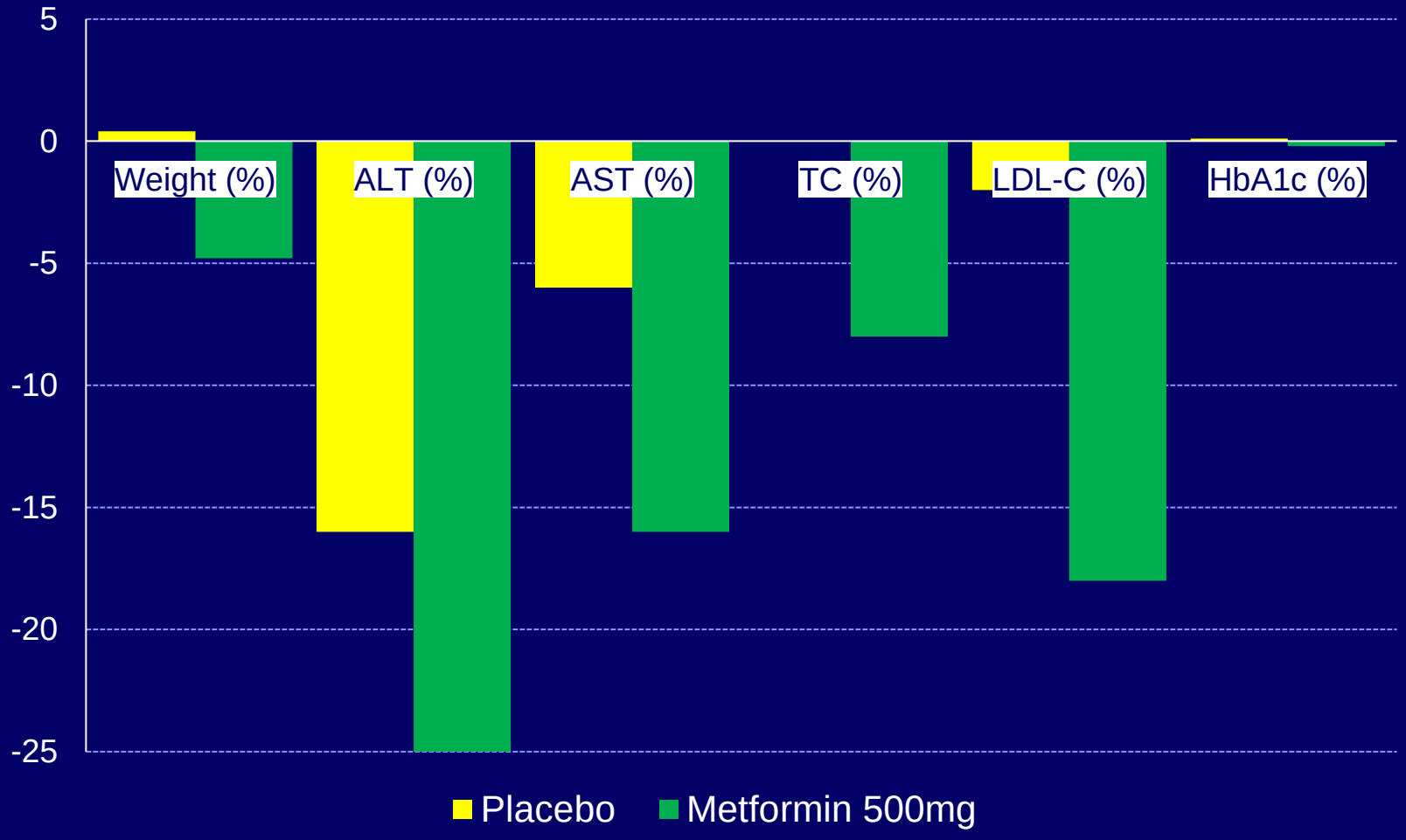
N = 606

EAS consensus panel



Mach F et al. Eur Heart J 2018; 39: 2526

