Lipid Management in 2026

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Conflict of Interest Disclosure

I have no actual or potential conflicts of interest in relation to this program or presentation to disclose.

I prepared this lecture in my personal capacity. The opinions expressed in this lecture are my own and do not reflect the view of the Veteran's Health Administration or the United States government.

Session Objectives

- Review efficacy of lifestyle interventions on lipid management
- Review effect of supplements on lipids
- Review pharmacotherapeutic treatment of dyslipidemia

Case 1

64 year-old sedentary man with obesity & hypertension recently suffered a myocardial infarction and underwent PCI. Currently asymptomatic. Eats a fast-food diet. Non-smoker. Drinks 2 beers most nights. Vitals WNL. Exam benign. Active meds: aspirin, clopidogrel, & losartan. Refuses statins. Total cholesterol 238 mg/dL, HDL 53 mg/dL, LDL 160, non-HDL 185, triglycerides 188.

- What lifestyle modification do you recommend?
- What is the expected impact on LDL? Triglycerides?

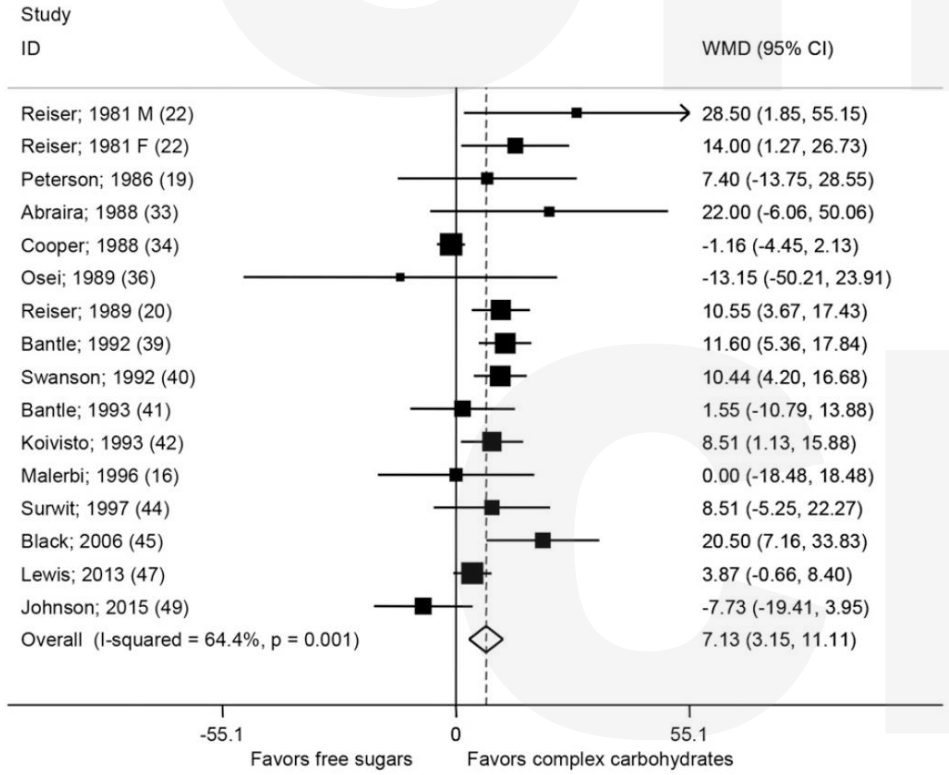
Lifestyle interventions to lower cholesterol

- Avoid excess sugar
- Add fiber
- Choose healthy fats, avoid trans/saturated fats
- Avoid alcohol
- Drink green tea
- Exercise
- Lose weight

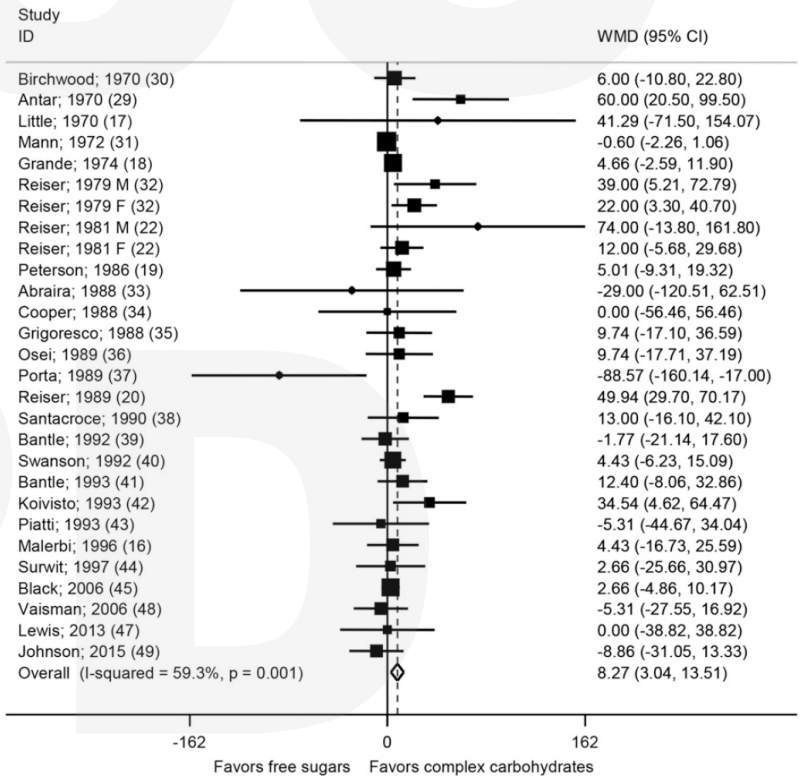
Avoid sugar

160
-7
151

LDL cholesterol



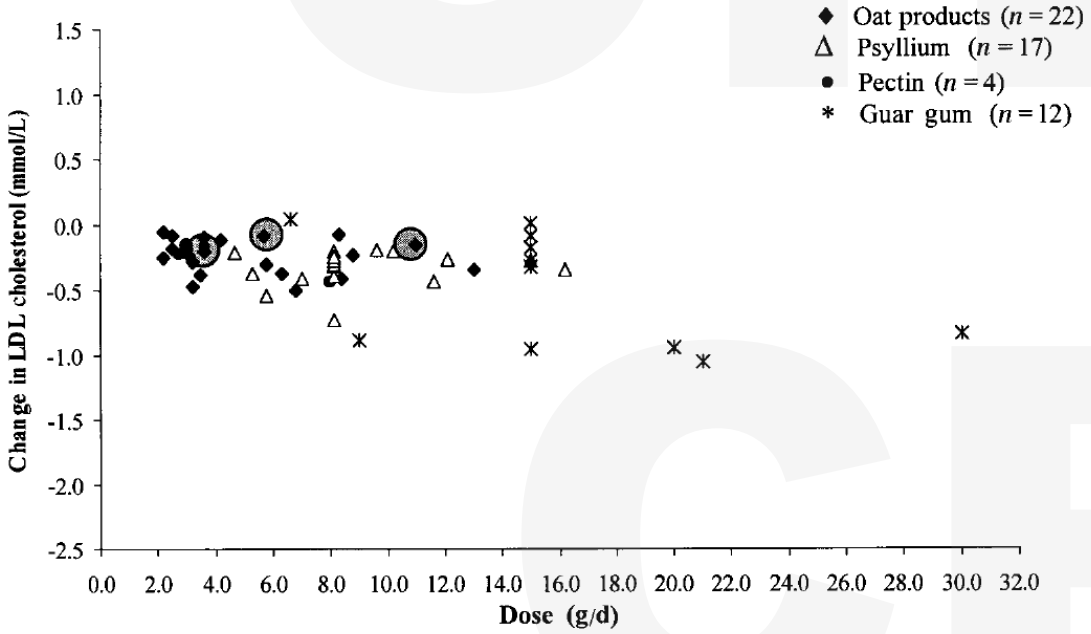
Triglycerides



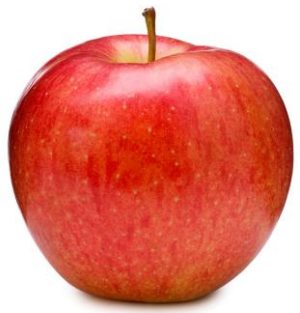
Am J Clin Nutr 2017;205:42-56.

Add fiber

151
-15
136



- Supplement 3 servings of 2.4 g of psyllium daily
  - LDL: -10 mg/dL
- Eat 3 apples or 3 bowls of oatmeal
  - LDL: -5 mg/dL



Am J Clin Nutr 1999;69:30-42.

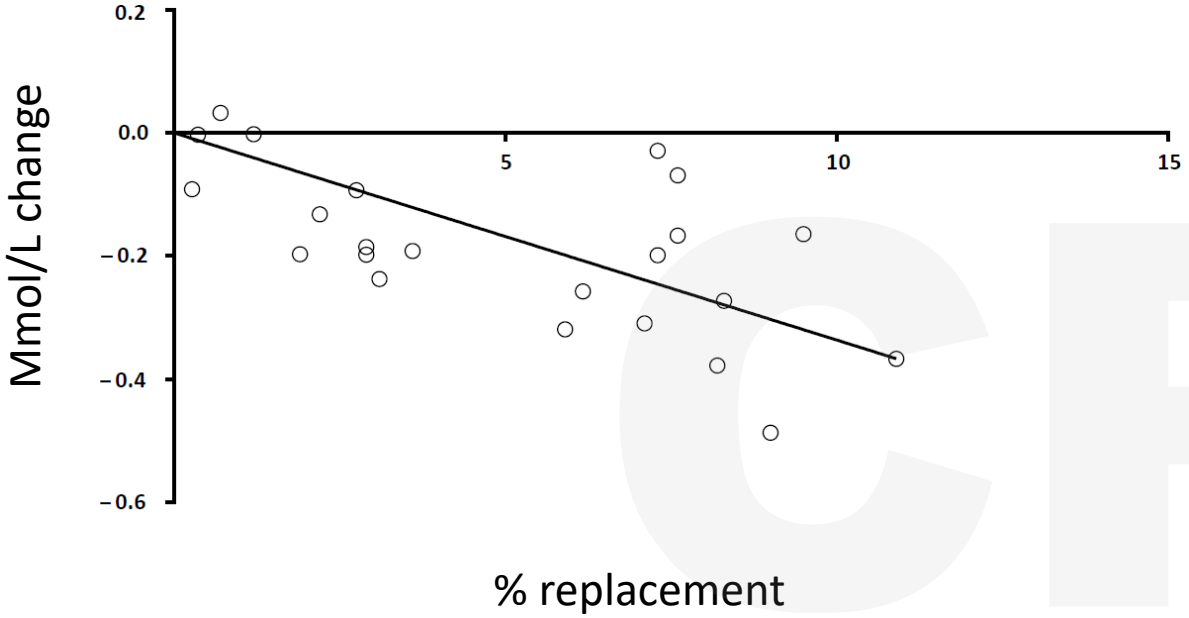
Am J Clin Nutr 2018;108:922-932.

136
-10
126

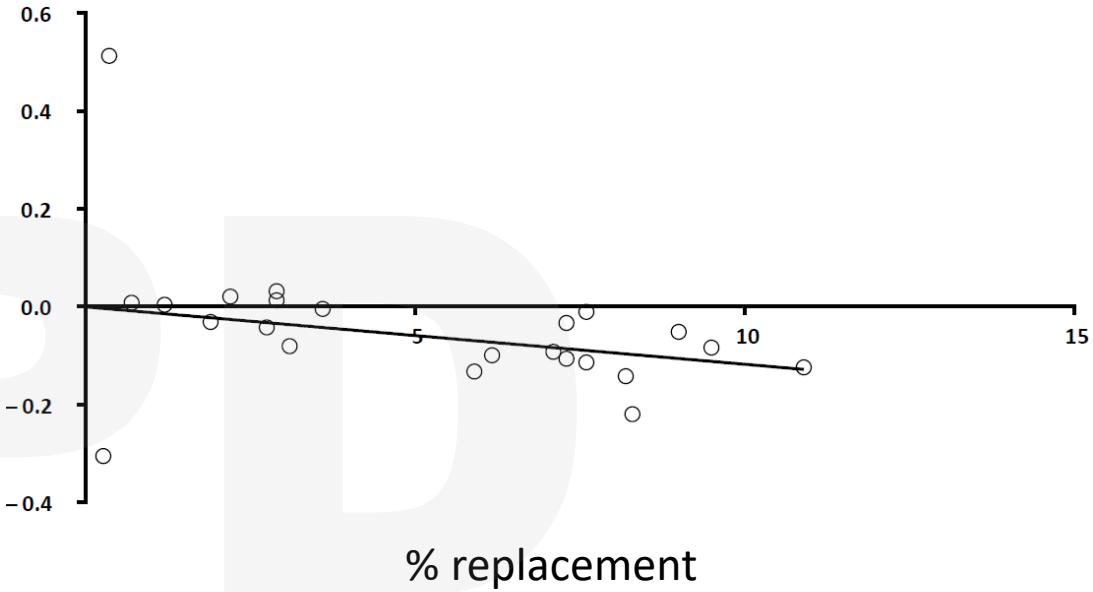
Choose healthy fats

Replacement of TFAs w/ UFAs

LDL Cholesterol



Triglycerides



Brouwer WHO 2016.

