

NATUROPATHIC APPROACH TO LIPIDS

STEPHEN W. PARCELL, ND

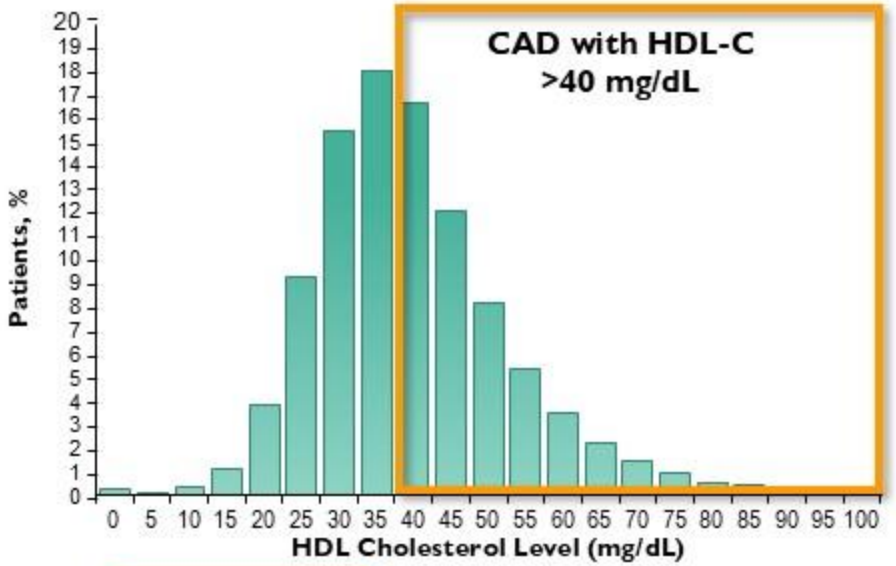
INTRO

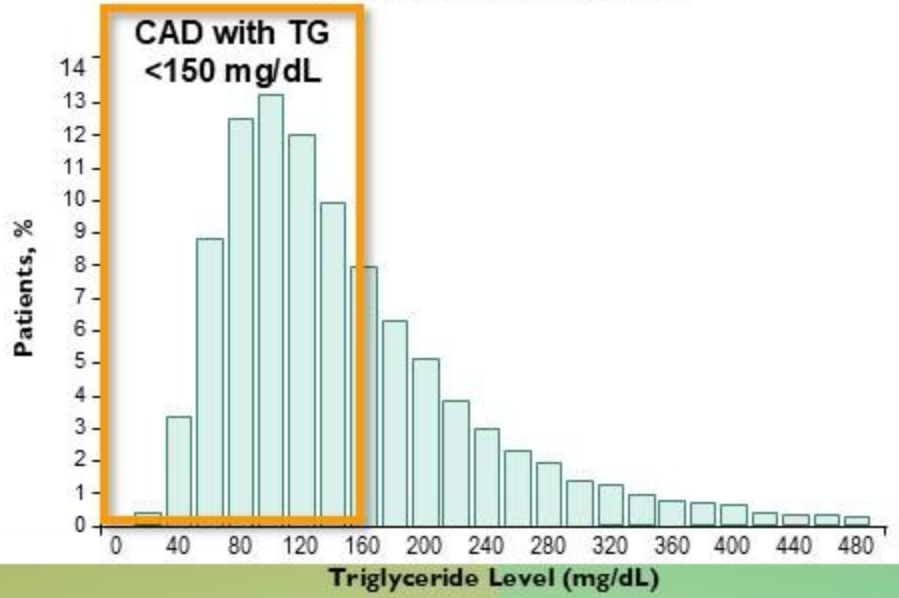
- Naturopathic doctors can do more to prevent heart attacks.
- High cholesterol accounts for ~20-30 % of CAD.
- Over 50% of patients with ACS have normal cholesterol on hospital admission.
- Lipids matter but are not the only risk factor, its an obstacle to cure!
- Doctors that claim cholesterol has no impact on atherosclerosis are wrong.
- Let's examine the role of lipids.
- Particle size, number and inflammation play a bigger role than total cholesterol of LDL/HDL ratio. Advanced testing for lipid subfractions is easy.
- Naturopathic treatment works but its not always easy compared to statin.

