LDL Subclasses and Carotid Atherosclerosis in the Multi-Ethnic Study of Atherosclerosis (MESA)

Samia Mora, MD, MHS
Divisions of Preventive and Cardiovascular Medicine
Brigham and Women's Hospital
Harvard Medical School

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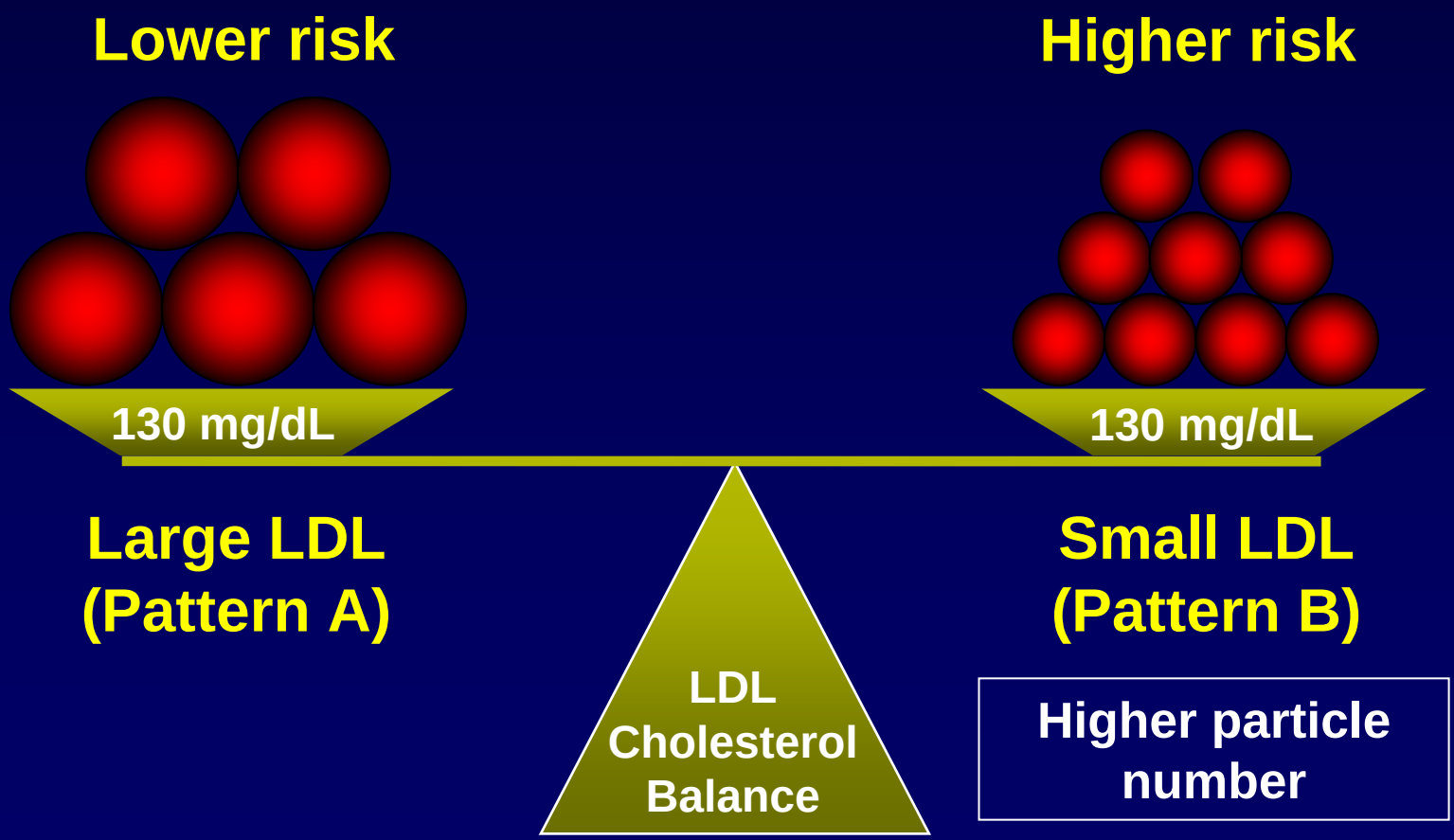
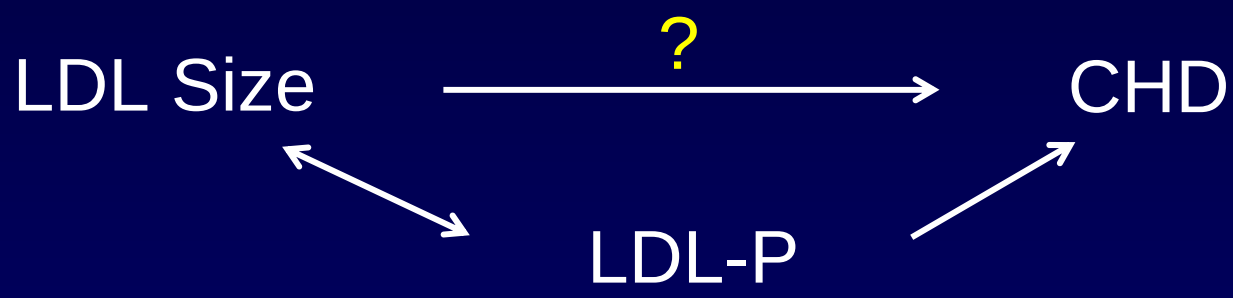
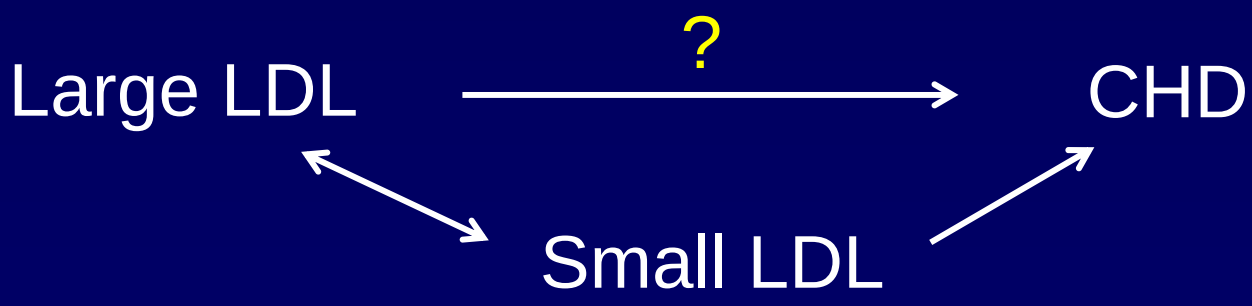
Many studies have shown that patients with smaller LDL size have greater CHD risk.