126
-0
126

Avoid alcohol

5 oz wine

12 oz beer

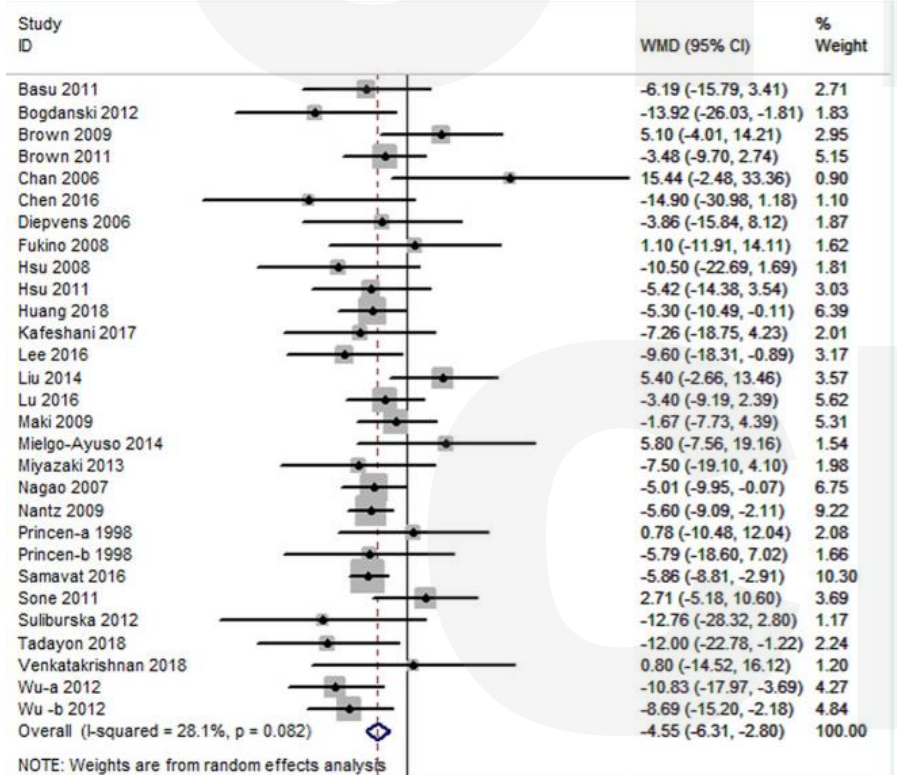
1.5 oz 80 proof

Crit Review Clin Lab Sci 2002;39(3):225-83.

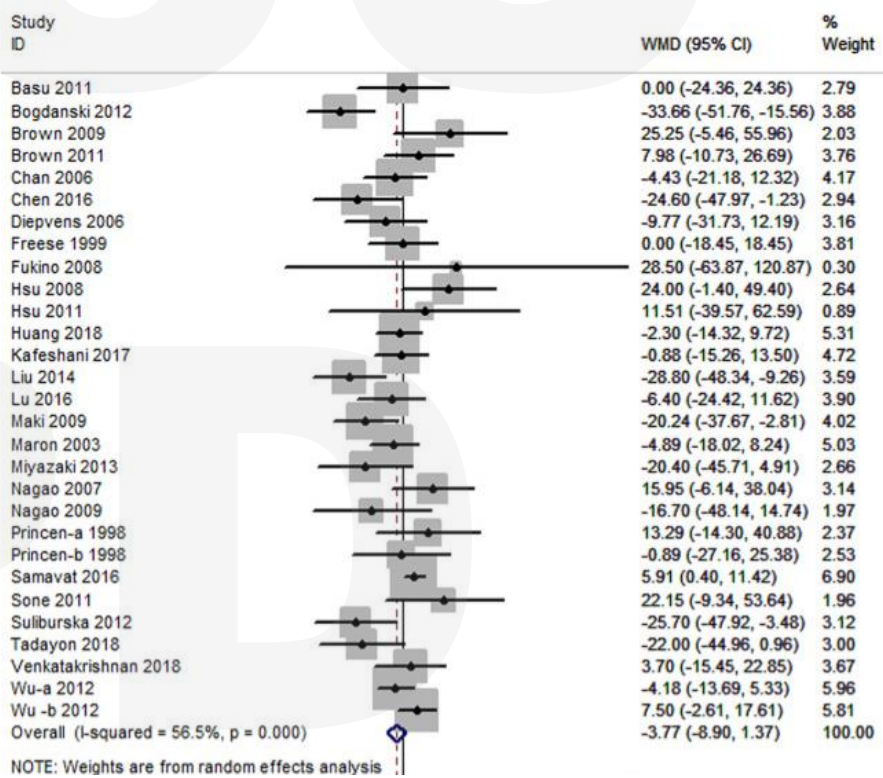
Drink green tea

126
-5
121

LDL



TGs

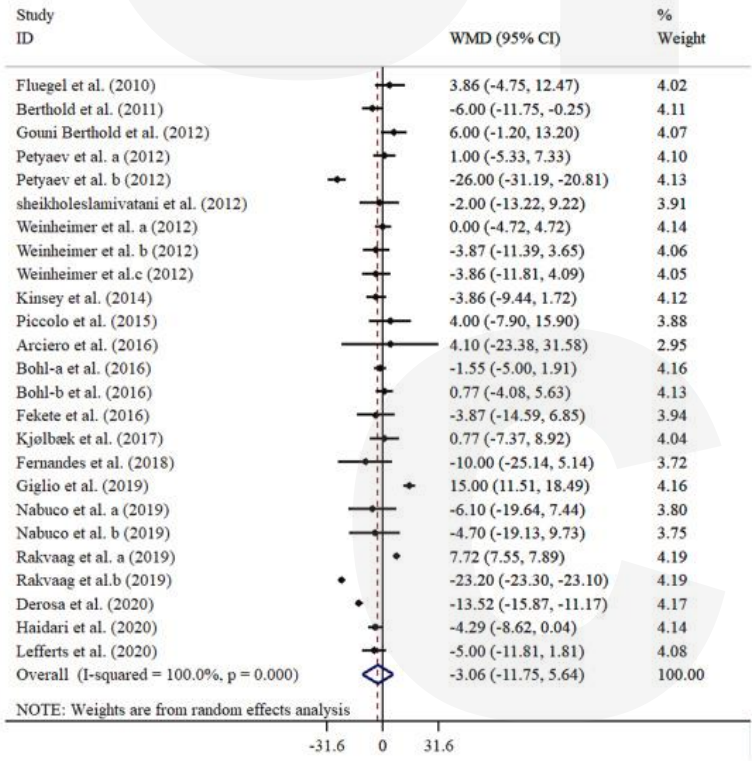


Nutr J 2020;19(1):48.

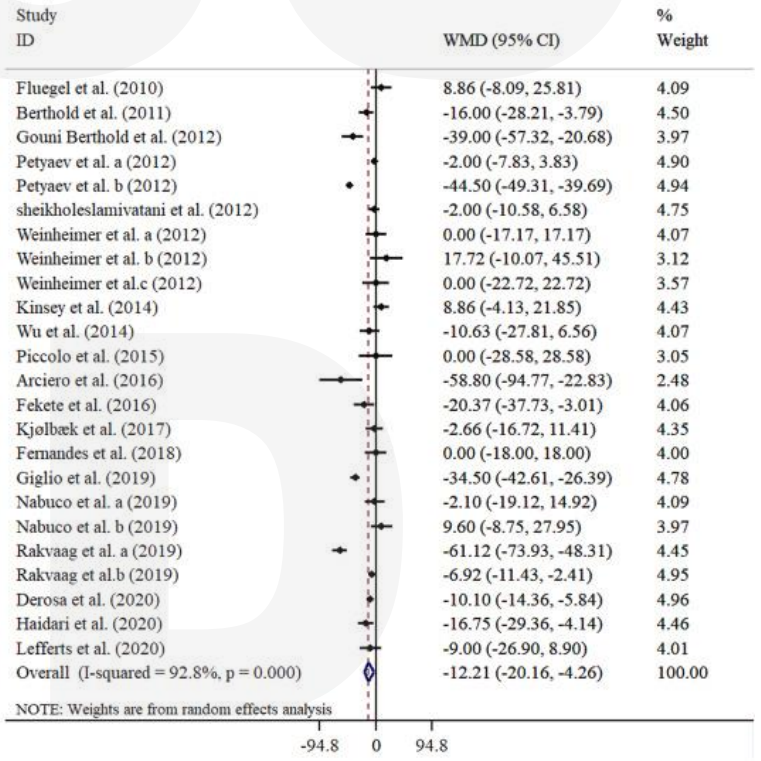
Supplement Whey Protein

121
-0
121

LDL



TGs



NMCD 2025;35(6):103858.

Exercise 

121
-9
112

Women

Variable	Base	Control	Diet	Exer	Combo
LDL	161	-3	-6	-7	-15*
Trig	159	+2	-12	-4	-10
Wt in kg	70	+1	-0.5	-3*	-3*

Men

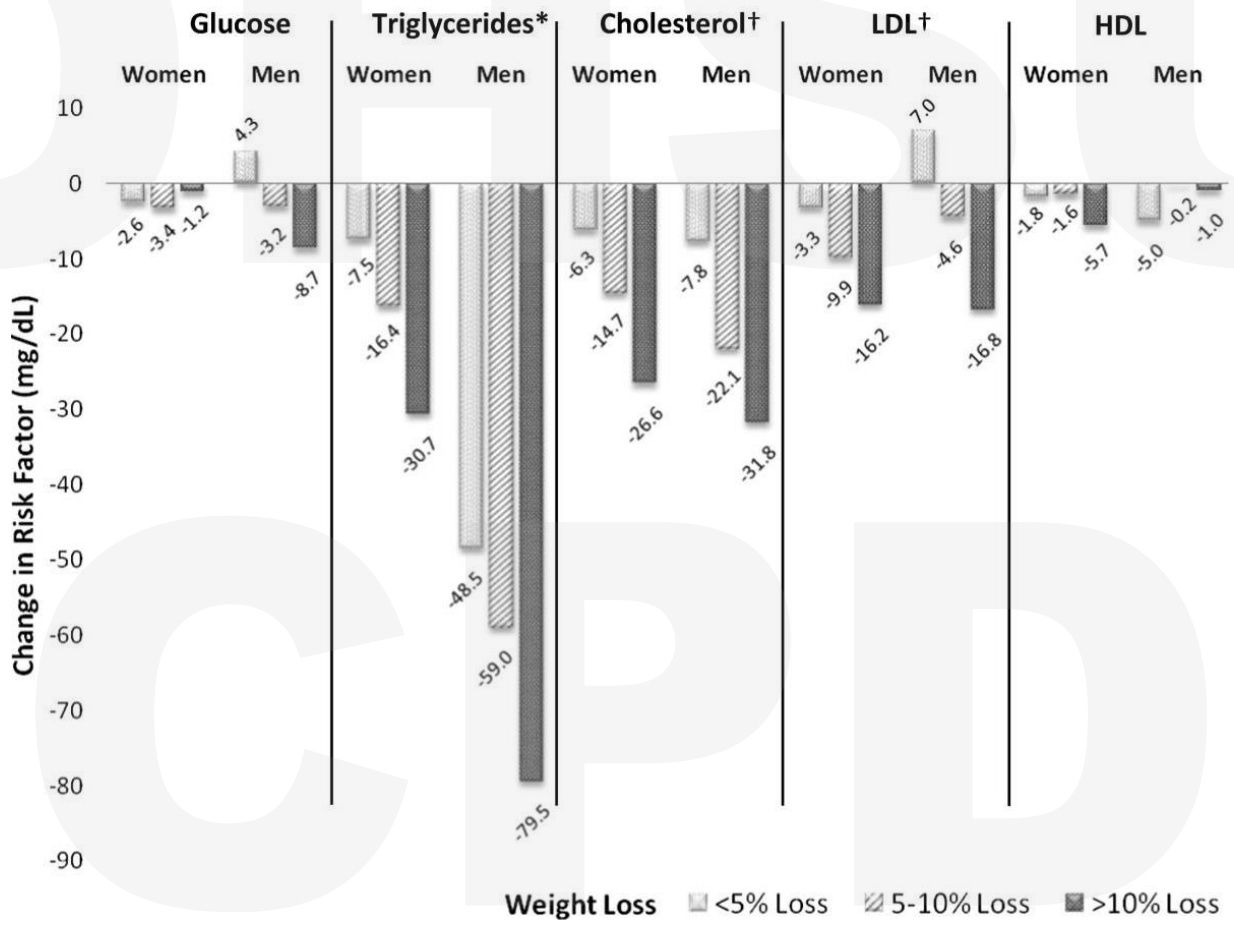
Variable	Base	Control	Diet	Exer	Combo
LDL	156	-5	-4	-11	-20*
Trig	171	+9	-14	-6	-7
Wt in kg	84	+0.5	-0.5	-3*	-4*

Key
Lipids are reported in mg/dL
* Indicates statistical significance

NEJM 1998;339:12-20.