These Arteries Will Pass a Stress Test
4 of them can cause a heart attack



PATIENTS AT HDL AND TRIGLYCERIDE GOAL REMAIN AT RISK



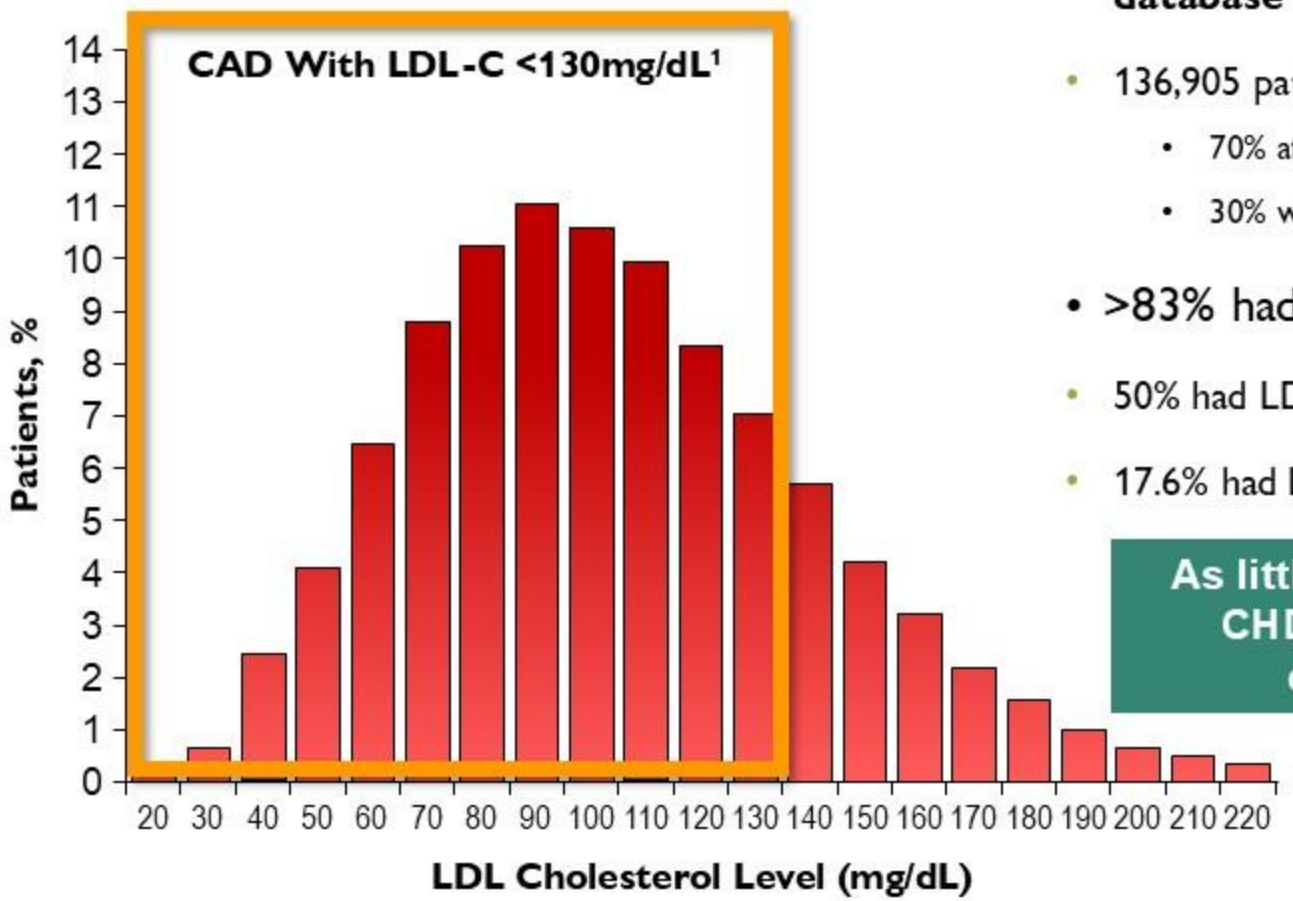


The *Get With the Guidelines* database reports:[1]

- 136,905 patients hospitalized with CAD
  - 70% after acute coronary syndrome
  - 30% chest pain (MI ruled out) and prior CAD
- ~45% had HDL-C levels >40 mg/dL
- ~70% had triglyceride levels <150mg/dL

Sachdeva A, Cannon CP, Deedwania PC, et al. *Am Heart J*. 2009;157:111-7.

PATIENTS AT GOAL FOR LDL-C STILL AT RISK…



The *Get With the Guidelines* database reports:[1]

- 136,905 patients hospitalized with CAD
  - 70% after acute coronary syndrome
  - 30% with chest pain and prior CAD
- >83% had LDL-C levels <130 mg/dL
- 50% had LDL <100 mg/dL
- 17.6% had LDL-C <70 mg/dL

As little as 25% of premature CHD was attributable to elevated LDL-C[2-4]

1. Sachdeva A, Cannon CP, Deedwania PC, et al. *Am Heart J*. 2009;157:111-7. **2.** Castelli W. *Atherosclerosis* 1996;124 Suppl:S1-9. **3.** Genest J Jr, McNamara JR, Ordovas JM, et al. *J Am Coll Cardiol*. 1992;19:792-802. **4.** Akosah KO, Schaper A, Cogbill C, Schoenfeld P. *J Am Coll Cardiol*. 2003;41:1475-9.

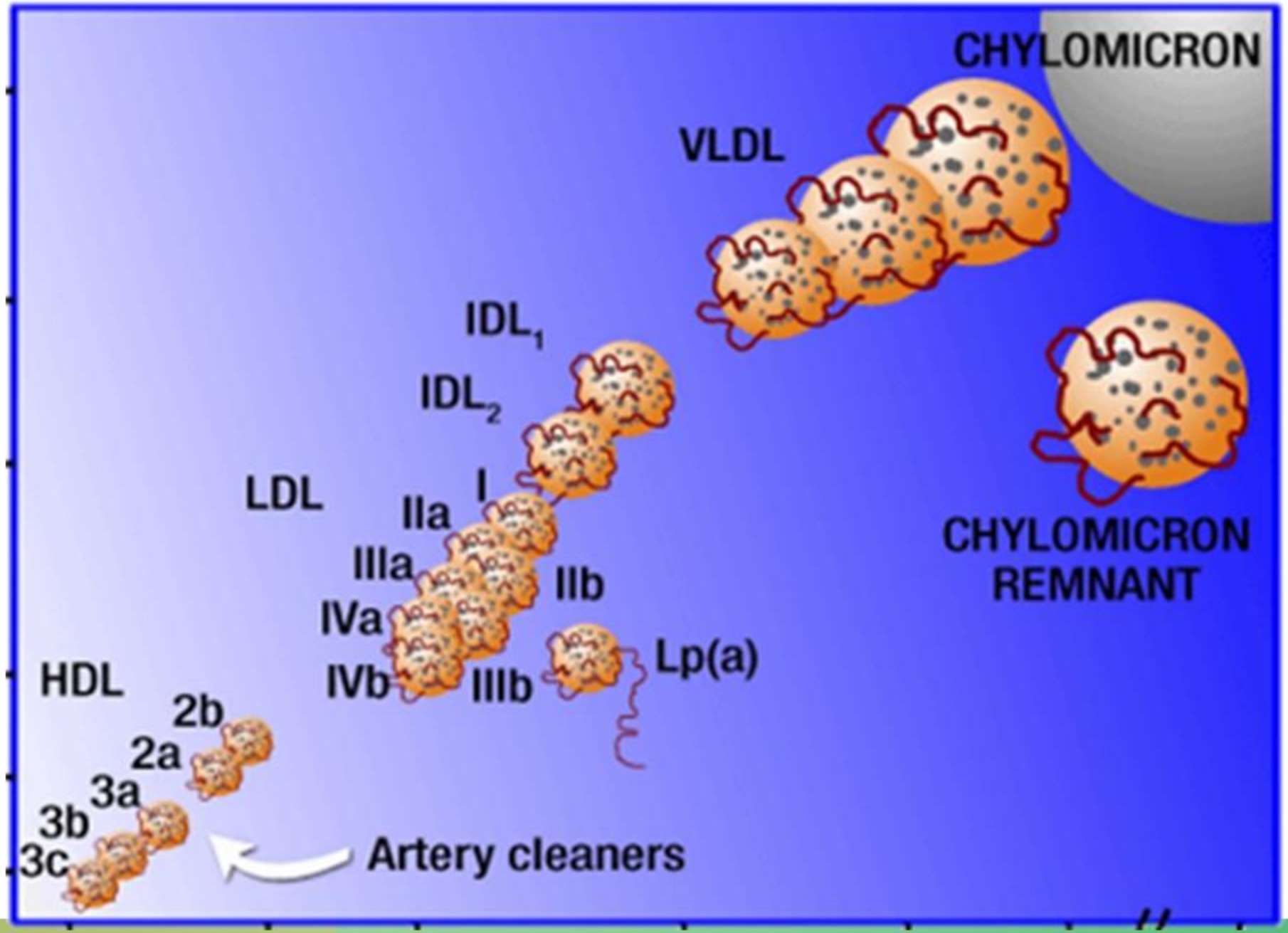
BIOMARKERS WHICH CAN BE MONITORED WITH ADVANCED TESTING HAVE BEEN SHOWN TO BE ASSOCIATED WITH AN INCREASED RISK FOR CVD