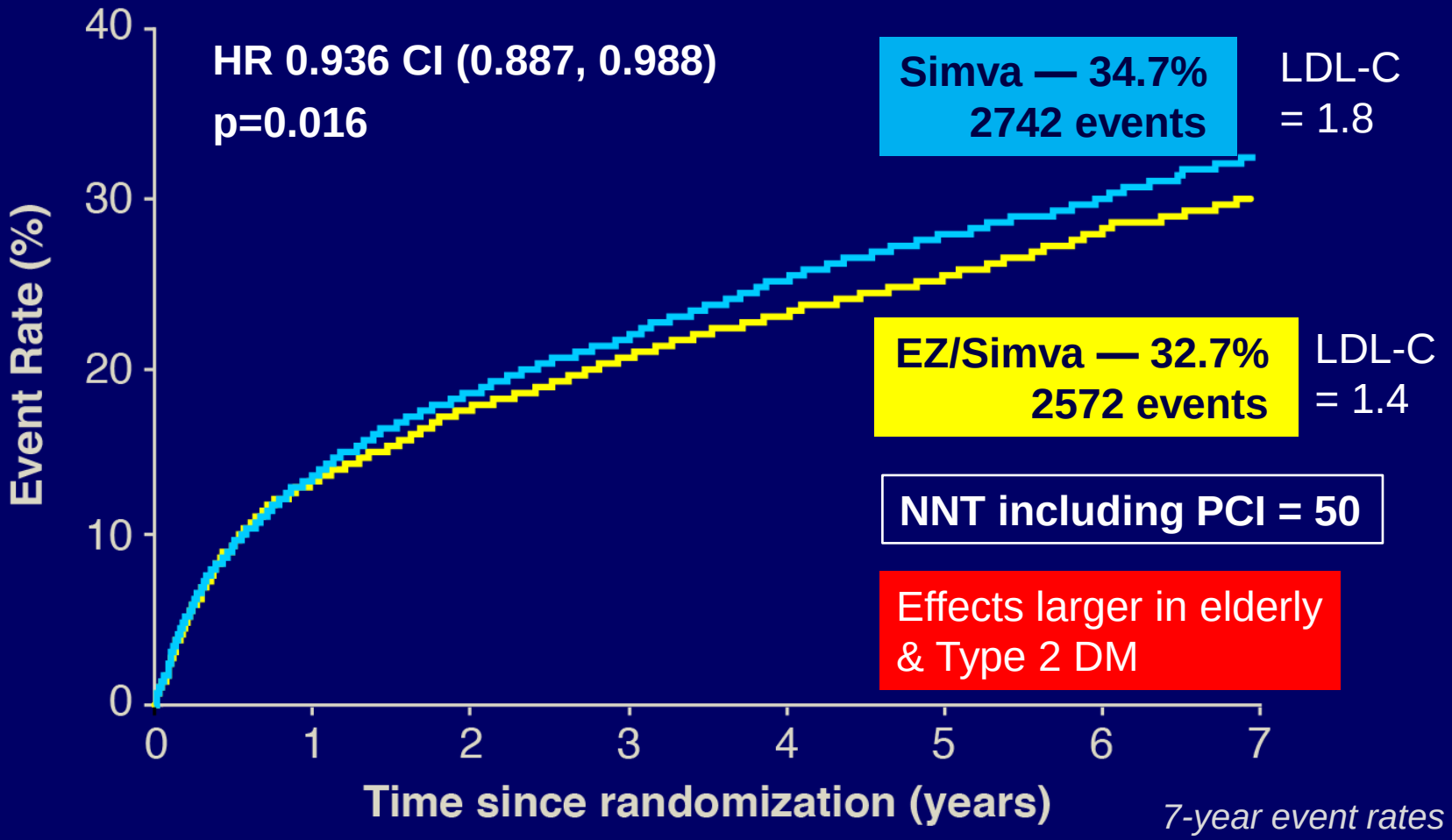
Low dose Metformin in treatment of NAFLD