Lose weight

112
-12
100

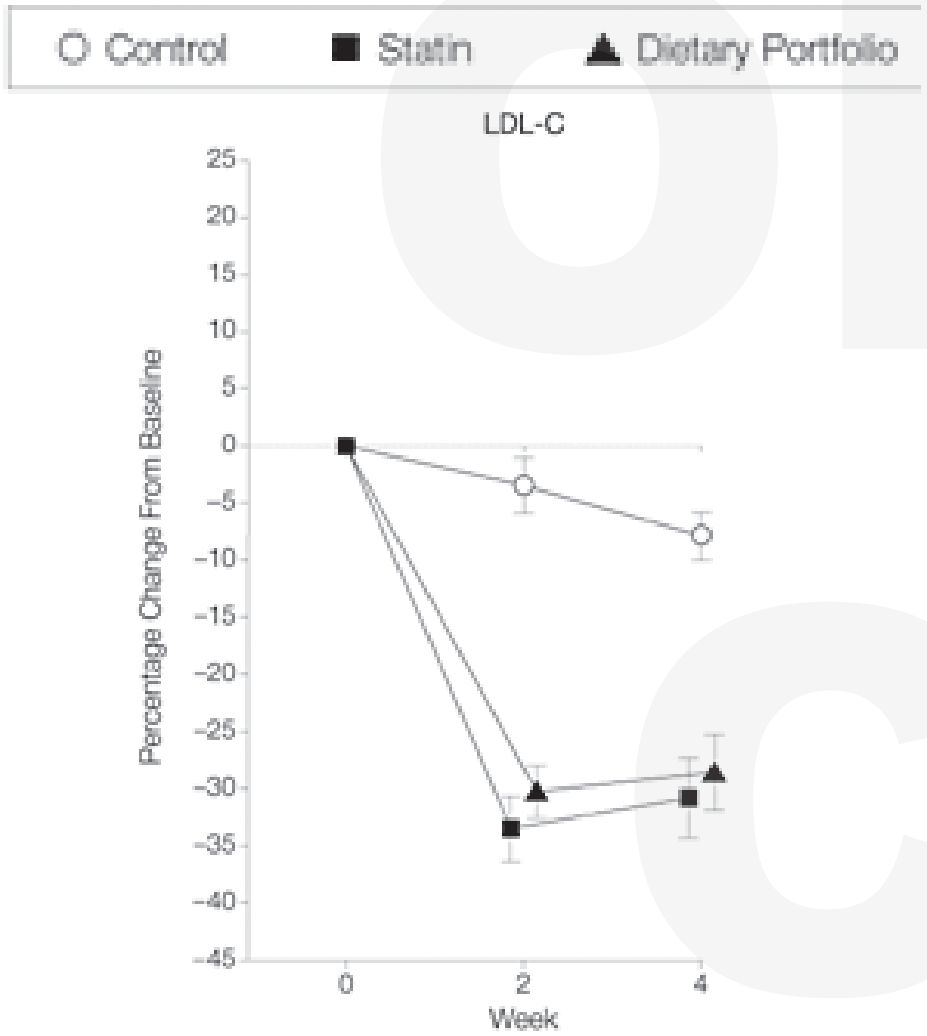


Transl Behav Med 2016;6(3):339-46.

Lifestyle interventions to lower cholesterol

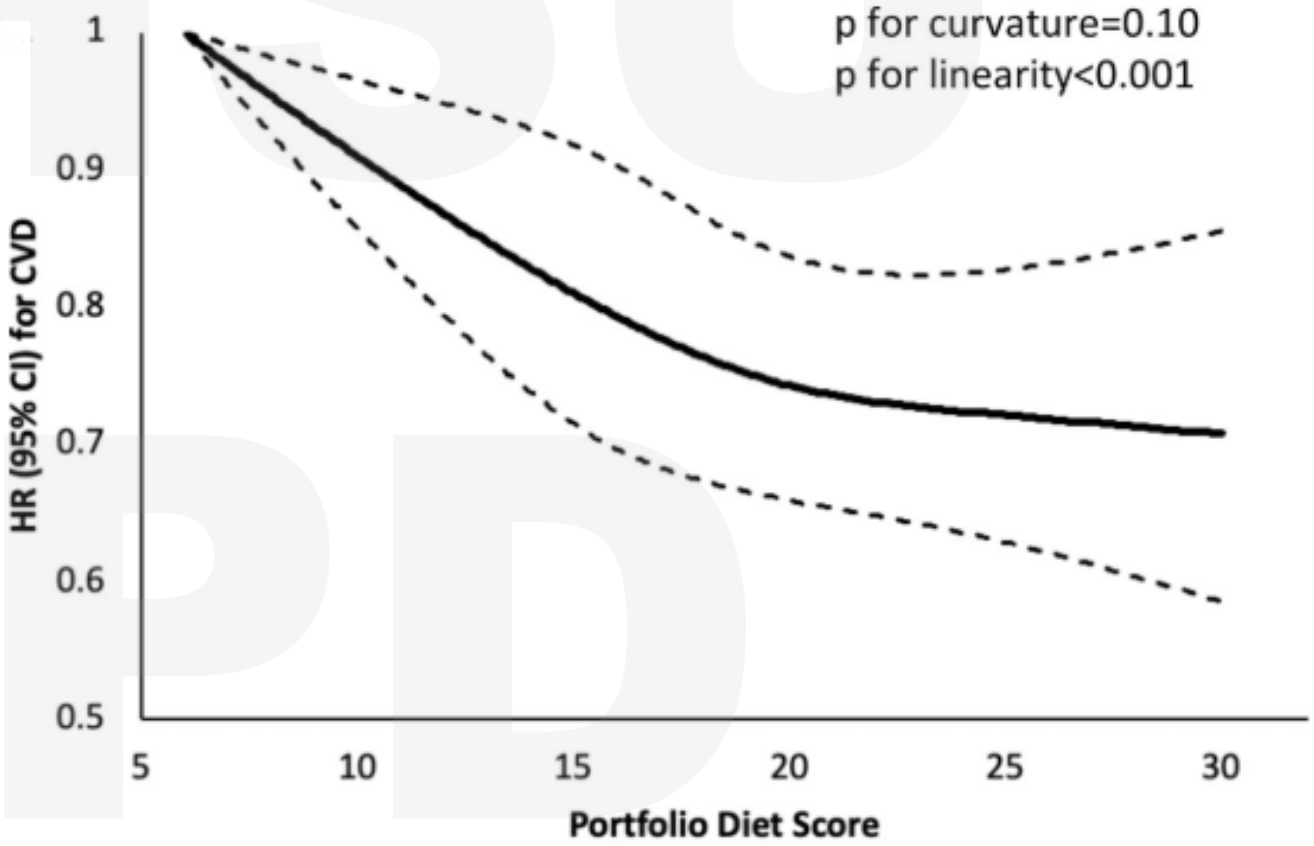
Intervention	LDL	Triglycerides
<10% of calories from sugar	-7 mg/dL	-8 mg/dL
Add Fiber (3 apples or 3 bowls of oatmeal)	-5 mg/dL	NS
Supplement Fiber (psyllium powder 2.4 g TID)	-10 mg/dL	NS
Replace ½ of your TFAs (10%→5%)	-10 mg/dL	NS
Cut out 2 alcoholic drinks/day	NS	-5 mg/dL
Drink 2 cups green tea/day	-5 mg/dL	NS
Whey protein	NS	-12 mg/dL
Exercise	-9 mg/dL	-5 mg/dL
Lose 10% of body weight	-12 mg/dL	-30 mg/dL
	-60 mg/dL	-60 mg/dL

Portfolio Diet



JAMA 2003;290(4):502-10.

Dose-Response relationship of Portfolio Diet Score with CVD



AHA 2023;148(22):1750-63

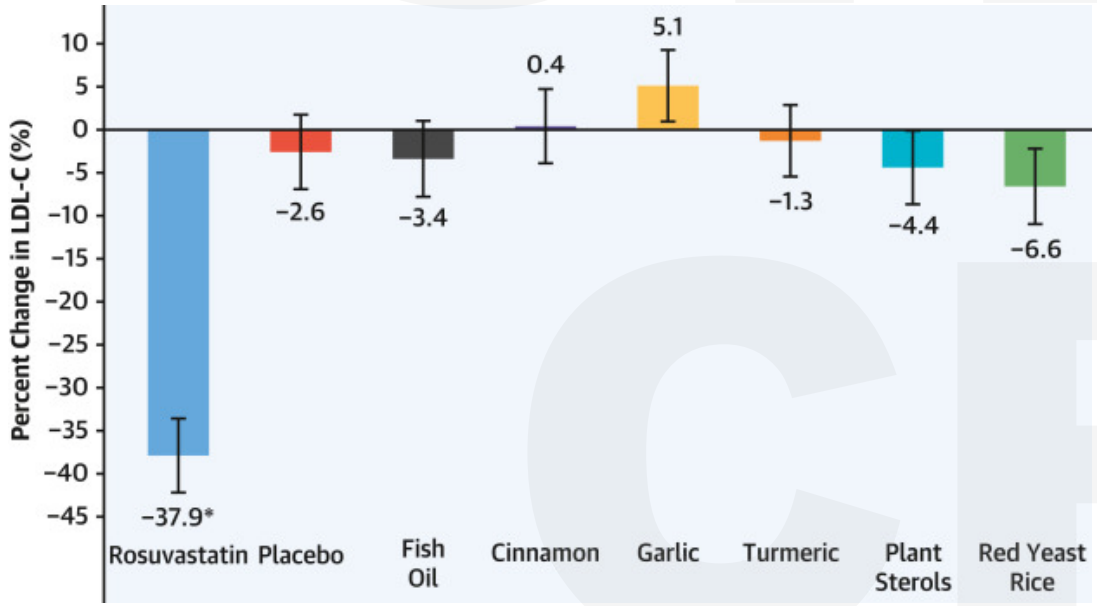
Case 1

Our 64 year-old comes back for follow-up 3 month later. He is following a healthy diet and exercises at least 150 minutes a week. Scale is down about 15 pounds and he is excited to review his lab results: LDL 160→117 & triglycerides 188→140. Still reluctant to start statins. He's interested in supplements and "alternatives to Western medicine" to treat his CAD.

- What do you tell him?