Advanced Lipoprotein Tests	Relative Risk
LDL particle number	1.4x[1]
Small LDL subclass particles	1.3x[1]
Medium LDL subclass particles	1.4x[1]
HDL subclasses	1.8x[1]
Lp(a)	1.5–5.3x[2]
ApoB	2.0–2.5x[3]

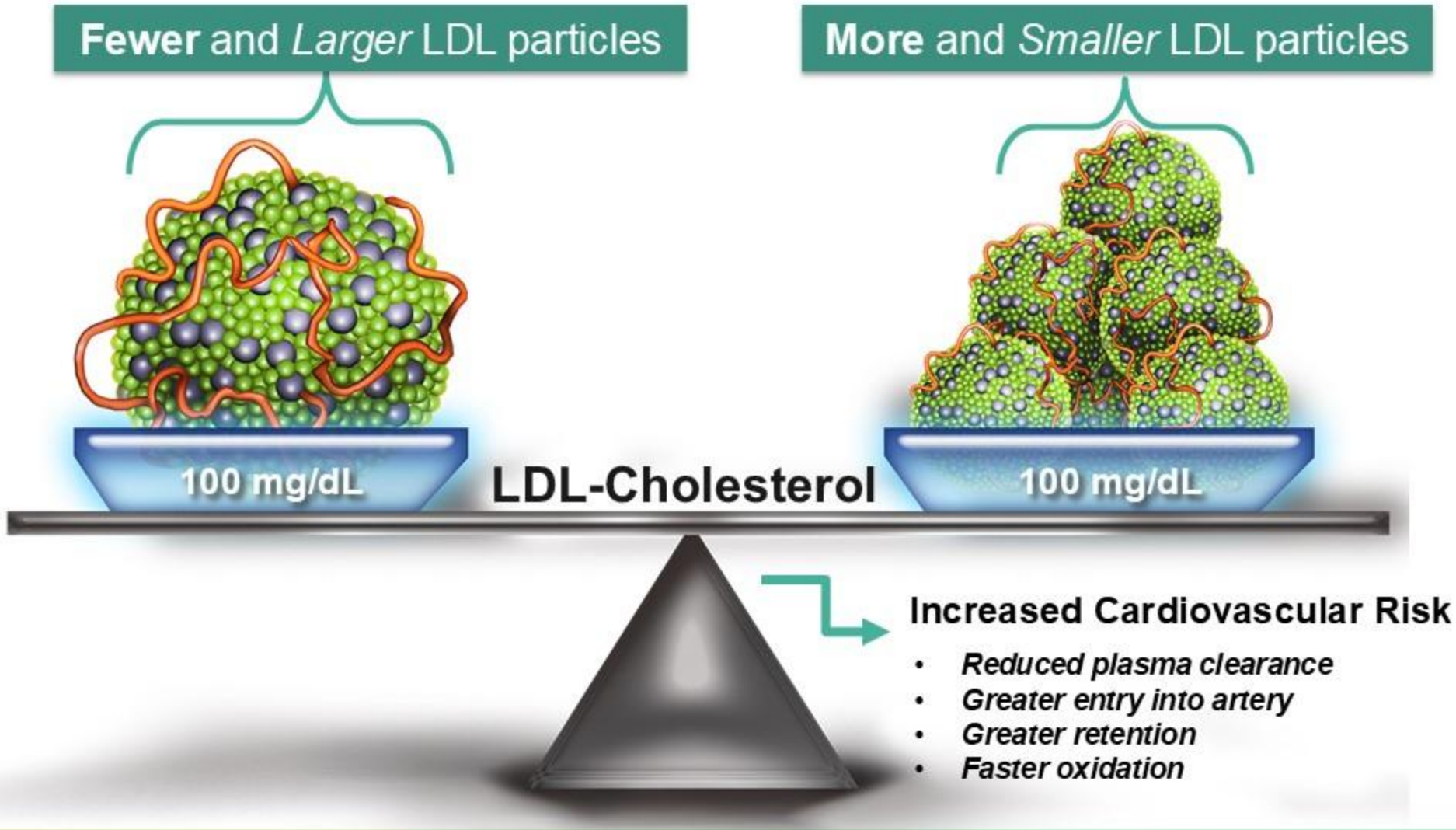
Inflammation Tests	Relative Risk
hs-CRP	1.5–2.0x[4]
Lp-PLA$_2$ (PLAC®)	1.7–2.9x* for CVD[4] 1.9–11.4x* for stroke[5]