Is the origin of this risk particle size or number?

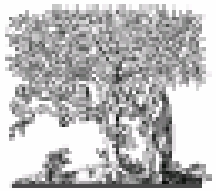


Is the relation of LDL size with CHD confounded by LDL particle number ?





Katz MH, Multivariable Analysis: A Practical Guide for Clinicians



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LDL particle subclasses, LDL particle size, and carotid atherosclerosis in the Multi-Ethnic Study of Atherosclerosis (MESA)

Samia Mora[a,*], Moyses Szklo[b], James D. Otvos[c], Philip Greenland[d], Bruce M. Psaty[e], David C. Goff[f], Daniel H. O'Leary[g], Mohammed F. Saad[h], Michael Y. Tsai[i], A. Richey Sharrett[b]

[a] *Center for Cardiovascular Disease Prevention, Department of Medicine, Brigham and Women's Hospital, and Harvard Medical School, Boston, MA, USA*

[b] *Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA*

[c] *LipoScience Inc., Raliegh, NC, USA*

[d] *Departments of Preventive Medicine and Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA*

[e] *Departments of Medicine, Epidemiology, and Health Services, University of Washington, SE, USA*

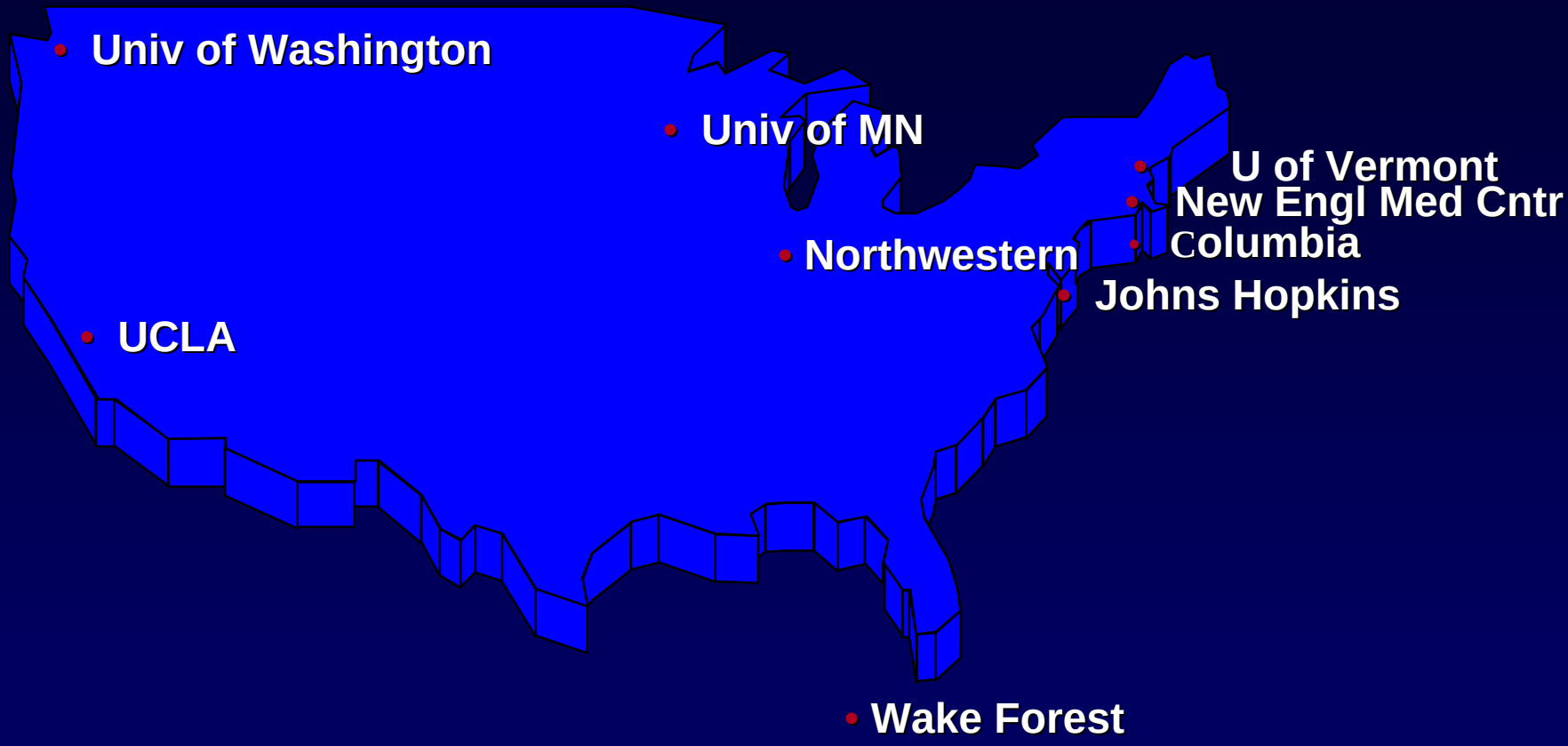
[f] *Department of Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC, USA*

[g] *Department of Radiology, Tufts-New England Medical Center, Boston, MA, USA*

[h] *Department of Preventive Medicine, Stony Brook School of Medicine, Stony Brook, NY, USA*

[i] *Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN, USA*

MESA Participants (N=5538)



Chinese 12%, African-American 28%, Hispanic 22%, White 38%