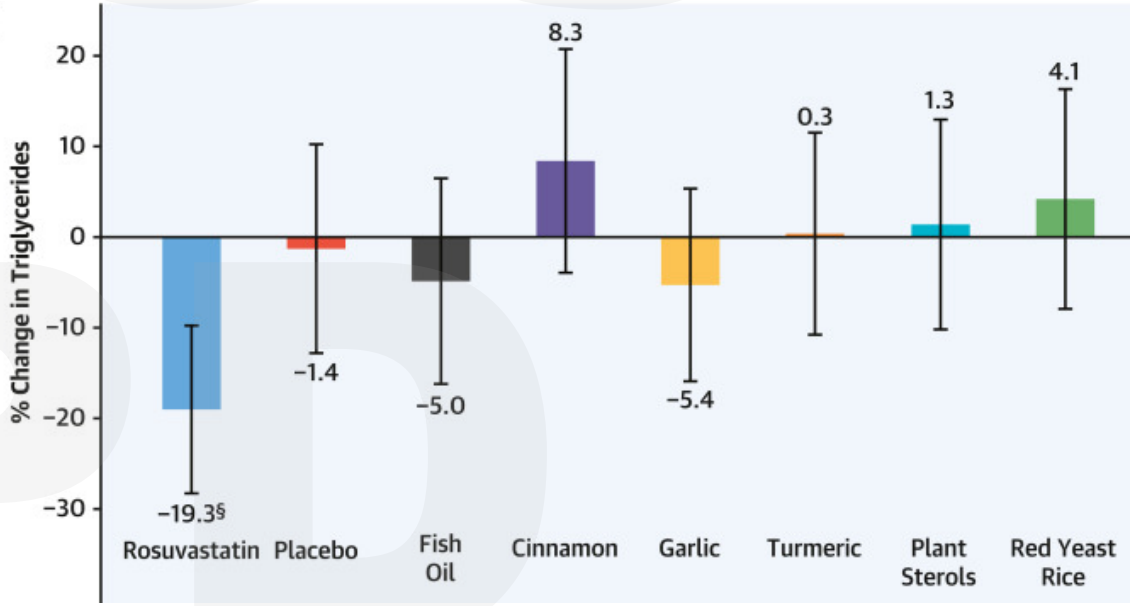
SPORT – Rosuvastatin v. Supplements

LDL



Δmg/dL	-49	-3	-4	+1	+7	-2	-6	-8

Triglycerides



Δmg/dL	-17	-1	-4	+7	-5	0	+1	+4

JACC 2023;81(3):1-12

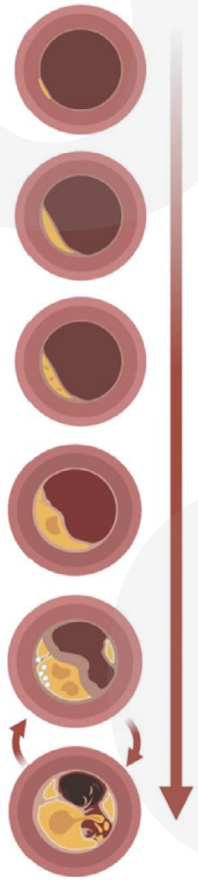
Case 1

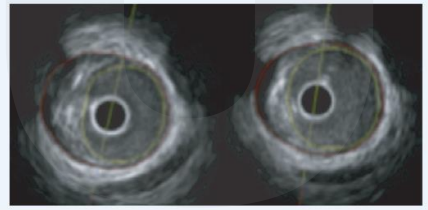
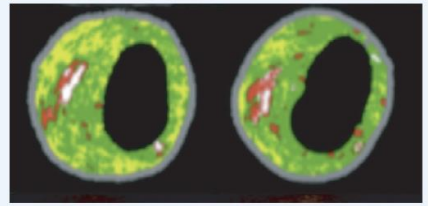
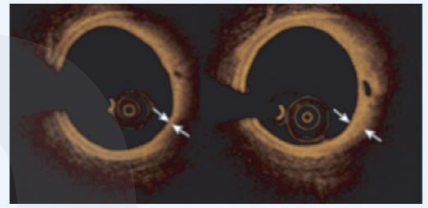
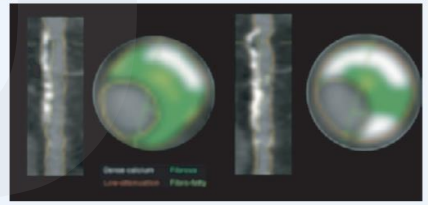
Our 64 year-old comes back for follow-up 3 months later. He is following a healthy diet and exercises at least 150 minutes a week. Scale is down about 15 pounds and he is excited to review his lab results: LDL 160→117 & triglycerides 188→140. After your discussion he is willing to "give statins a try" if they can reverse his coronary artery disease.

- What do you tell him?

Plaque definitions & imaging modalities

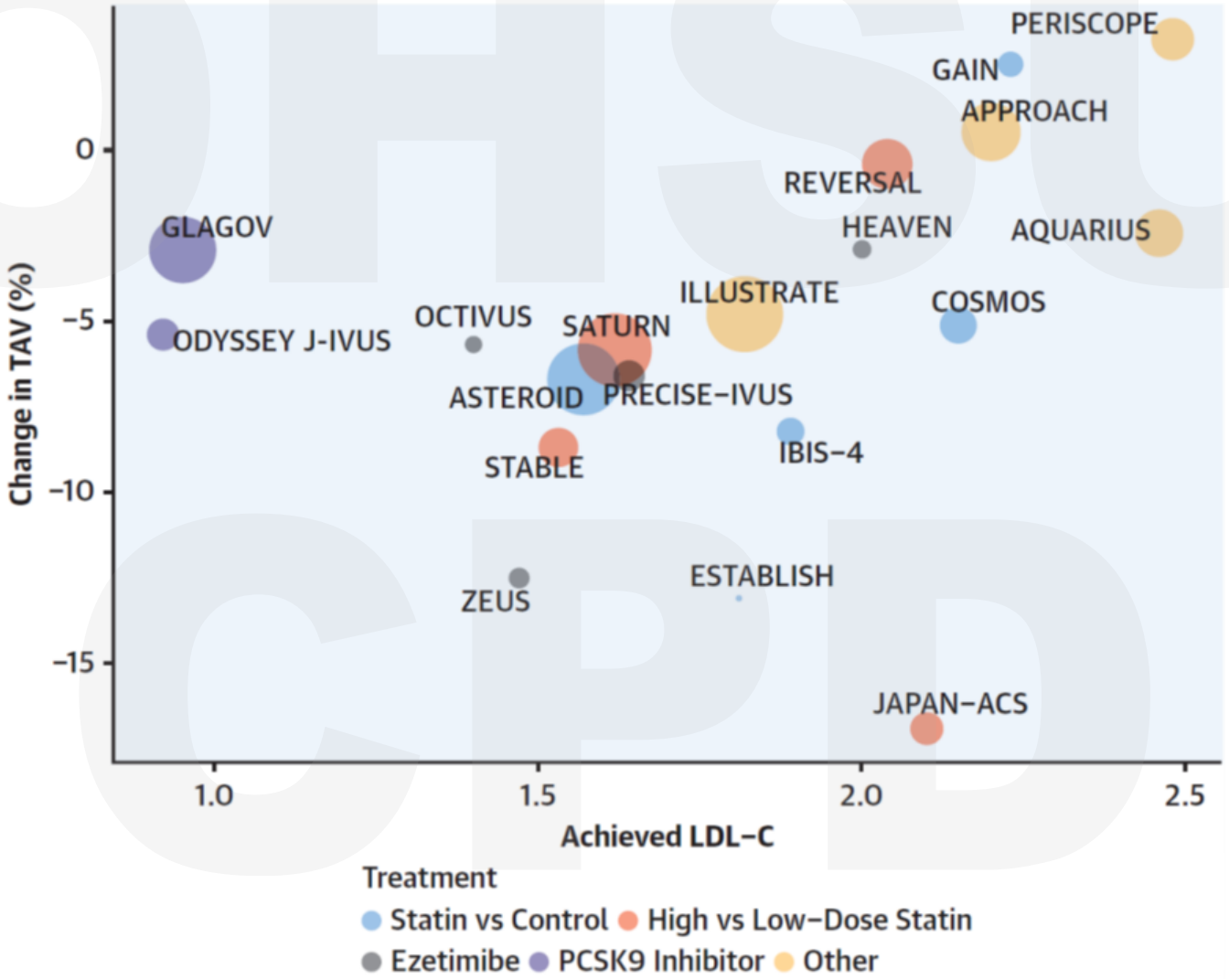
Term	Definition
Type I Initial lesion	Isolated macrophage foam cells
Type II Fatty streak	Mainly intracellular lipid accumulation
Type III Intermediate lesion	Fatty streak plus small extracellular lipid pools
Type IV Atheroma lesion	Fatty streak and core of extracellular lipid
Type V Fibroatheroma lesion	Lipid core and fibrotic layer, or multiple lipid cores and fibrotic layer; or mainly calcific, or mainly fibrotic
Type VI Complicated lesion	Surface defect, hematoma-hemorrhage, thrombus



Modality	Baseline	Follow-Up
IVUS		
VH-IVUS		
OCT		
CCTA		

JACC 2022;79(1):66-82.

Coronary atherosclerotic plaque regression



JACC 2022;79(1):66-82.

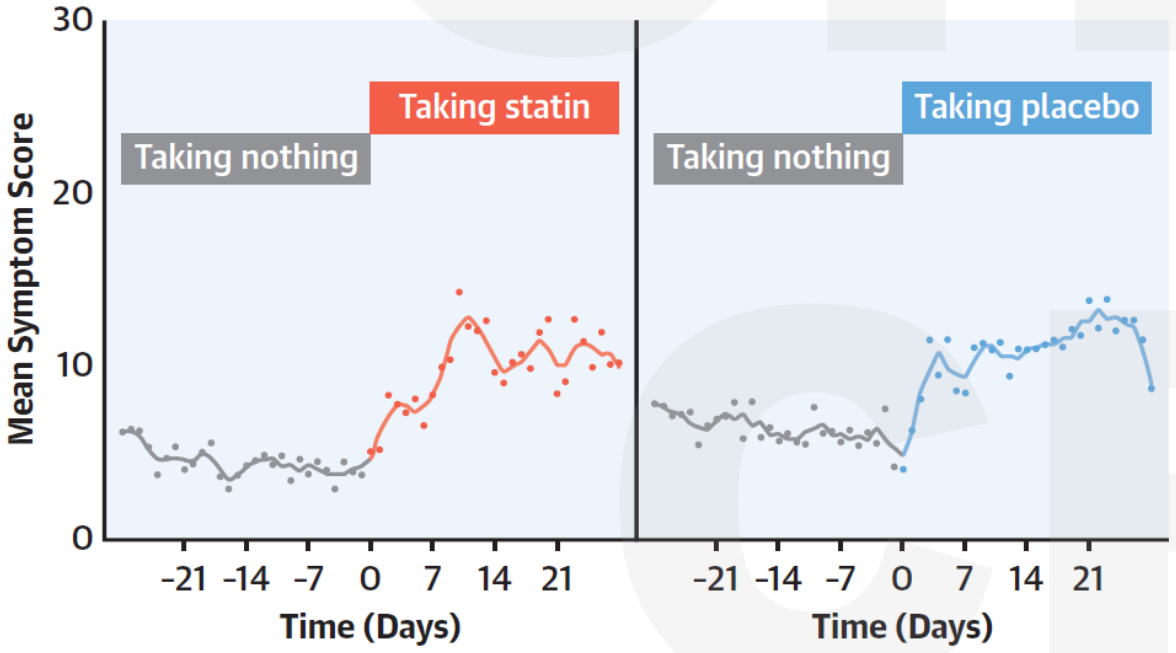
Case 1

Our 64 year-old comes back for follow-up a few months later & he continues to live a healthy lifestyle. He elected to take a statin & initial lab work following initiation of atorvastatin 40 mg daily demonstrated a further reduction in his LDL 160→117→58, but he notes he developed some muscle aches and stopped taking it a few weeks ago. The muscle aches resolved with discontinuation. Rechecking his lipids, the LDL is now back up to 120.

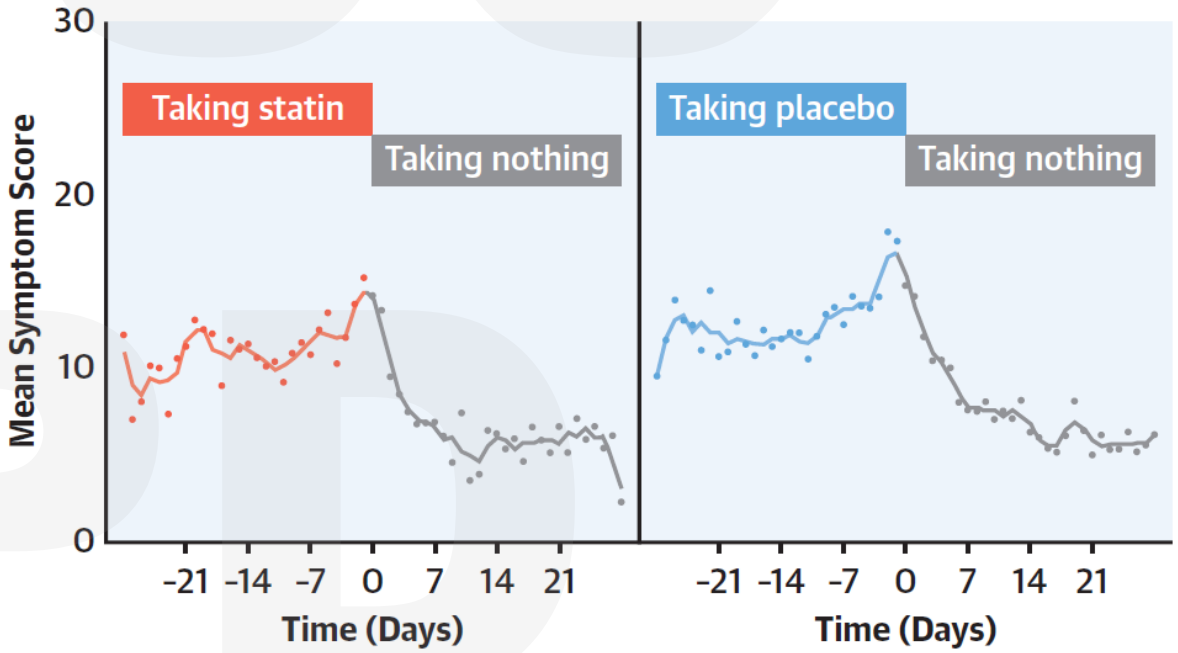
- What is your next move?