*The risk associated with elevated Lp-PLA2 levels is substantially increased in patients with both Lp-PLA2 and hs-CRP elevated

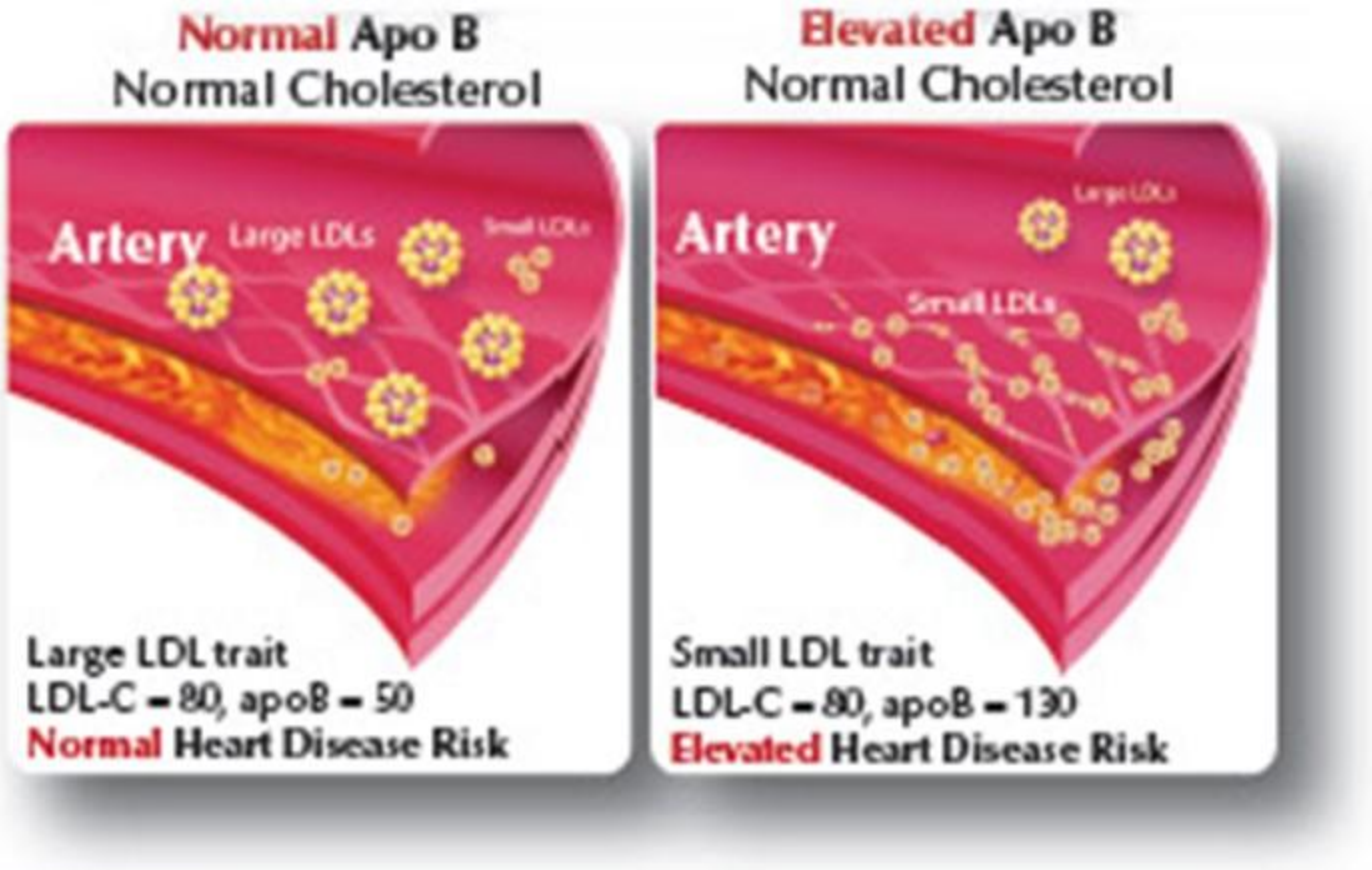
1. Musunuru K, Orho-Melander M, Caulfield MP, et al. Ion mobility analysis of lipoprotein subfractions identifies here independent axes of cardiovascular risk. *Arterioscler Thromb Vasc Biol.* 209;29:1975-80. **2**. Nordesgaard B, Chapman MJ, Ray K, Boren J, et al. Lipoprotein(a) as a cardiovascular risk factor: current status. *Eur Heart J.* 2010;31:2844-53. **3**. Sniderman AD, Williams K, Contois JH, Monroe HM, McQueen MJ, et al. A Meta-Analysis of Low Density Lipoprotein Cholesterol, Non-High-Density Lipoprotein Cholesterol, and Apolipoprotein B as Markers of Cardiovascular Risk. *Circ Cardiovasc Qual Outcomes.* 2011;4:337-45. **4.** Ballantyne CM, Hoogeveen RC, Bang H, et al. *Circulation.* 2004;109:837-42. **5.** Ballantyne CM, Hoogeveen RC, Bang H et al. *Arch Intern Med.* 2005;165:2479-84.