53% women

Individual Lipid Associations with IMT

Chemical Lipid Measures	ΔIMT (SE) in μm per 1-SD	P value
LDL Cholesterol	37.2 (4.1)	<0.001
HDL Cholesterol	-22.4 (4.5)	<0.001
Triglycerides	13.1 (4.1)	0.002

Each variable examined in a separate model, adjusted for age, sex, race, smoking, hypertension.

Atherosclerosis. 2006 Jun 9 [epub ahead of print]

Individual LDL Particle Associations with IMT

NMR LDL Particle Measures	ΔIMT (SE) in μm per 1-SD	P value
LDL Size	-20.9 (4.5)	<0.001
Total LDL-P	40.2 (4.1)	<0.001
Large	4.9 (4.4)	0.27
Small	31.7 (4.2)	<0.001

Each variable examined in a separate model, adjusted for age, sex, race, smoking, hypertension.

Atherosclerosis. 2006 Jun 9 [epub ahead of print]

Potential sources of confounding

Spearman Rank Correlations

	Small LDL-P	Large LDL-P	Total LDL-P
Small LDL-P	**	-0.63	0.88
Large LDL-P	-0.63	**	-0.24
LDL Size	-0.91	0.87	-0.64

Atherosclerosis. 2006 Jun 9 [epub ahead of print]

Association of NMR LDL Size with IMT

	ΔIMT (SE) in μm per 1-SD	P value
LDL Size (unadjusted)	-20.9 (4.5)	<0.001
LDL Size (adjusted for LDL-P)	14.5 (7.2)	0.05

Models adjusted for age, sex, race, smoking, and hypertension.

unpublished data

Associations of LDL Subclasses with IMT

NMR LDL Subclass	ΔIMT (SE) in μm per 1-SD	P value
Large LDL-P	4.9 (4.4)	0.27
Large LDL-P (adjusted)	42.9 (6.7)	<0.001
Small LDL-P	31.7 (4.2)	<0.001
Small LDL-P (adjusted)	39.1 (7.1)	<0.001

Each variable examined in a separate model, adjusted for age, sex, race, smoking, hypertension.