Nocebo effect

Symptom time course in days before and after *starting* tablets



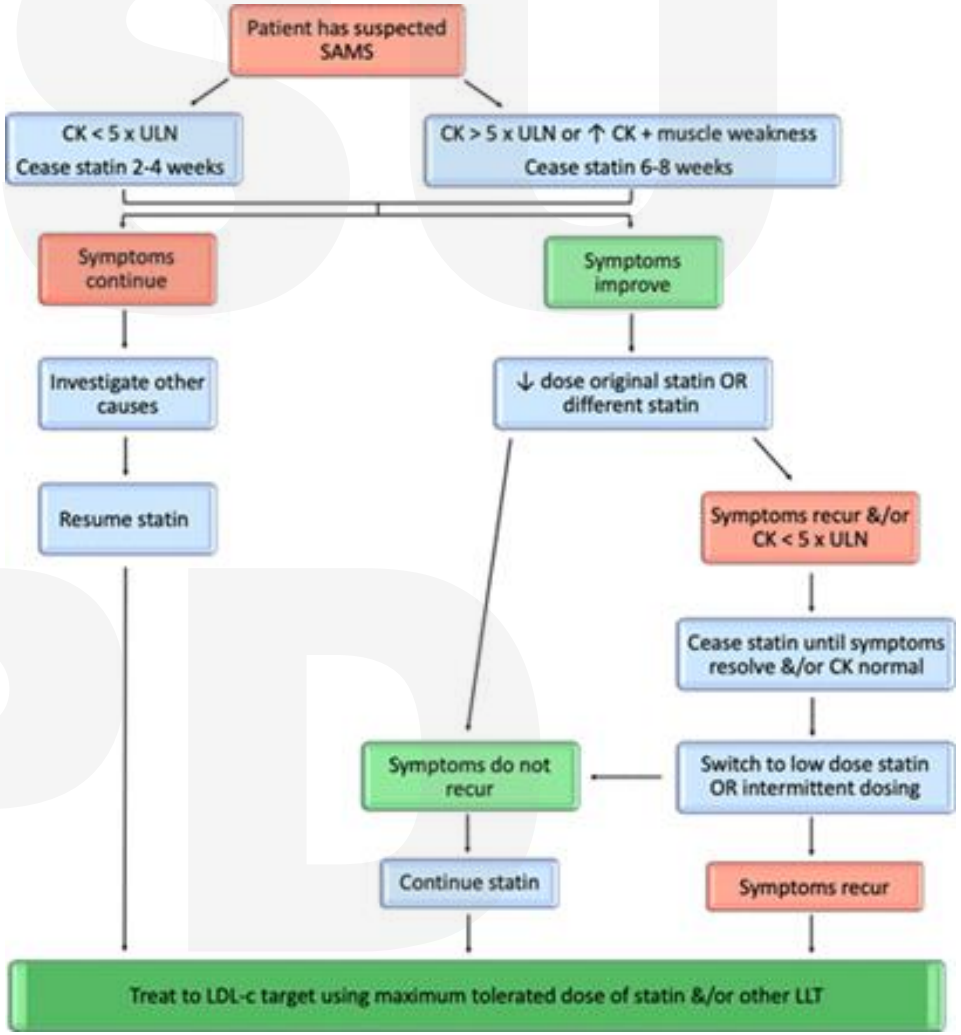
Symptom time course in days before and after *stopping* tablets



JACC 2021;78:1210-22.

Statin-Associated Muscle Symptoms (SAMS)

Clinical Symptoms	Score
Regional distribution/pattern	
Symmetrical hip flexors/thigh aches	3
Symmetrical calf aches	2
Symmetrical upper proximal aches	2
Nonspecific asymmetrical, intermittent	1
Temporal pattern	
Symptom onset <4 wk	3
Symptom onset 4–12 wk	2
Symptom onset >12 wk	1
Dechallenge	
Improves upon withdrawal <2 wk	2
Improves upon withdrawal 2–4 wk	1
Does not improve upon withdrawal >4 wk	0
Challenge	
Same symptoms reoccur upon rechallenge <4 wk	3
Same symptoms reoccur upon rechallenge 4–12 wk	1
Statin myalgia clinical index score	
Probable	9–11
Possible	7–8
Unlikely	<7



Circ Res 2019;124(2):328-50.

Estimated effects for outcomes comparing statin and placebo periods for aspects of daily life

	Mean difference, cm (99% CI), **N =152**
General activity	0.09 (−0.25 to 0.42)
Mood	0.26 (−0.04 to 0.56)
Ability to walk	0.11 (−0.22 to 0.43)
Normal work	0.15 (−0.17 to 0.46)
Relationships with other people	0.15 (−0.09 to 0.39)
Sleep	−0.02 (−0.32 to 0.29)
Enjoyment of life	0.13 (−0.22 to 0.48)

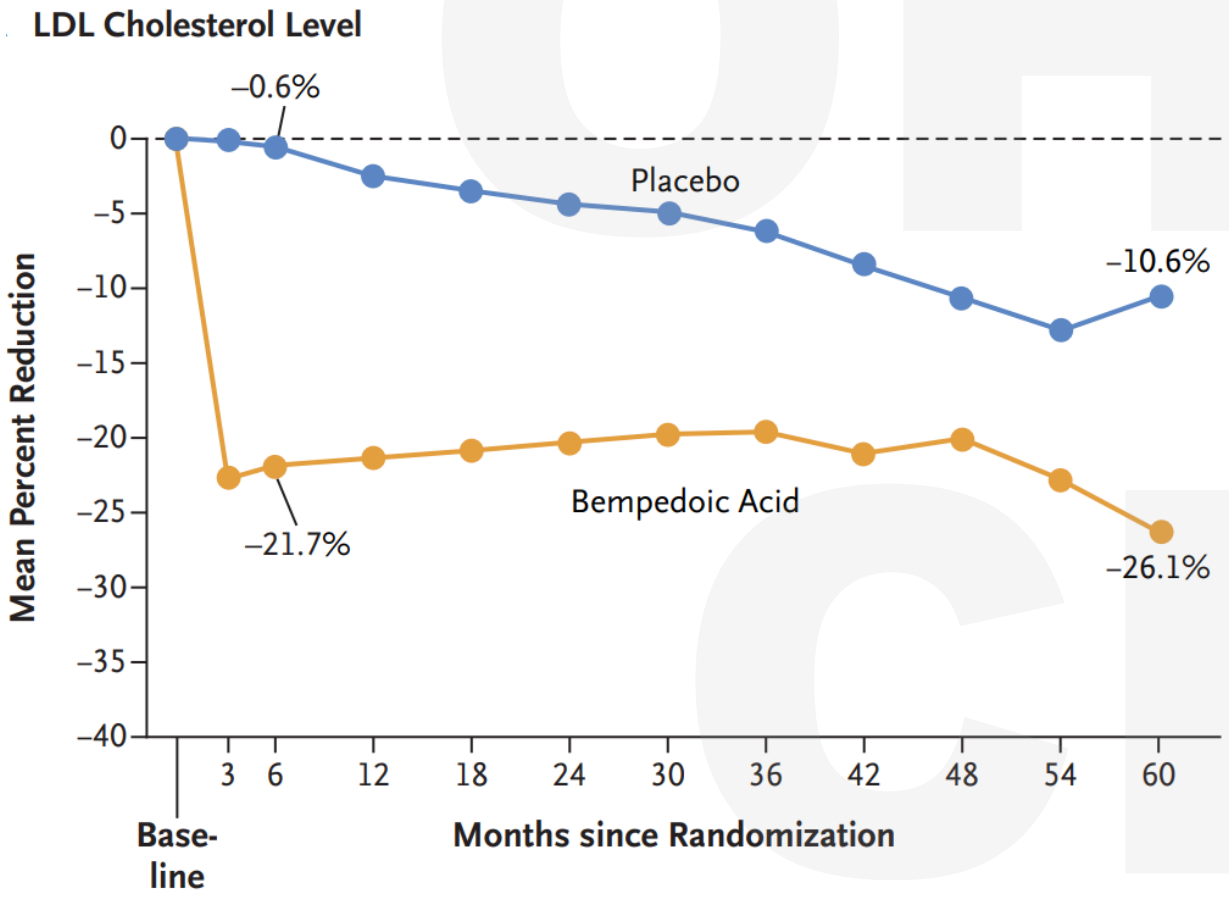
BMJ 2021;372:n135

With SAMS…can supplements help?

- Coenzyme Q10: maybe effective…it's safe to try 200 mg daily
- Vitamin D: correct the deficiency…a supplement is probably fine
- Magnesium: no demonstrated benefit ensure it's in the normal range…a supplement is probably fine

J Nutr Sci 2025;10(14):e72
JAMA Cardiol 2023;8(1):74-80
Curr Issues Mol Biol 2023;45(4):3146-67

CLEAR Outcomes: Bempedoic Acid (ATP citrate lysase inhibitor)



Outcome	Bempedoic Acid	Placebo	Difference (95% CI)	P value
MACE	11.7%	13.3%	0.87 (0.79-0.96	0.004
Death (CV)	3.8%	3.7%	1.04 (0.88-1.24)	
MI	3.7%	4.8%	0.77 (0.66-0.91)	0.002
Stroke	1.9%	2.3%	0.85 (0.67-1.07)	0.16
CABG/PCI	6.2%	7.6%	0.81 (0.72-0.92)	0.001
Death (any)	6.2%	6.0%	1.03 (0.90-1.18)	

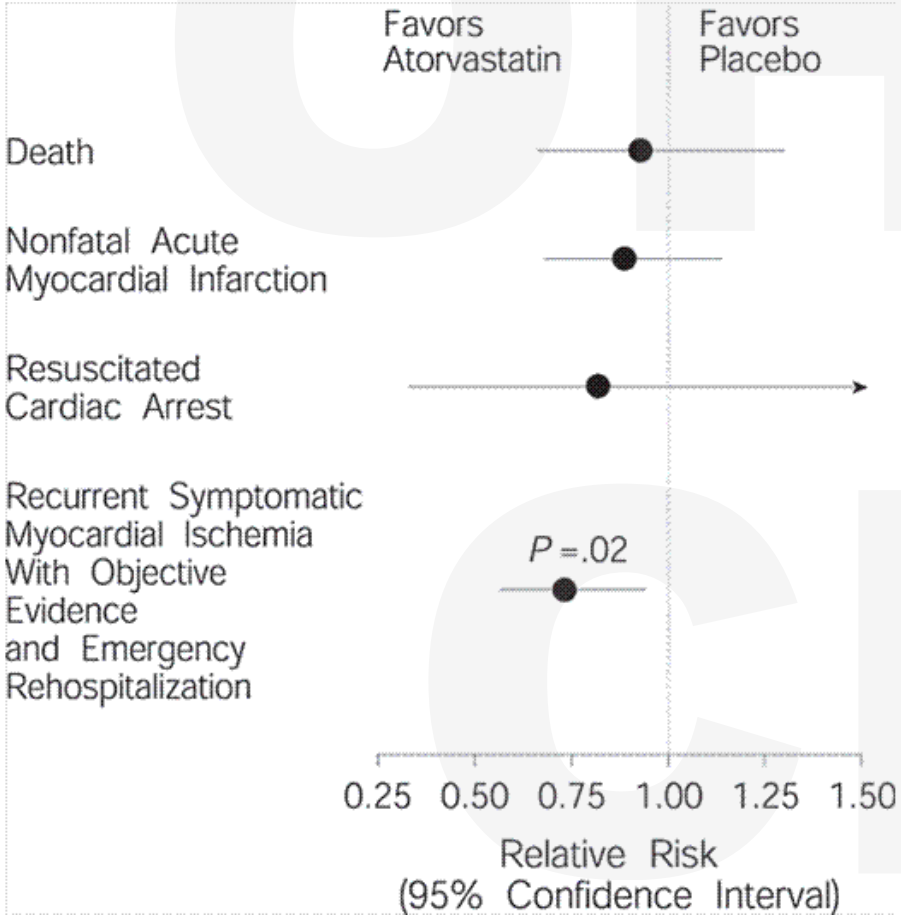
NEJM 2023;388:1353-1364

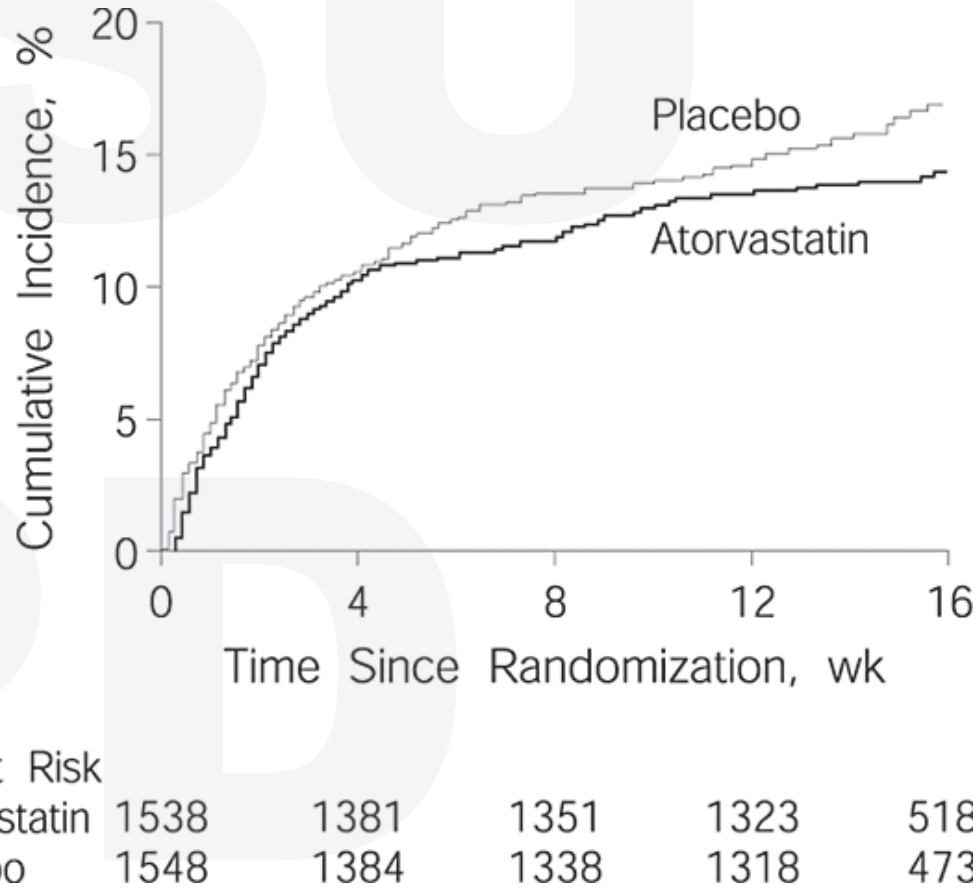
Case 2

A 54 year-old female veteran with a history of premature coronary artery disease and PCI to the RCA several years ago presents to establish care. She eats a healthy diet and exercises regularly. BP 128/78 mmHg. Benign exam. Current meds: aspirin 81 mg daily, lisinopril 5 mg daily, and atorvastatin 20 mg daily. Chemistry panel & CBC are WNL. HBA1C 5.0%. No recent lipid panel.