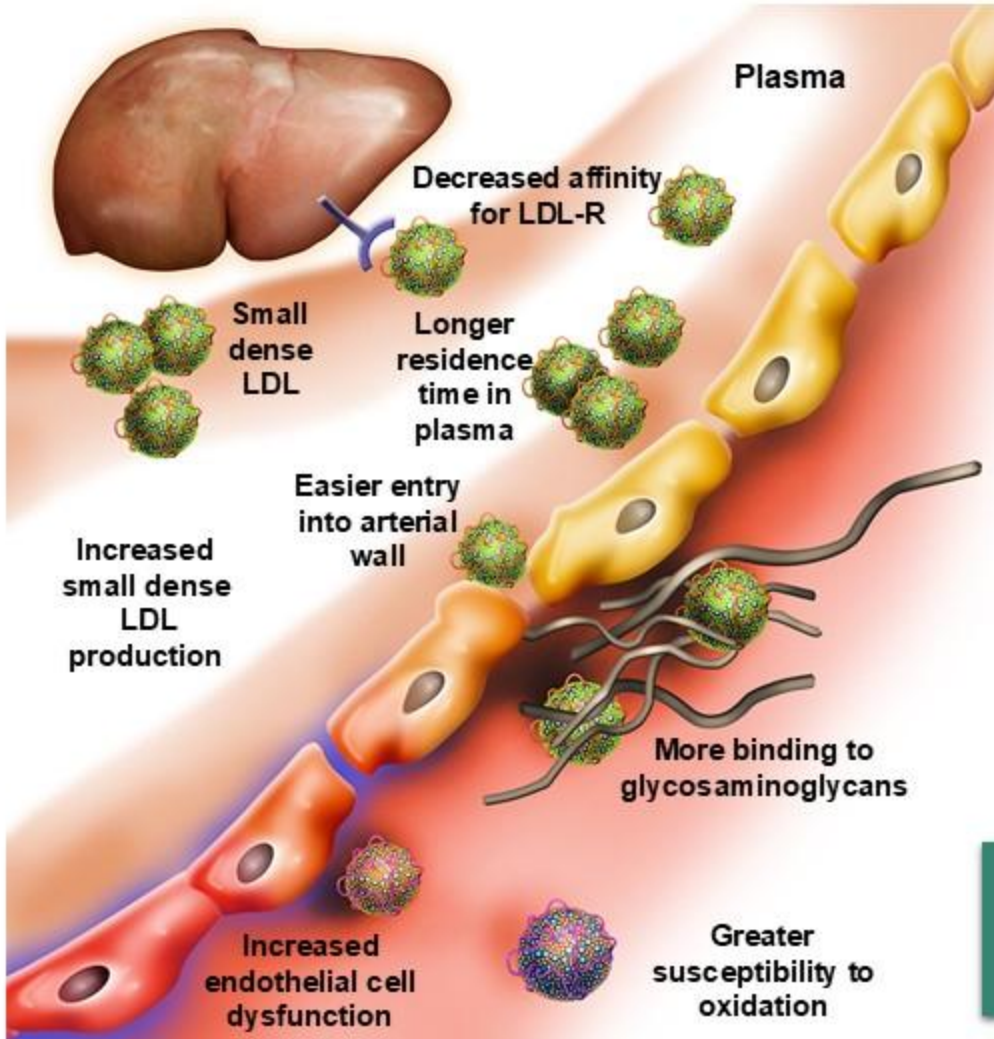

CHYLOMICRON
VLDL
IDL1
IDL2
LDL
I
IIa
IIIa
IIb
IVa
IVb
IIIb
Lp(a)
HDL
2b
2a
3a
3b
3c
Artery cleaners
CHYLOMICRON
REMNANT

PARTICLE SIZE AND NUMBER MATTER



Like Adding Cheese to a Sandwich





- LDL particle number may increase due to:
  - Increased production of small dense LDL-P
  - Decreased LDL-receptor affinity
  - Long residence time in plasma
- When LDL particle number increases:
  - Smaller LDL particles cross arteries, bind proteoglycans, and are oxidized more easily – **promoting atherogenesis and plaque vulnerability**
  - Endothelial cells are induced to produce more PAI-1 and thromboxane A2

LDL particle number (LDL-P) offers valuable prognostic information beyond traditional factors

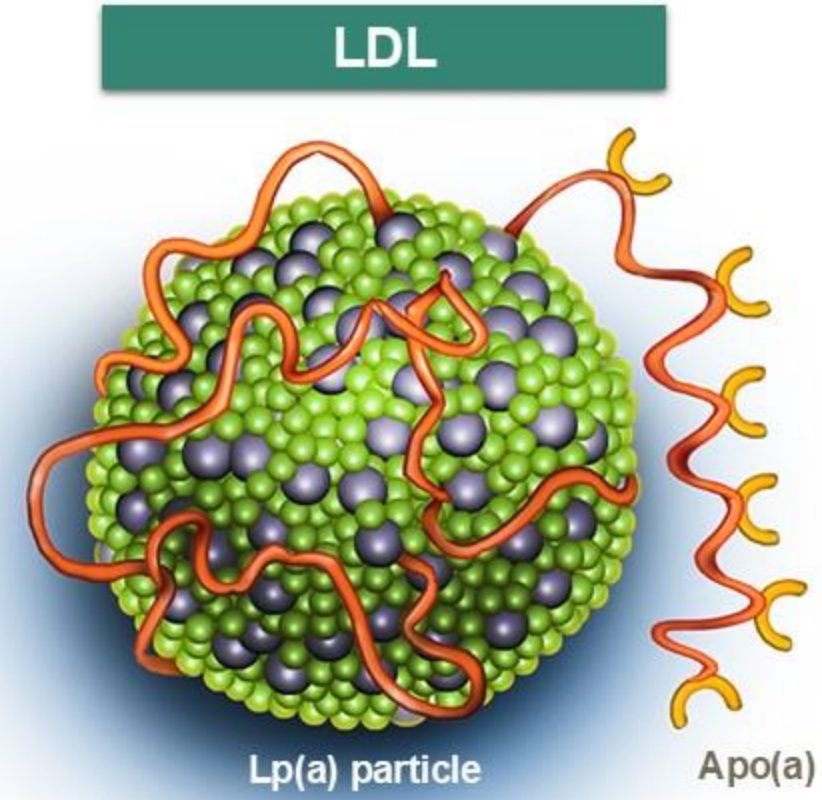
Sources: Superko, HR. Beyond LDL-C Reduction *Circulation* 1996;94:2351-2354. Mudd JO, Borlaug BA, Johnston et al. Cannon CP, Deedwania PC, et al. Beyond Lowdensity Lipoprotein Cholesterol *J Am Coll Cardiol* 2007;50:1735-1741. Krauss RM. Heterogeneity of plasma low-density lipoproteins and atherosclerosis risk. *Curr Opin Lipidol.* 1994;5:339-349. Krauss RM, Dreon DM. Low-density-lipoprotein subclasses and response to a low-fat diet in healthy men. *Am J Clin Nutr* 1995;62:478S-487S; Musunuru K. Atherogenic Dylslipidemia: Cardiovascular risk and Dietary Intervention. *Lipids* 2010;45:907-914.