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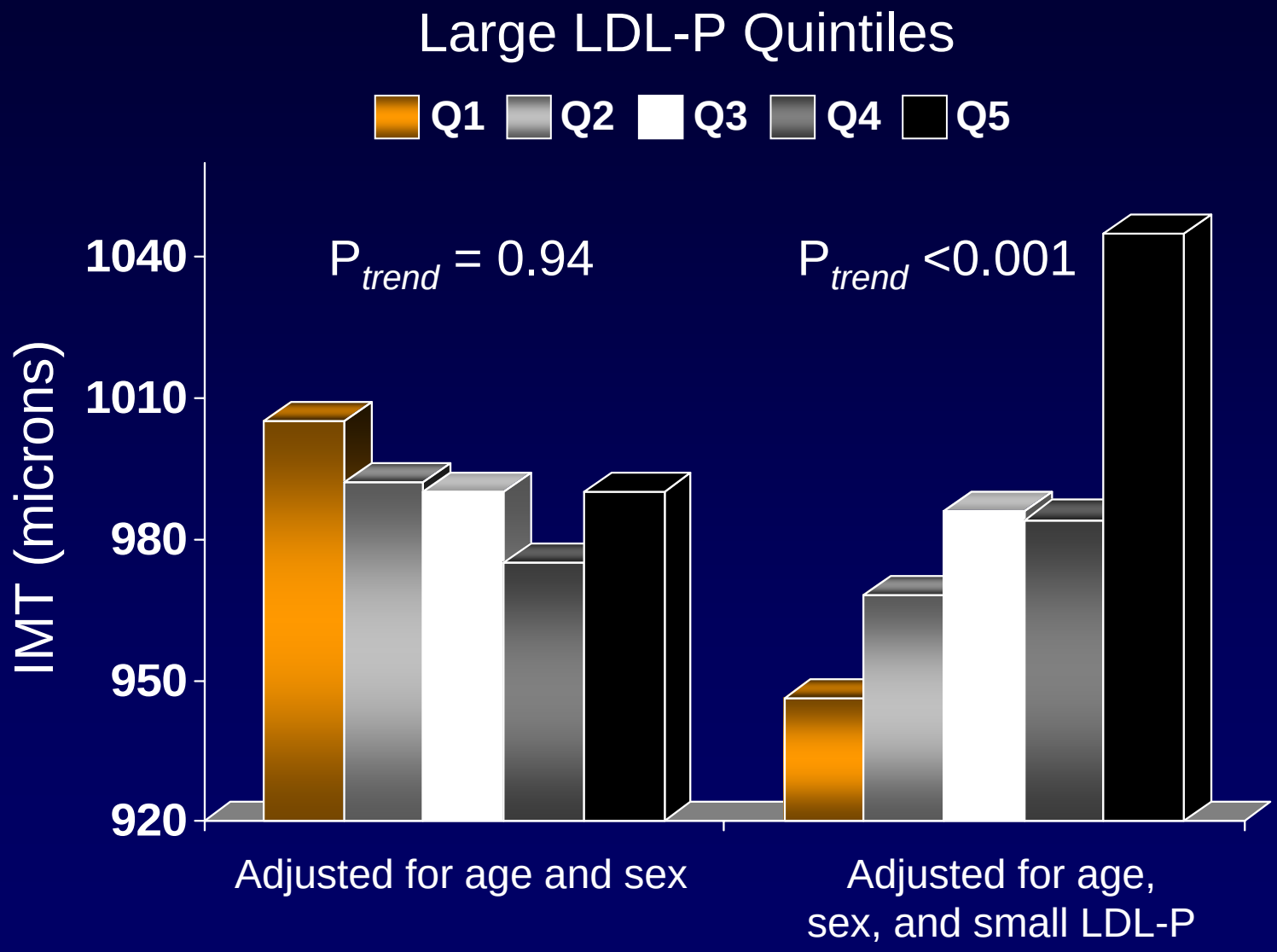
Adjusting for small LDL-P unmasks the true relation of large LDL-P with IMT



Atherosclerosis. 2006 Jun 9 [epub ahead of print]

Associations of On-Trial LDL Subclasses with CHD Events in VA-HIT

NMR LDL Subclass	OR (95% CI) per 1-SD	P value
Large LDL-P	1.06 (0.93-1.22)	0.35
Large LDL-P (adjusted)	1.34 (1.11-1.62)	0.002
Small LDL-P	1.17 (1.02-1.34)	0.03
Small LDL-P (adjusted)	1.41 (1.14-1.73)	0.001

Adjusted values were from a model containing all LDL and HDL subclasses together, adjusted additionally for treatment group, age, hypertension, smoking, body mass index, and diabetes.

Circulation. 2006;113:1556-63

MESA Results Summary

- Without adjusting for small LDL-P, we found large LDL-P was only weakly associated with IMT, consistent with prior studies
- Both small and large LDL-P, when examined jointly, were highly significantly associated with IMT, even after adjustment for traditional risk factors
- LDL particle size contributed little after accounting for LDL-P

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