N=48

Haukeland JW et al. Scand J Gastro 2009; 44: 853

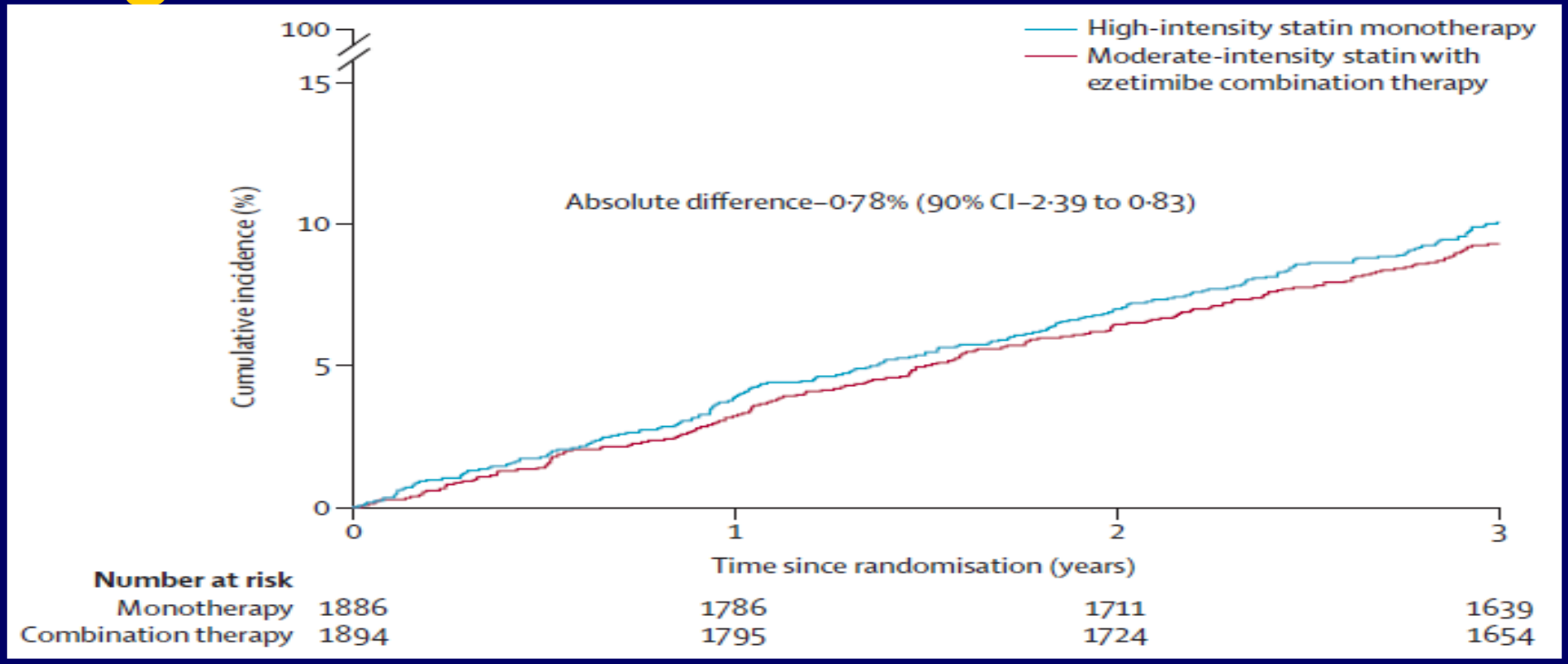
IMPROVE-IT: Ezetimibe in ACS Primary Endpoint — ITT



CVD death, MI, UAS, CVA & PCI (≥30 days)

Cannon CP et al; NEJM 2015; 372 : 2387

RACING:
High dose Statin vs. Statin-Ezetimibe



	Statin-Eze	High statin	Difference
New-onset diabetes	145 (7·9%)	159 (8·7%)	–0·82 (–2·65 to 1·00)
New-onset diabetes with anti-diabetic medication initiation	95 (5·1%)	107 (5·8%)	..
Muscle-related adverse events	21 (1·1%)	34 (1·9%)	0·69 (–2·22 to 0·82)
Myalgia	17 (0·9%)	29 (1·6%)	0·66 (–1·46 to 1·06)
Myopathy	2 (0·1%)	4 (0·2%)	–0·11 (–0·50 to 0·25)
Myonecrosis*	11 (0·6%)	13 (0·7%)	0·11 (–0·72 to 0·48)

Kim B-K et al. Lancet 2022; 400 : 380

N=3780

Guidelines for use of PCSK-9 inhibitors

USA	Europe

NLA
• CVD & LDL-C>2.5mM
  ◦ (nHDL-C >3.4 mM)
• FH no CVD LDL-C >3.4mM
  ◦ (nHDL-C >4 mM)
AACE/ASE
• CVD-ACS & LDL-C>1.9mM
• Others as above
	NICE TA
	• CVD & LDL-C >4.0 (2.5*)
	  ◦ Multi-vessel disease >3.5mM
	• FH no CVD & LDL-C >5mM
	EAS/ESC
	• CVD/DM & LDL-C >3.6
	  ◦ Rapid disease >2.6mM
	• FH no CVD & LDL-C >5mM
	  ◦ Other CVD RFs > 4.5mM