LDL-P IS A STRONGER PREDICTOR OF CVD RISK

Study	Endpoint
Malmö Diet and Cancer Study Cardiovascular Cohort	Incident CVD events
Women's Health Study	Incident MI, CHD death
MESA Trial	Carotid intima-media thickness
Framingham Heart Study	Incident CVD events
Cardiovascular Health Study	Incident MI

Musunuru K, Orho-Melander M, Caulfield MP, et al. *Arterioscler Thromb Vasc Biol*. 2009;29:1975-80 Blake GJ, Otvos JD, Rifai N, Ridker PM.. *Circulation*. 2002;106:1930-1937. Mora S, Szklo M, Otvos JD, et al.. *Atherosclerosis*. 2007;192:211-217. Cromwell WC, Otvos JD, Keyes MJ, et al. *J Clin Lipidol*. 2007;1:583-592. Kuller L, Arnold A, Tracy R, et al.. *Arterioscler Thromb Vasc Biol*. 2002;22:1175-1180.

- Lp(a) is an LDL-like particle with the protein apo(a) attached
- Apo(a) is structurally similar to plasminogen amino acid sequences (kringles)
- 33% of CVD patients have elevated Lp(a) levels
- Lp(a) level is inherited
    - 50% of first-degree relatives are at risk of elevated Lp(a)[1,2]



Lipoprotein(a) consists of an LDL-like particle and apolipoprotein(a), which is covalently bound to apoB

1. Utermann G, Menzel HJ, Kraft HG, et al. *J Clin Invest*. 1987;8:458-65. **2.** Kamstrup PR, Tybjaerg-Hansen A, Steffensen R, Nordestgaard BG. *JAMA*. 2009 10;301:2331-9.

Drug/Modification	Effect on Lp(a)	Effect on ApoB
Statins[1,2]	—/↑	↓
Fibrates[1,3]	—	↓
Niacin[3–5]	↓	↓
Omega-3 fatty acids[4,6–9] (fish oil)	—↓	—
Diet[1,10]	—	↓

References cited are representative.

1. Berthold HK, Gouni-Berthold I. *Atheroscler Suppl.* 2013;14:1-5. **2.** Homma Y, Michishita I, Hayashi H, et al. *J Atheroscler Thromb.* 2010;17:1049-53. **3.** Feher MD, Caslake M, Foxton J, et al. *Diabetes Metab Res Rev.* 1999;15:395-9. **3.** Riche DM, East HE, Priest HM. *J Am Pharm Assoc (2003).* 2008;48:803-7. **4.** Maki KC, Bays HE, Dicklin MR, et al. *J Clin Lipidol.* 2011;5:483-92. **5.** Bays HE, Shah A, Lin J, et al. *Am J Cardiovasc Drugs.* 2012;12:197-206. **6.** Nelson TL, Hokanson JE, Hickey MS. *Eur J Nutr.* 2011;50:185-93. **7.** Pedersen MW, Koenig W, Christensen JH, Schmidt EB. *Eur J Nutr.* 2009;48:1-5. **8.** Herrmann W, Biermann J, Kostner GM. *Am J Cardiol.* 1995;76:459-62. **9.** Superko HR, Superko SM, Nasir K, Agatston A, Garrett BC. *Circulation* 2013;128:2154-2161 **10.** Jones JL, Comperatore M, Barona J, et al. *Metabolism.* 2012;61:366-72.