- Should you increase her statin?
- Would you check her lipid panel first?

MIRACL: Statins for 2^{o} Prevention





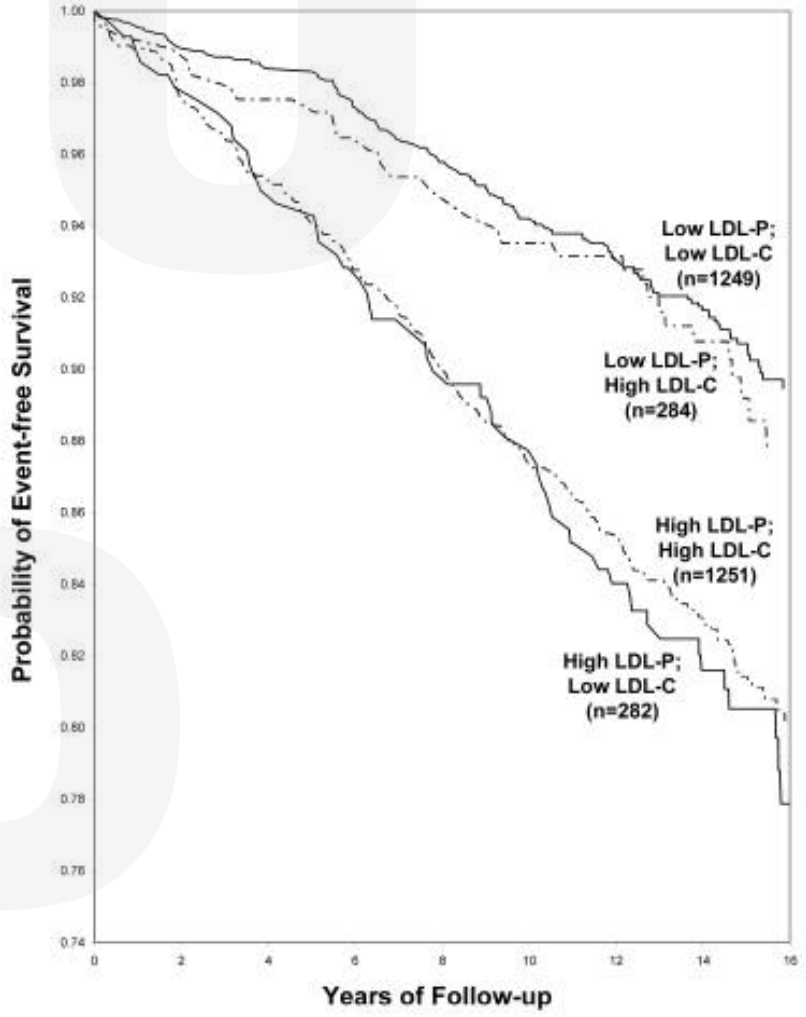
JAMA 2001;2859(13):1711-18.

Risk tracks with particle number

Age and Gender Adjusted Incidence of CVD by Quartile of Atherogenic Lipoprotein

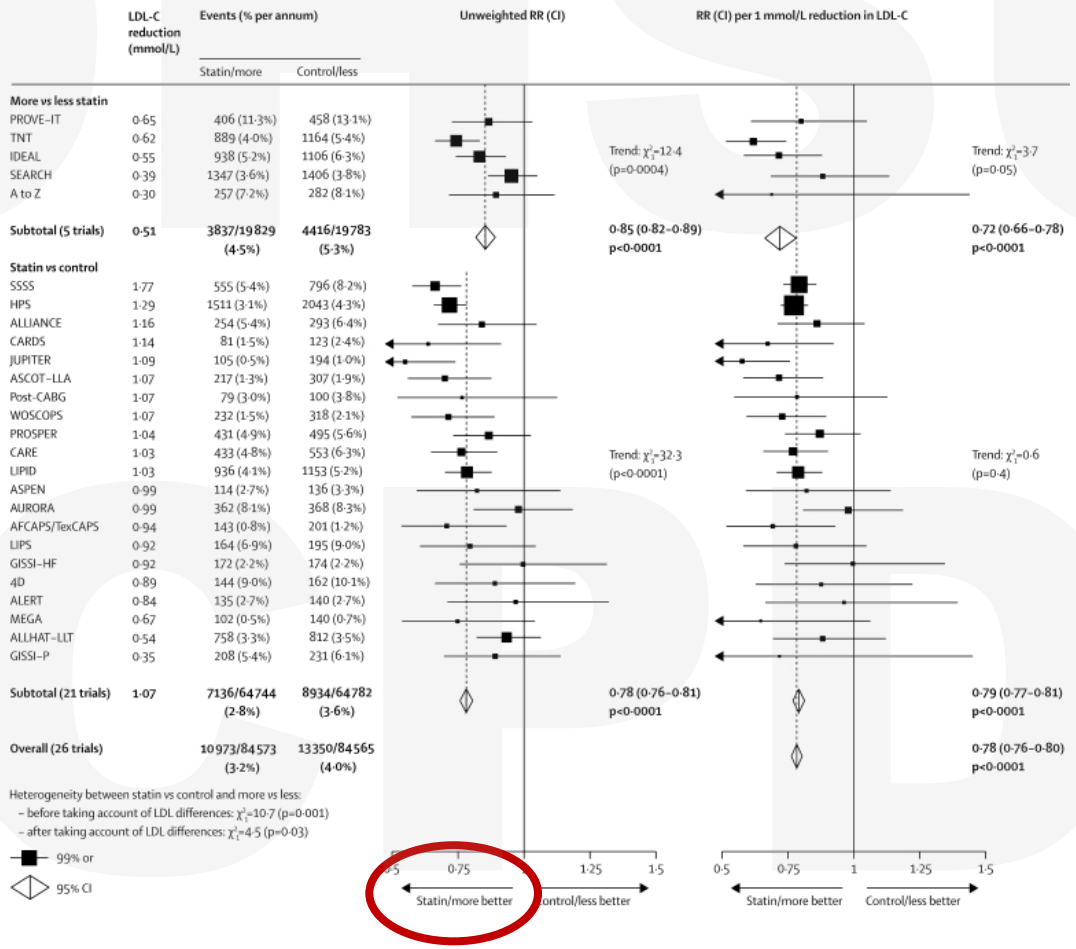
		Quartile 1	Quartile 2	Quartile 3	Quartile 4
LDL-C	Median	92	118	142	170
	# events	75	100	114	142
	CVD rate/1000 person years	81	86	88	119
LDL-P	Median	967	1279	1548	1931
	# events	55	109	101	166
	CVD rate/1000 person years	59	89	81	139

Event-free survival



J Clin Lipidol 2007;1(6):583-92.

For secondary prevention use *at least* a moderate-dose statin



Lancet 2010;376(9753):1670-81.

Sidebar: Drug Doses

Drug	Metabolism	Moderate-dose (mg)	High-dose (mg)
Rosuvastatin	CYP2C9/CYP2C19 (minor)	5-10	20-40
Atorvastatin	CYP3A4	10-20	40-80
Lovastatin	CYP3A4	40-80	NA
Simvastatin	CYP3A4	20-40	NA
Fluvastatin	CYP2C9	80 (XL) or 40 BID	NA
Pravastatin	Glucuronidation	40-80	NA
Pitavastatin	Glucoronidation, CYP2C9 & CYP3A4 (minor)	1-4	NA

For secondary prevention in higher risk patients offer risk/benefit discussion for high intensity

- Increased incidence of new onset diabetes
- Abnormal LFTs twice as common
- High doses statins are “less well tolerated”
- No increased risk of dementia
- No increased risk of CK elevation or rhabdomyolysis
- No effect on cancer

Case 2

A 54 year-old female veteran with a history of premature CAD and PCI. Lipid panel on atorvastatin 20 mg daily:

- total cholesterol 253 mg/dL
- LDL 160 mg/dL
- HDL 84 mg/dL
- triglycerides 240 mg/dL

She agrees to intensify therapy to atorvastatin 40 mg daily following risk-benefit discussion.

Case 2

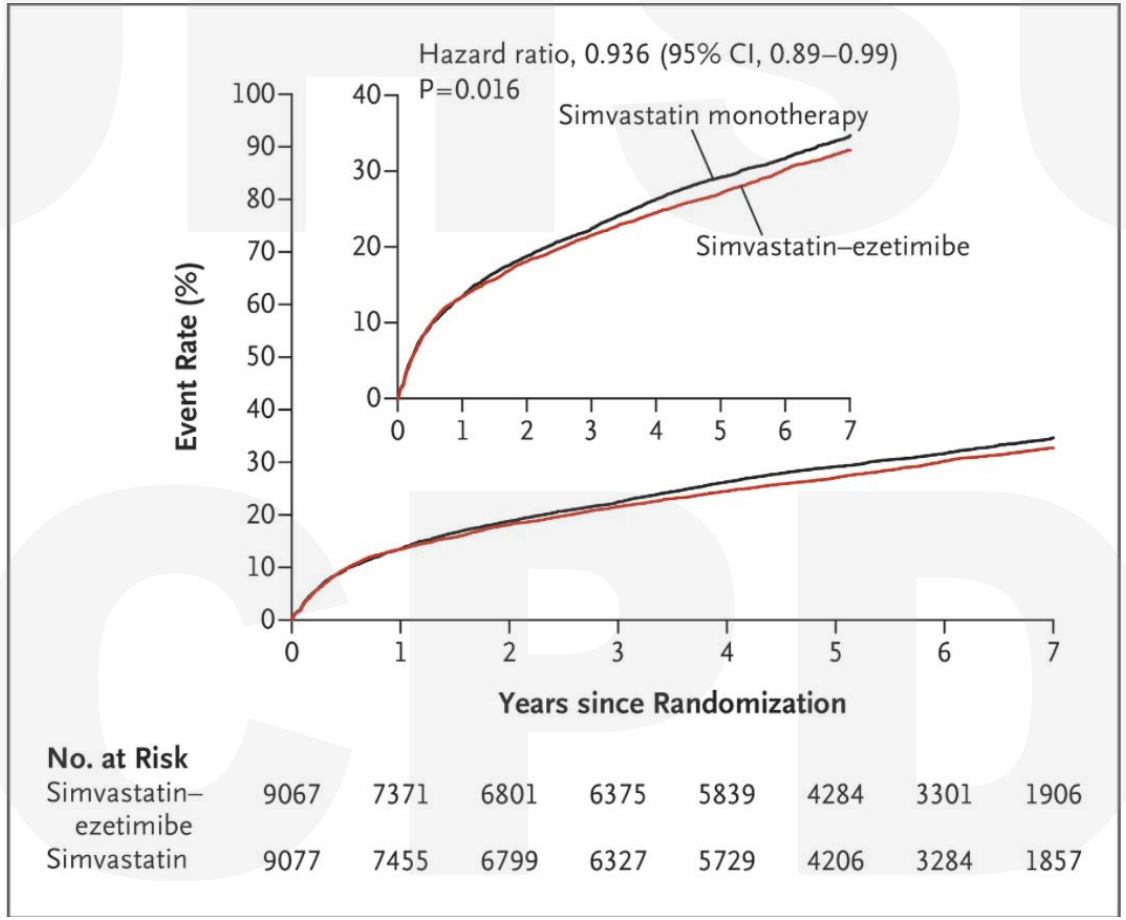
A 54 year-old female veteran with a history of premature CAD and PCI. Lipid panel after 10 weeks on atorva 40 mg daily:

- total cholesterol 253 → 220 mg/dL
- LDL 160 → 106 mg/dL
- HDL 84 → 98 mg/dL
- triglycerides 240 →194 mg/dL.

