# Clinical Utilization of Lipoprotein Subclasses in the Management of Cardiovascular Disease (CVD) Risk

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Consultant for LipoScience, Inc.

# Case CG

Patient is a 42-year-old male who enters for screening evaluation. Patient has no prior history of dyslipidemia or CHD.

Major CHD Risk Factors:

Family history is significant for father who experienced a non-fatal MI at age 50 and a fatal MI at age 65. One brother also experienced a non- fatal MI at age 45.

# Case CG

| | |
|---|---|
| Past Medical History: | GERD |
| Current Medications: | Prevacid 30 mg q day<br>Ranitidine 75 mg prn<br>ASA 81 mg q day |
| Family History: | CHD as noted above |
| Review of Systems: | Unremarkable |

PE: BP 104/66 Pulse 72 Wt. 203 Ht. 6’2”
Otherwise unremarkable

# Case CG

**Baseline Lipids**

| | |
|---|---|
| Total-C | 146 mg/dL |
| LDL-C | 94 mg/dL |
| HDL-C | 24 mg/dL |
| TG | 142 mg/dL |

Is lipoprotein-related risk present?

What is the source of lipoprotein-related risk?

What are the lipoprotein goals of treatment?

**ATP III Guidelines**

1. 2 Risk Factors

   10 year Framingham Risk Score = 1%

2. LDL-C Goal < 130 mg/dl

Other Considerations

- Does not meet criteria for "Metabolic Syndrome"
- "Isolated low HDL-C"

# Relationship of LDL Particle Size with CHD Outcomes

1. To date, 17 cross-sectional epidemiologic, 8 prospective epidemiologic, and 6 clinical intervention trials have examined the relationship of LDL particle size and CHD risk.

2. The relationship of small LDL size with CHD risk is intertwined with a complex physiologic syndrome that includes high triglycerides (TG), low HDL cholesterol (HDL-C) and increased LDL-P.

3. Following multivariate analysis for these co-segregating risk factors (high TG, low HDL-C, increased LDL-P) LDL size is rarely a significant, independent predictor of CHD events.