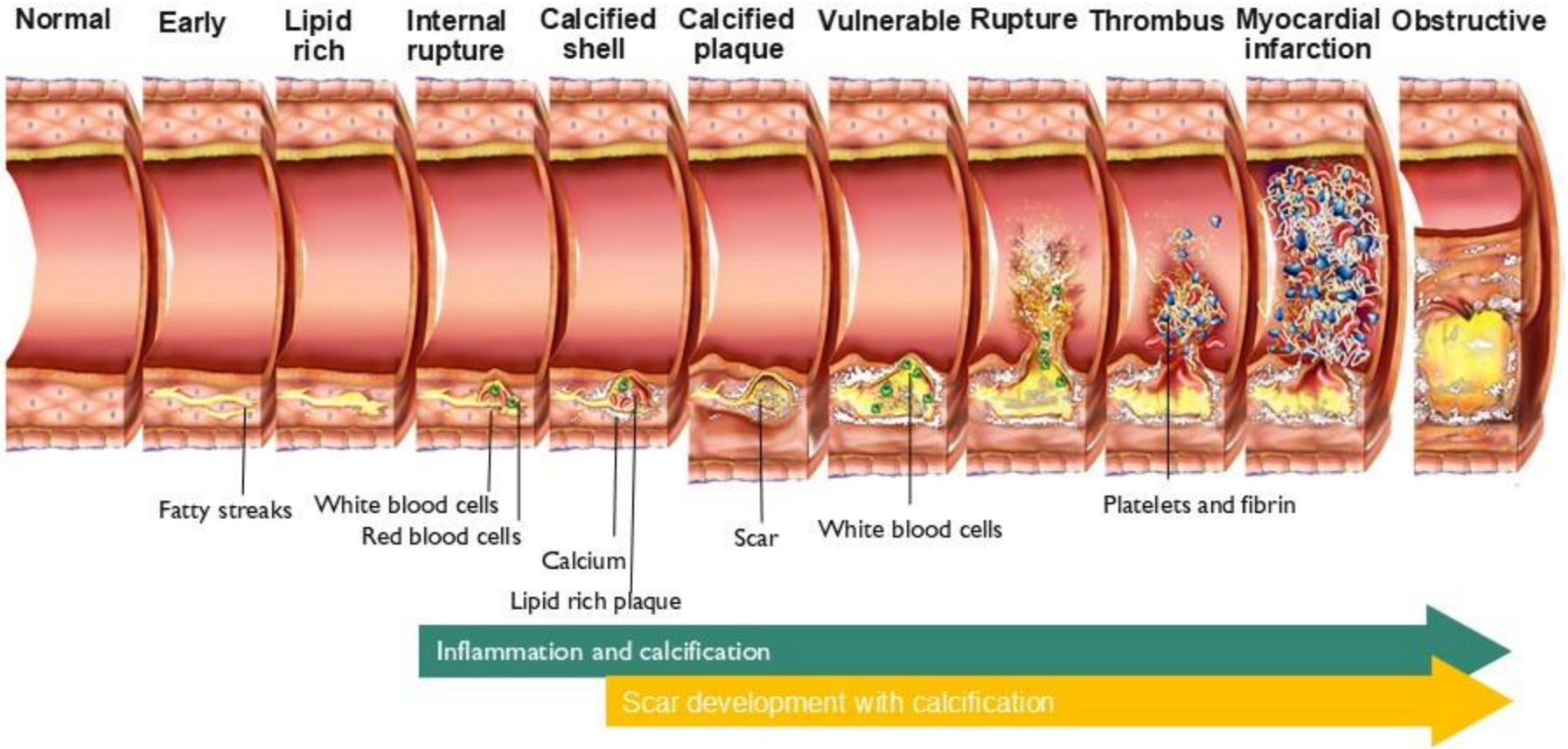
HS-CRP AND LP-PLA$_2$ (PLA2)

Drug	Effect on hs-CRP	Effect on Lp-PLA2[2-9]
Statins[1–3]	↓	↓
Fibrates[1,3]	↓	↓
Niacin[4–6]	↓ —	↓
Omega-3 fatty acids (fish oil)[7–10]	↓ —	↓ —
Diet[11,12]	↓ ↑	↓

References cited are representative of many showing stated result.

1. Ridker PM, Hennekens CH, Buring JE, Rifai N. *N Engl J Med.* 2000;342:836-43. **2.** Agouridis AP, Tsimihodimos V, Filippatos TD, et al. *Expert Opin Pharmacother.* 2011;12:2605-11. **3.** Wägner AM, Sánchez-Quesada JL, Benítez S, et al. *Diabetes Res Clin Pract.* 2011;93:e25-8. **4.** Hamoud S, Kaplan M, Meilin E, et al. *Am J Med Sci.* 2013;345:195-9 .**5.** Kuvin JT, Dave DM, Sliney KA, et al. *Am J Cardiol.* 2006;98:743-5. **6.**Wi J, Kim JY, Park S, et al. *Atherosclerosis.* 2010;213:235-40. **7.** Wang TD, Chen WJ, Lin JW, et al. *Atherosclerosis.* 2003;170:315-23. **8.** Malekshahi Moghadam A, Saedisomeolia A, Djalali M, et al. *Singapore Med J.* 2012;53:615-9. **9.** Maki KC, Bays HE, Dicklin MR, et al. *J Clin Lipidol.* 2011;5:483-92. **10.** Nelson TL, Hokanson JE, Hickey MS. *Eur JNutr.* 2011;50:185-93. 11. Kim EJ, Cho SW, Kang JY, et al. *J Am Coll Nutr.* 2012;31:352-60. **12.** Chen CW, Lin CT, Lin YL,et al. *Yonsei Med J.* 2011;52:13-9.

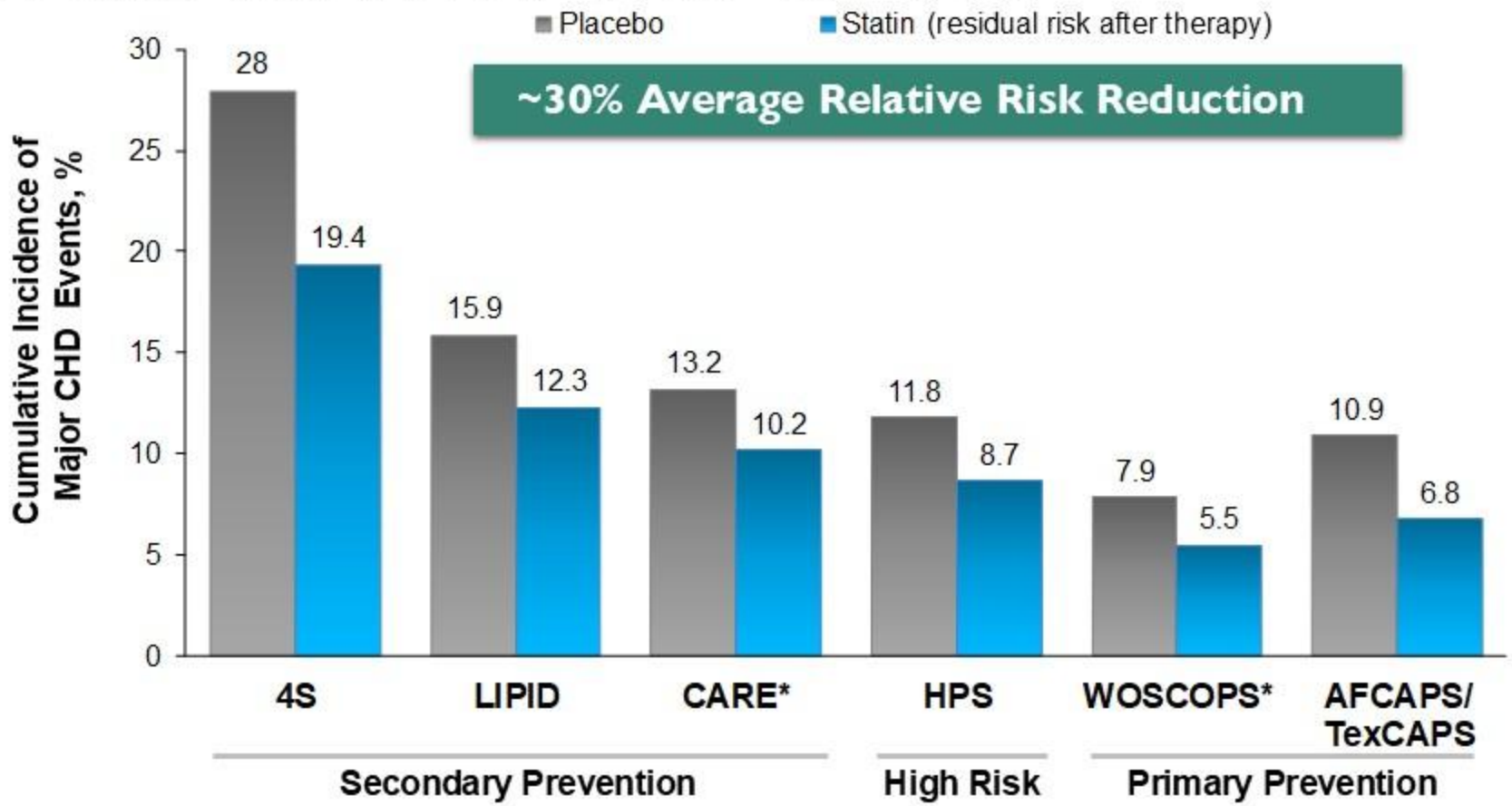
INFLAMMATION!