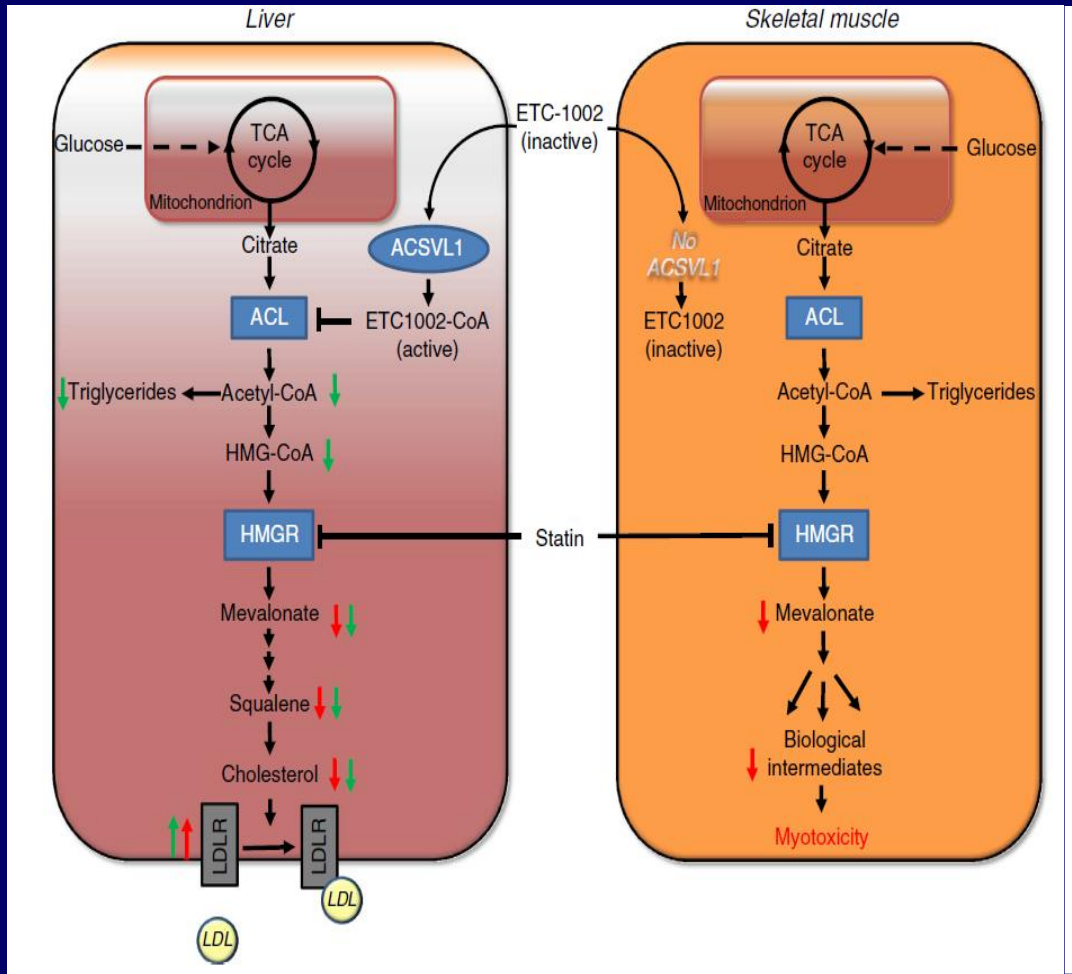
Orringer C et al; J Clin Lipid 2017; 11: 880
Jellinger PS et al; Endo Pract 2017; 23 : 479
Landmesser U et al; EHJ 2017; 38 : 2245
NICE.org.uk (TA394; TA393; TA 733)