Cromwell WC and Otvos JD. *Curr Athero Reports* 2004;6:381-387

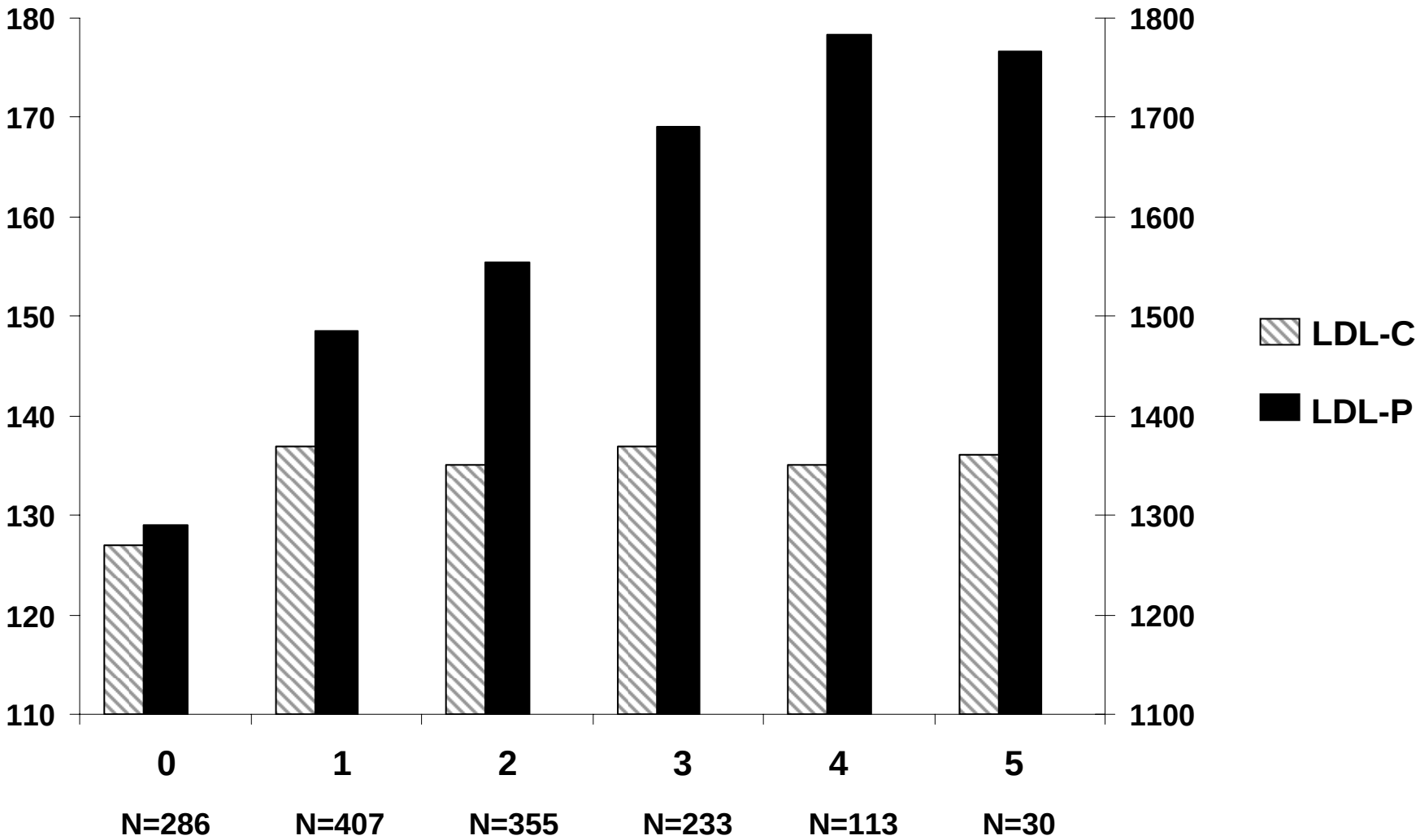
# Outcome Associations of NMR LDL Particle Number (LDL-P) versus LDL Cholesterol (LDL-C)

| Study | CHD Status | Atherosclerotic Endpoint | Associations Stronger for LDL-P than LDL-C * |
|---|---|---|---|
| Women's Health Study ** *Circulation* 2002; 106:1930-1937 | Primary Prevention | Incident MI, CHD death, CVA | YES |
| VA-HDL Intervention Trial ** *Circulation 2006*;113:1556-63 | Secondary Prevention | Non-fatal MI or CHD Death | YES |
| MESA Trial *Atherosclerosis* 2006, in press | Primary Prevention | Carotid IMT | YES |
| Framingham Heart Study 2004 AHA | Primary Prevention | Incident MI or Angina | YES |
| Cardiovascular Health Study *ATVB* 2002; 22:1175-1180 | Primary Prevention | Incident MI or Angina | YES |
| PLAC-I *AJC* 2002;90:89-94 | Secondary Prevention | Angiographic MLD | YES |
| Health Women Study *AJC* 2002;90(suppl): 71i-77i | Primary Prevention | EBCT Coronary Calcium Score | YES |