- Important to identify inflammation and aggressively treat plaque progression
- Elevated levels of Lp-PLA2 and hs-CRP indicate that inflammation is active

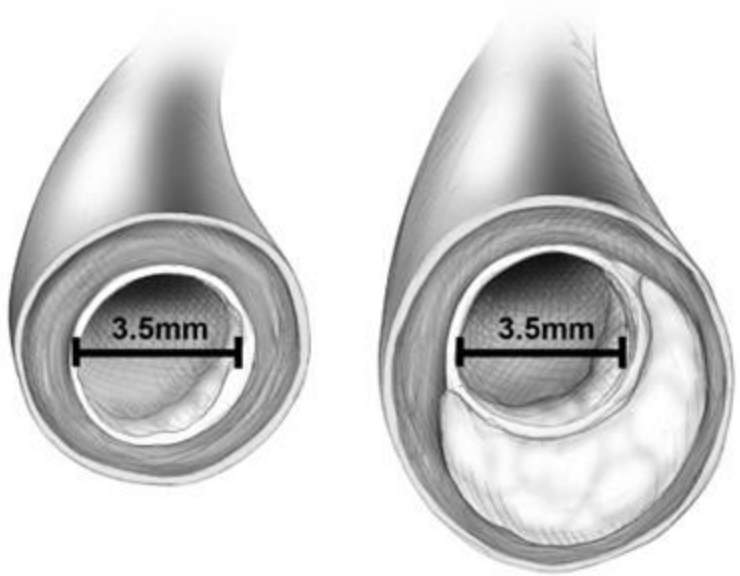
EVENT REDUCTION STATIN TRIALS

RESIDUAL RELATIVE RISK IS ~70%



Modification of Superko HR, King S. *Circulation*. 2008;117:560-568

Glagov Remodeling



Early atherosclerosis

Advanced atherosclerosis - artery expands outward, outside diameter of artery increases, inside diameter stays the same.

TREATMENTS

- Niacin
- Statins
- psk9
- Cholesterol absorption blockers (zetia, welchol, sterols)
- Red yeast rice
- Ground flax seed
- Black cumin (Nigella sativa)
- Fish oil
- Green tea, black tea
- Plant sterols
- Myoinositol
- Bergamot?
- Tocotrienols?
- Panthenate?
- Garlic
- Berberine
- Fiber
- Diet (fiber, low sat fat, nuts, soy, flax, keto +/-, weight loss?)
- Exercise

NIACIN CONTROVERSY

Integr Med (Encinitas). 2014 Oct; 13(5): 8–11.

PMCID: PMC4684109

PMID: 26770111

"Niacin Doesn't Work and Is Harmful!" Proclaim the Headlines. Yet Another Highly Publicized Questionable Study to Discredit Integrative Medicine

Mark Houston, MD, MS, MSc and Joseph Pizzorno, ND, Editor in Chief

Conclusions

Go to:

1. Niacin is an efficacious agent for the treatment of dyslipidemia and prevention of CVD as monotherapy, as well as with statins and other lipid-lowering agents.
2. The vast majority of clinical trials with niacin or niacin with other drug therapies for dyslipidemia show significant reductions in CVD, CHD, and carotid atherosclerosis.
3. Therapeutic dosages of ERN has a relatively low side effect profile.
4. The addition of laropiprant may have induced many of the adverse effects. The data do not support the conclusion that niacin alone caused the adverse effects on clinical or metabolic parameters.
5. Niacin monotherapy has many positive effects on lipids such as LDL reduction and LDL particle number reduction. It also increases LDL size, increases HDL, HDL-2B, HDL particle number, and HDL function. It reverses cholesterol transport, cholesterol efflux capacity, and triglyceride. Patient not at LDL goal or patients with CVD and dyslipidemia with HDL < 32 mg/dL and triglyceride > 200 mg/dL may benefit from ERN added to intensive statin-based LDL cholesterol–lowering therapy.
6. Niacin has many nonlipid actions that are clinically important to prevent and treat CVD and CHD.