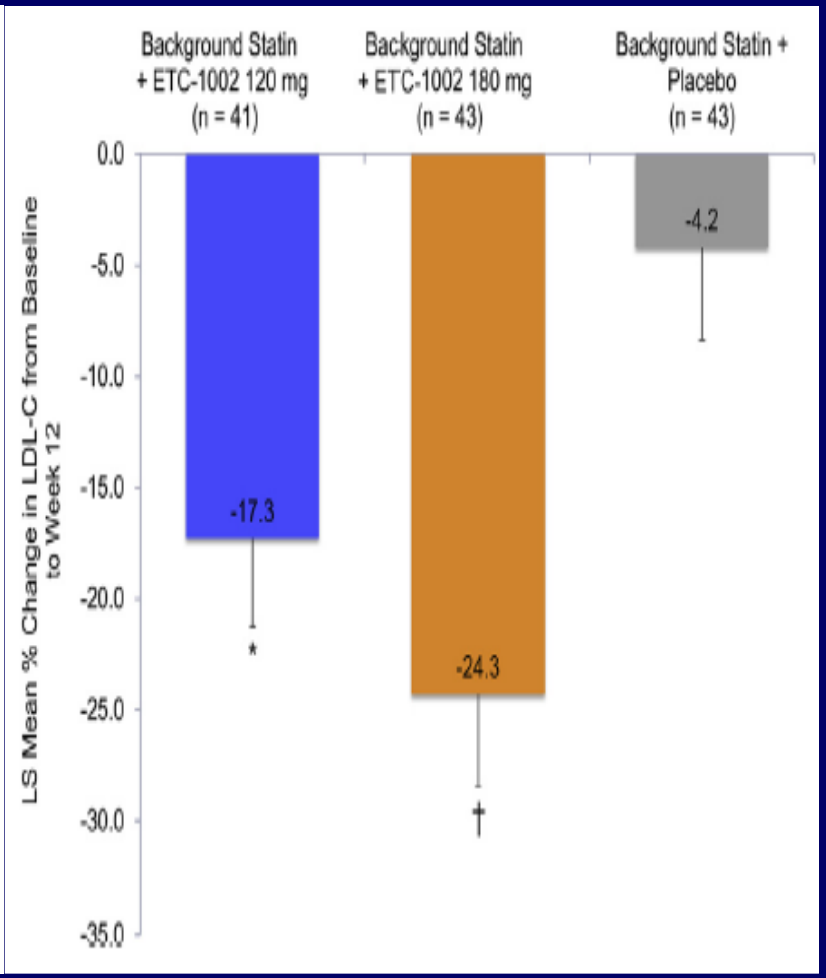
PCSK-9 inhibitors in statin-intolerant patients

Condition	Age	Gender	Pre-PCSK-9 LDL-C (mmol/L)	Post-PCSK9 LDL-C (mmol/L)	LDL-C PCSK-9 response (%)	Adverse events/comments
HoFH (LDLR & PCSK9)	31	Female	5.66	2.78	−51	Nil
FH (PCSK9 mutation)	78	Female	2.05	(4.32) 1.80	(+210) −18	Statin & ezetimibe stopped. No response to PCSK9 monotherapy. Response after ezetimibe added.
Remnant hyperlipidaemia (apoE2/E2); IHD	68	Male	1.88	(6.88) 1.50	(+350) −17	Statin stopped. No response to PCSK9 monotherapy. Response after fibrate added.
Myasthenia gravis	65	Female	4.02	2.92	−27	Nil
FH, HOCM, FSH muscular dystrophy carrier	49	Male	3.02	1.30	−57	Nil
Duchenne muscular dystrophy (carrier)	60	Female	5.73	1.39	−76	Nil
FH PE01 mitochondrial myopathy	75	Male	5.30	2.54	−51	Nil
RYR1 mutation carrier	37	Male	5.34	2.16	−60	Nil
Nephrotic syndrome	52	Female	2.12 TC = 19.8 mmol/L TG = 34.8 mmol/L	0.86 TC = 3.7 mmol/L TG = 5.06 mmol/L	(nil) −59	No response to PCSK9 monotherapy. Response only after pioglitazone added
Renal transplant	45	Male	5.41	3.13	−42	Nil
HIV CVD Bile salt malabsorption	62	Male	3.33	1.19	−66	Nil