Patient c/o occasional myalagias & declines additional statin titration.

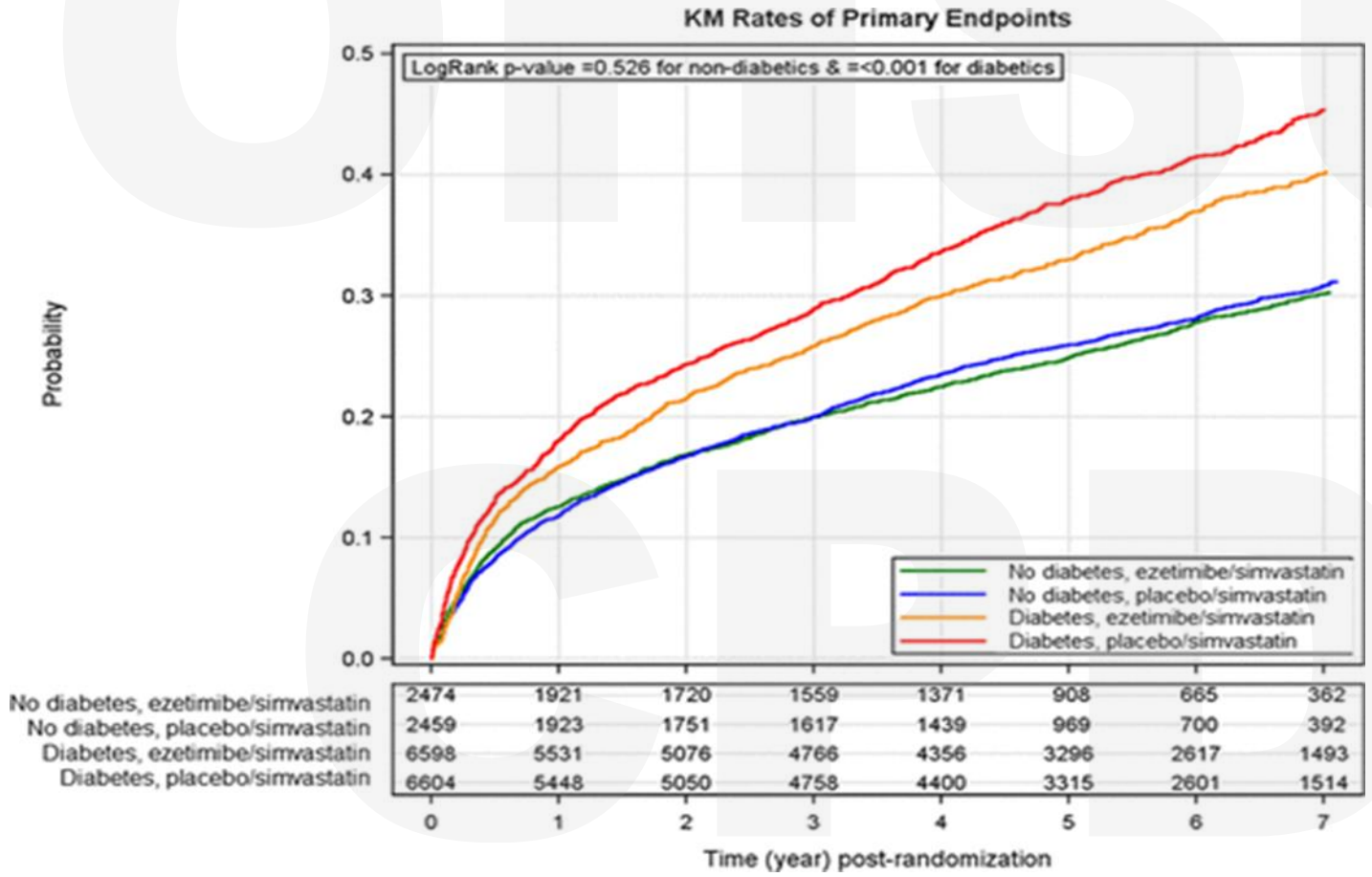
- What else can you offer?

IMPROVE-IT: Consider addition of ezetimibe



NEJM 2015;372:2387-97.

Consider ezetimibe…especially in diabetics



Circ 2018;137(15):1571-82.

Case 2

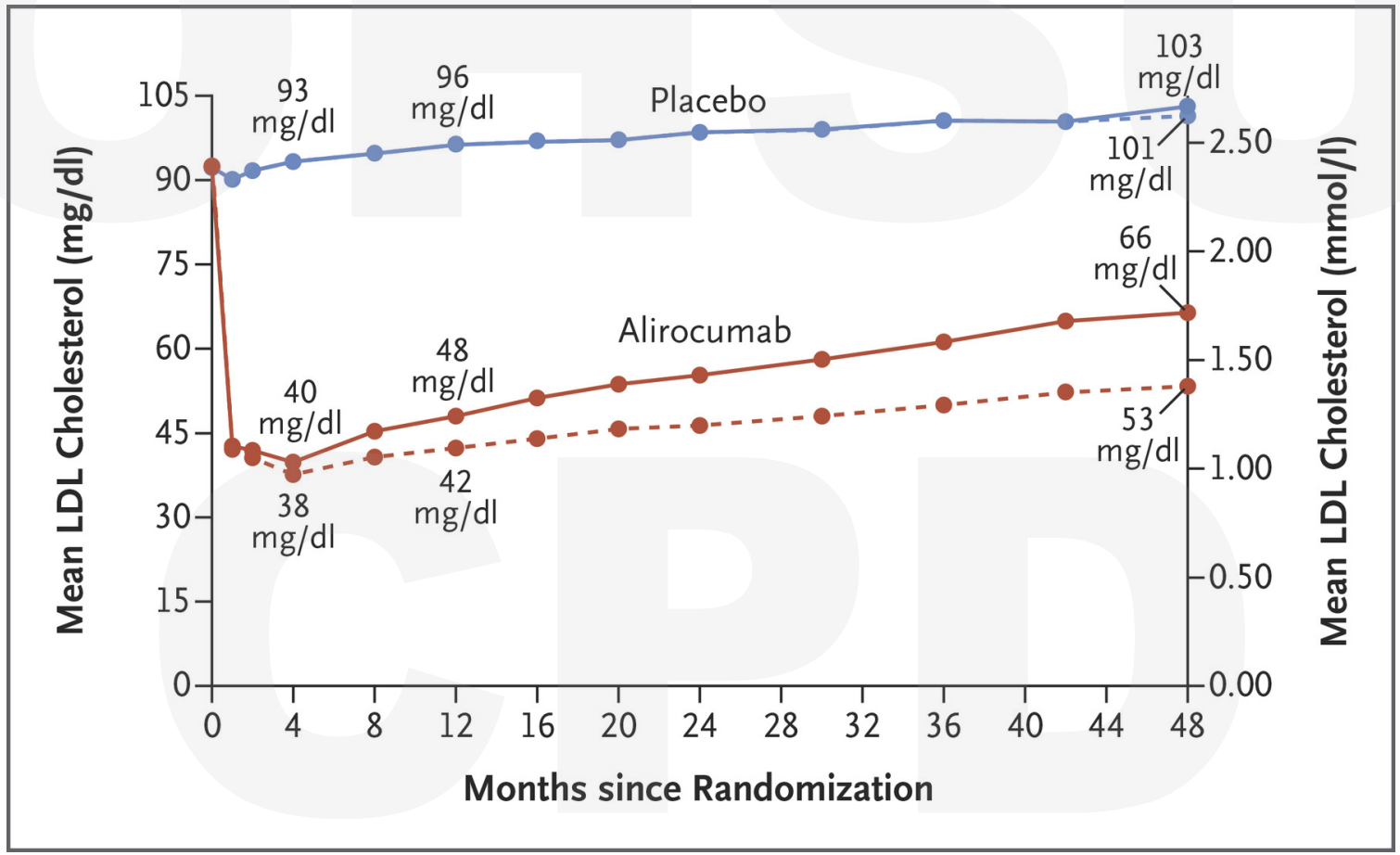
A 54 year-old female veteran with a history of premature CAD and PCI. Lipid panel after 12 weeks on atorva 40 mg daily + ezetimibe 10 mg daily:

- total cholesterol 253 → 220 →217 mg/dL
- LDL 160 → 106 →96 mg/dL
- HDL 84 → 98 → 82 mg/dL
- triglycerides 240 →194 → 206 mg/dL.

She asks is interested in further therapy.

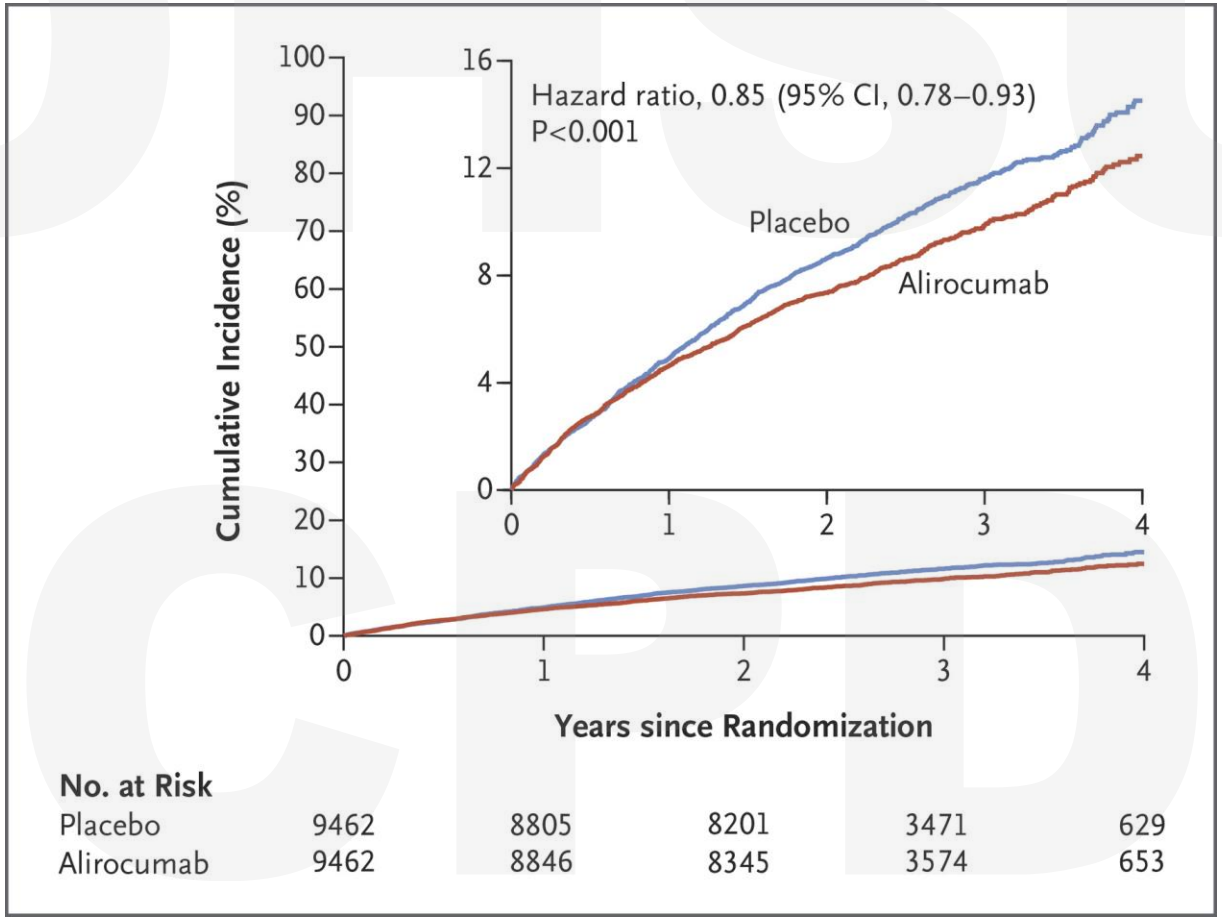
- Would you initiate PCSK9i therapy?