* Significant and independent in multivariate models

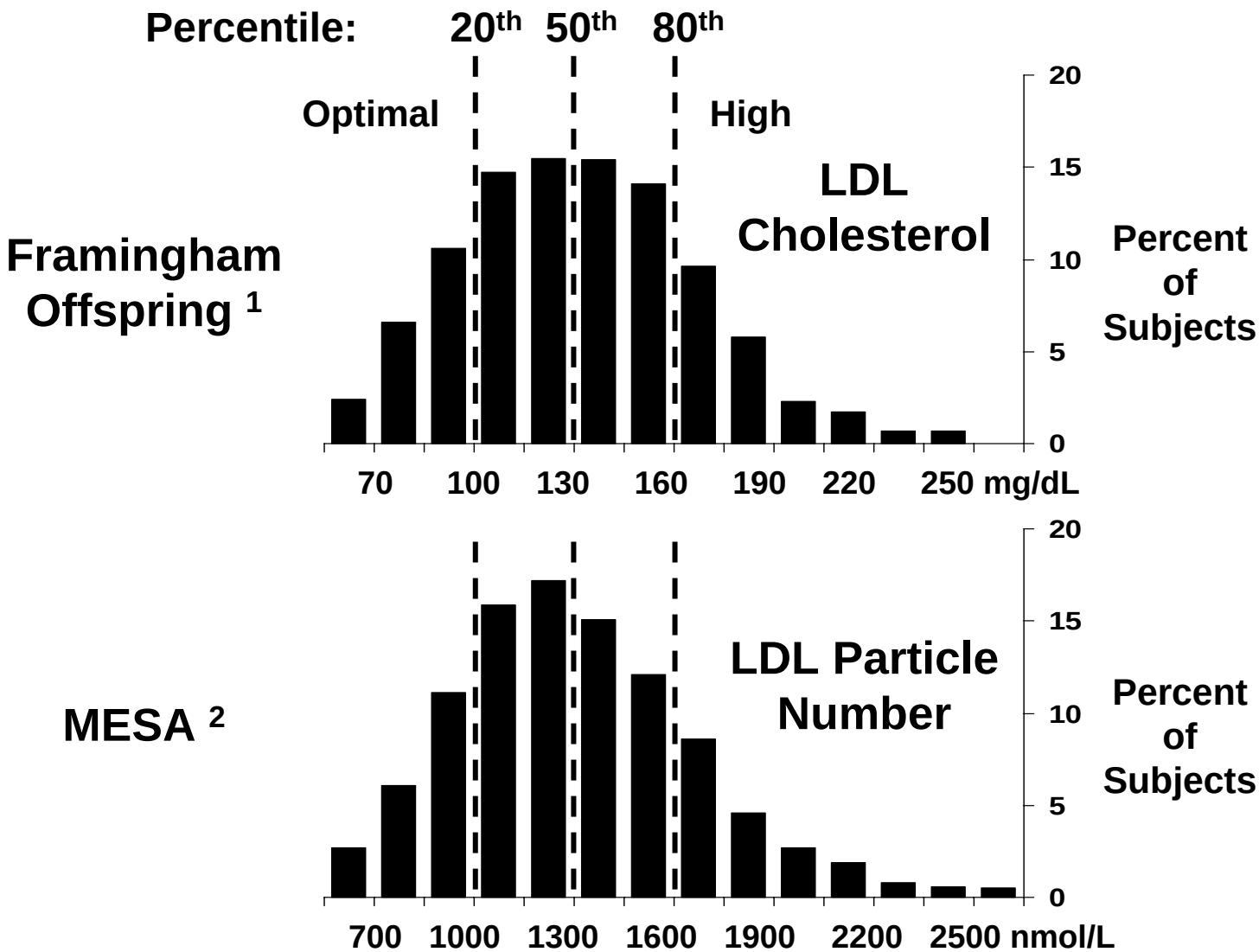
** LDL-P relations stronger than Apo B

# Alternate Measures of LDL in Framingham Men with Increasing Numbers of Metabolic Syndrome Features




Kathiresan S, et al. *Circulation* 2006;113:20-27