Kohli M et al; Int J Clin Pract 2017; 71: e13032

Other ways of lowering LDL-C
ATP-citrate lyase & bempedoic acid

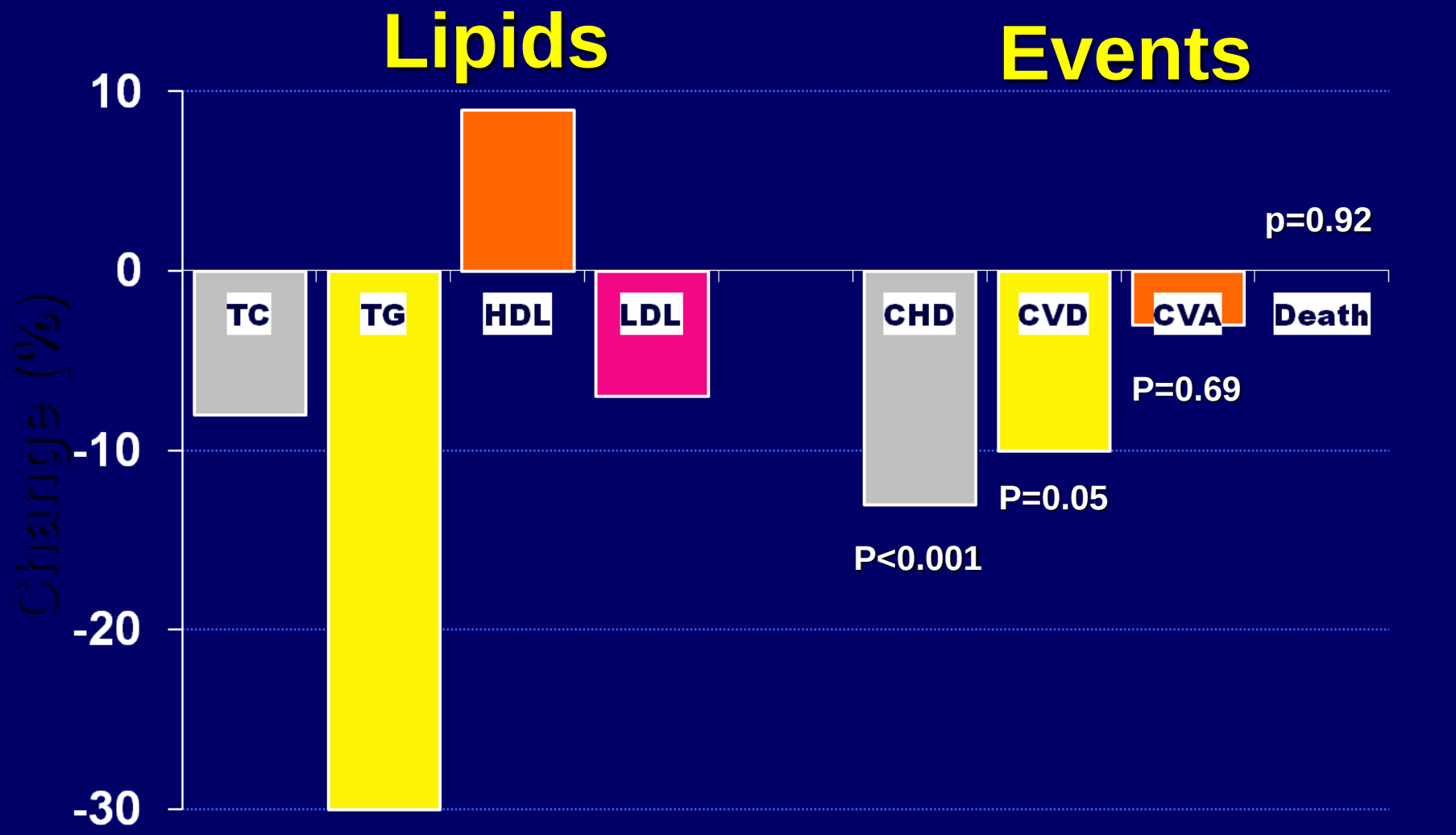




Pinkosky SL et al. Nature Comm 2016; 7: 13457
Ballantyne CM et a;. Am J Cardiol 117: 1928

Fibrates : meta-analyses

Secondary& primary prevention;



Saha S et al; Am Heart J 2007; 154: 943

Jun M et al; Lancet 2010 ; 375 : 1875

10 & 18 studies;
n= 36489 & 45,058

Conclusions

- Operator error
  - Doctor/Prescriber
- Poor standards
  - Guidelines dated
- Faulty design
  - Not ideal molecule
- Faulty construction
  - Ignoring co-morbidities
- Unexpected factors
  - Life

- Only prescribe statins to people that need them
- Exclude secondary causes
- Check for medication interactions
- If statin intolerance occurs
  - Switch statin
  - Consider intermittent dosing regimes
  - Consider/add non-statin lipid-lowering drugs

Knowledge, care, practice & routine are essential for safe prescribing