ODYSSEY: LDL cholesterol levels during trial



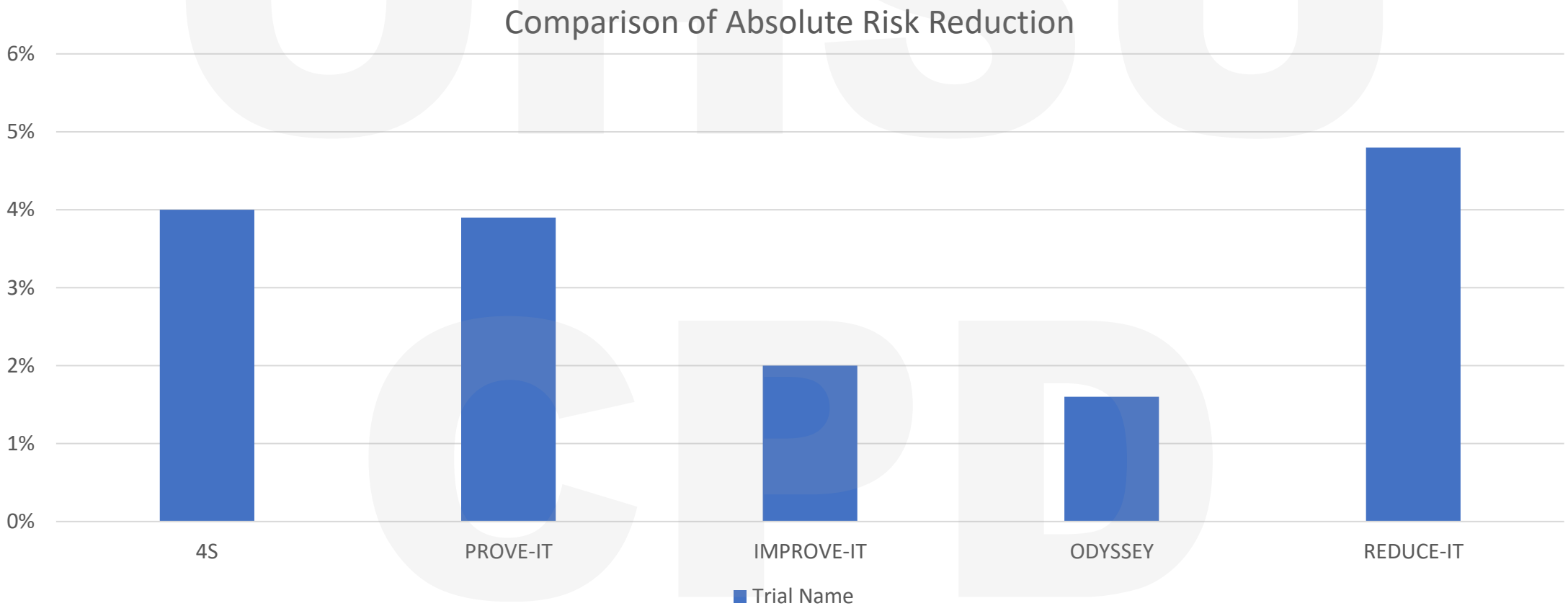
NEJM 2018;379:2097-107. JACC 2017;69(5):471-82.

ODYSSEY: Cumulative Incidence of Primary Endpoint



NEJM 2018;379:2097-107.

Secondary Prevention of MACE



Case 2

A 54 year-old female veteran with a history of premature CAD and PCI. Lipid panel after 12 weeks on atorva 40 mg daily + ezetimibe 10 mg daily:

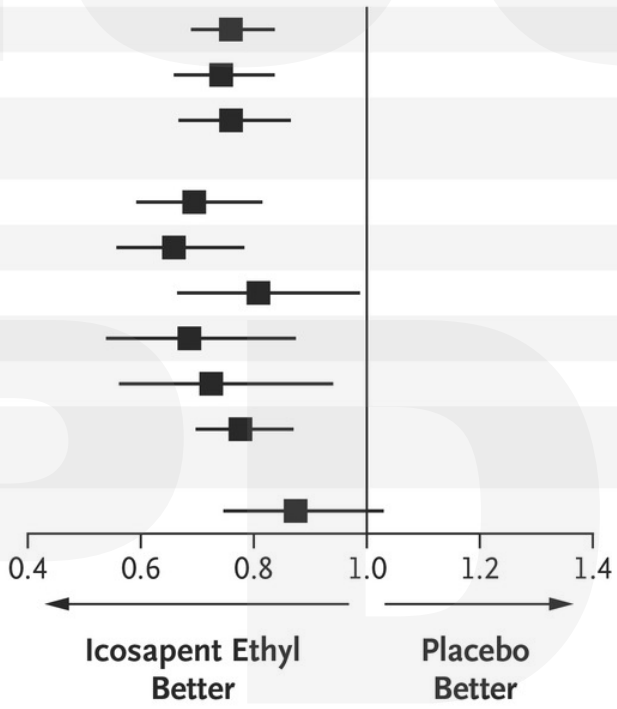
- total cholesterol 253 → 220 →217 mg/dL
- LDL 160 → 106 →96 mg/dL
- HDL 84 → 98 → 82 mg/dL
- *Fasting* triglycerides 240 →194 → **206** mg/dL.

She isn't really excited about injections, but is still interested in further therapy.

- Is there an unexplored avenue?

REDUCE-IT

End Point	Icosapent Ethyl (N=4089)	Placebo (N=4090)	Hazard Ratio (95% CI)	P Value
	no. of patients with event (%)			
Primary composite	705 (17.2)	901 (22.0)	0.75 (0.68–0.83)	<0.001
Key secondary composite	459 (11.2)	606 (14.8)	0.74 (0.65–0.83)	<0.001
Cardiovascular death or nonfatal myocardial infarction	392 (9.6)	507 (12.4)	0.75 (0.66–0.86)	<0.001
Fatal or nonfatal myocardial infarction	250 (6.1)	355 (8.7)	0.69 (0.58–0.81)	<0.001
Urgent or emergency revascularization	216 (5.3)	321 (7.8)	0.65 (0.55–0.78)	<0.001
Cardiovascular death	174 (4.3)	213 (5.2)	0.80 (0.66–0.98)	0.03
Hospitalization for unstable angina	108 (2.6)	157 (3.8)	0.68 (0.53–0.87)	0.002
Fatal or nonfatal stroke	98 (2.4)	134 (3.3)	0.72 (0.55–0.93)	0.01
Death from any cause, nonfatal myocardial infarction, or nonfatal stroke	549 (13.4)	690 (16.9)	0.77 (0.69–0.86)	<0.001
Death from any cause	274 (6.7)	310 (7.6)	0.87 (0.74–1.02)	—



NEJM 2019;380:11-22.

Causes of secondary hypertriglyceridemia

Diagnoses

- Hypothyroidism
- Uncontrolled diabetes
- Nephrotic syndrome
- Alcohol abuse
- Obesity/metabolic syndrome

Medication Induced

- Oral estrogens
- Tamoxifen
- Corticosteroids
- Thiazides
- Protease inhibitors
- Clozapine/olanzapine
- Non-cardioselective beta-blockers (except carvedilol)

Management of hypertriglyceridemia

- Moderate (fasting TG 150 to 499 mg/dL)
  1. Moderate-high potency statin
  2. Icosapent ethyl 2g BID
- Moderate to severe (fasting TG 500 to 999 mg/dL)
  1. Moderate-high potency statin
  2. Icosapent ethyl 2g BID
  3. Fenofibrate 145 mg daily
- Severe (fasting TG >1000 mg/dL)
  - Extreme dietary fat restriction, alcohol abstinence

What's next?

- Inclisiran – small interfering RNA (siRNA) that inhibits hepatic synthesis of proprotein convertase subtilisin-kexin type 9 (PCSK9)
  - Achieves a 50% reduction in LDL.
  - Currently no clinical trials document a reduction in cardiovascular events.
    - ORION-4
    - VICTORION-1-PREVENT and VICTORION-2P

Conclusion

- Diet and lifestyle remain a mainstay of lipid therapy, but…
- Frequently pharmacologic therapy is necessary.
- There are multiple anti-lipemic agents on the market including alternatives to statins
- The stepwise initiation & titration is effective at reducing cholesterol and improving ASCVD outcomes
- (Most) supplements aren’t worth the ha$$le.

Questions?

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Familial Hypercholesterolemia

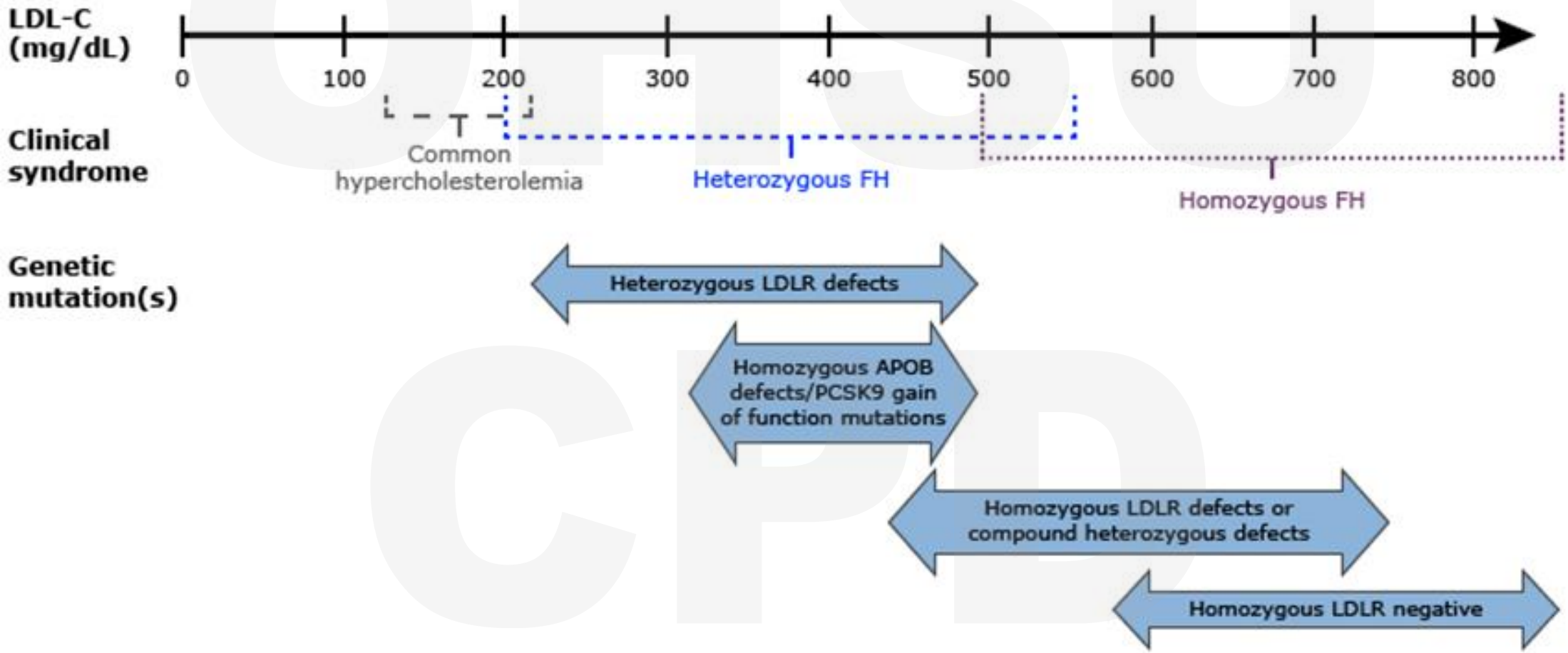
Bonus Case 2 conclusion!

Dutch Lipid Clinic Network diagnostic criteria for familial hypercholesterolemia

Criteria	Points
1) Family history	
▪ First-degree relative with known premature (men: <55 years; women: <60 years) coronary or vascular disease, or ▪ First-degree relative with known LDL-C above the 95th percentile	1
▪ First-degree relative with tendinous xanthomata and/or arcus cornealis, or ▪ Children <18 years of age with LDL-C above the 95th percentile	2
2) Clinical history	
▪ Patient with premature (men: <55 years; women: <60 years) coronary artery disease	2
▪ Patient with premature (men: <55 years; women: <60 years) cerebral or peripheral vascular disease	1
3) Physical examination	
▪ Tendinous xanthomata	6
▪ Arcus cornealis before age 45 years	4
4) LDL-C levels	
▪ LDL-C ≥8.5 mmol/L (325 mg/dL)	8
▪ LDL-C 6.5 to 8.4 mmol/L (251-325 mg/dL)	5
▪ LDL-C 5 to 6.4 mmol/L (191-250 mg/dL)	3
▪ LDL-C 4 to 4.9 mmol/L (155-190 mg/dL)	1
5) DNA analysis	
▪ Functional mutation in the LDLR, apoB, or PCSK9 gene	8
Choose only one score per group, the highest applicable diagnosis (diagnosis is based on the total number of points obtained) ▪ A "definite" FH diagnosis requires >8 points ▪ A "probable" FH diagnosis requires 6 to 8 points ▪ A "possible" FH diagnosis requires 3 to 5 points	

http://apps.who.int/iris/handle/10665/66346

Low density lipoprotein cholesterol levels and genetic mutations in familial hypercholesterolemia



Eur Heart J 2014;35:2146.

Case 2

A 54 year-old female veteran with a history of premature CAD and PCI. Assessed patient for familial hypercholesterolemia (FH):

- FHx notable for father with MI in his early 50s (1 point)
- Personal h/o premature CAD (2 points)
- Untreated LDL-C 238 mg/dL (3 points)
- Referred for genetic test (not completed)

With 6 points on the Dutch Lipid Clinic Network diagnostic criteria, she has probable FH.