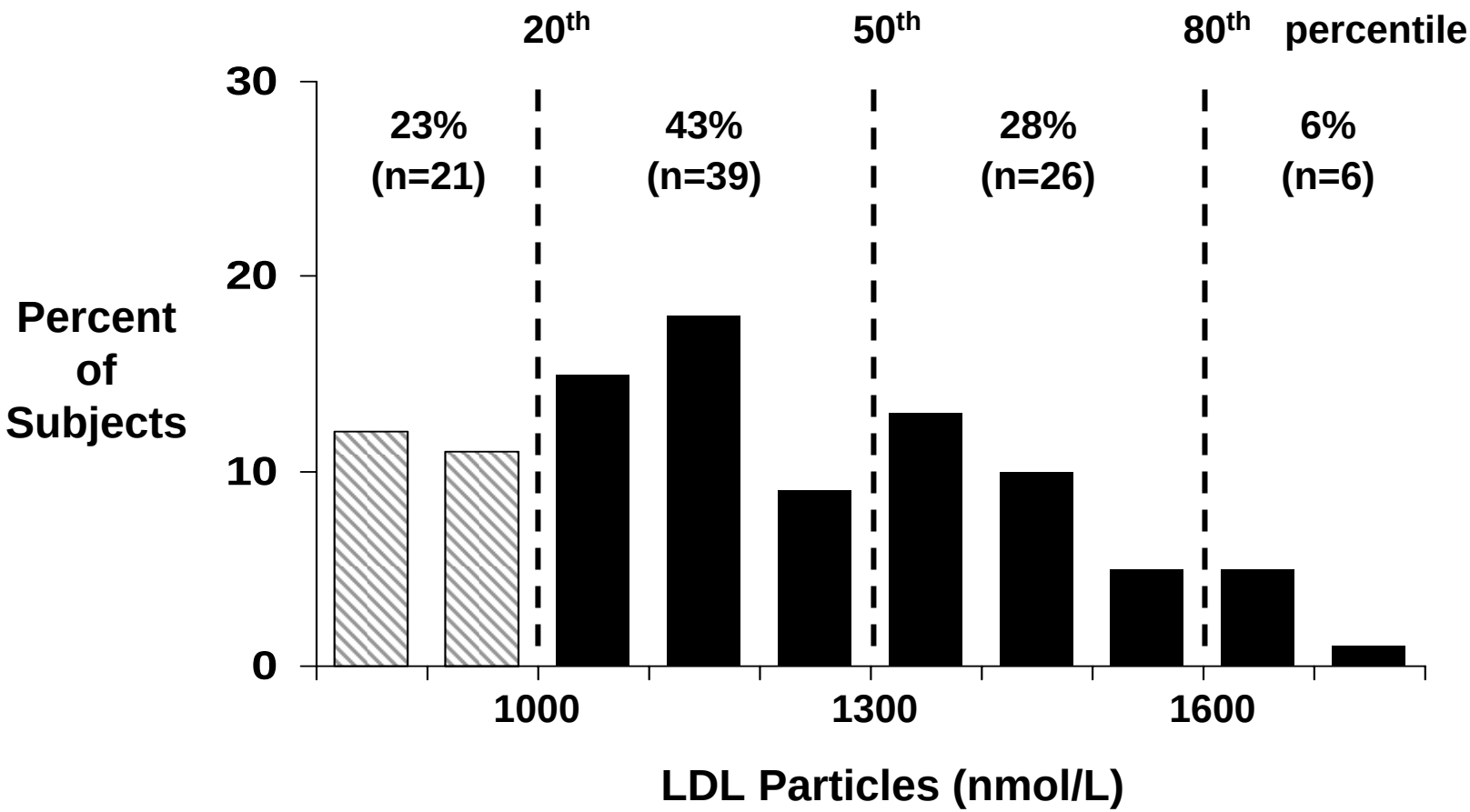
# Clinical Cutpoints for LDL




[1] Otvos JD, Jayarajah E, Cromwell, WC. *AJC* 2002;90(8A):22i-29i

[2] Mora S, et al. AHA/ADA Met Syn/Met Risks, San Francisco, May 3-5, 2006

# LDL Particle Number in Framingham MetSyn Patients with LDL-C < 100 mg/dL (<20th Percentile)



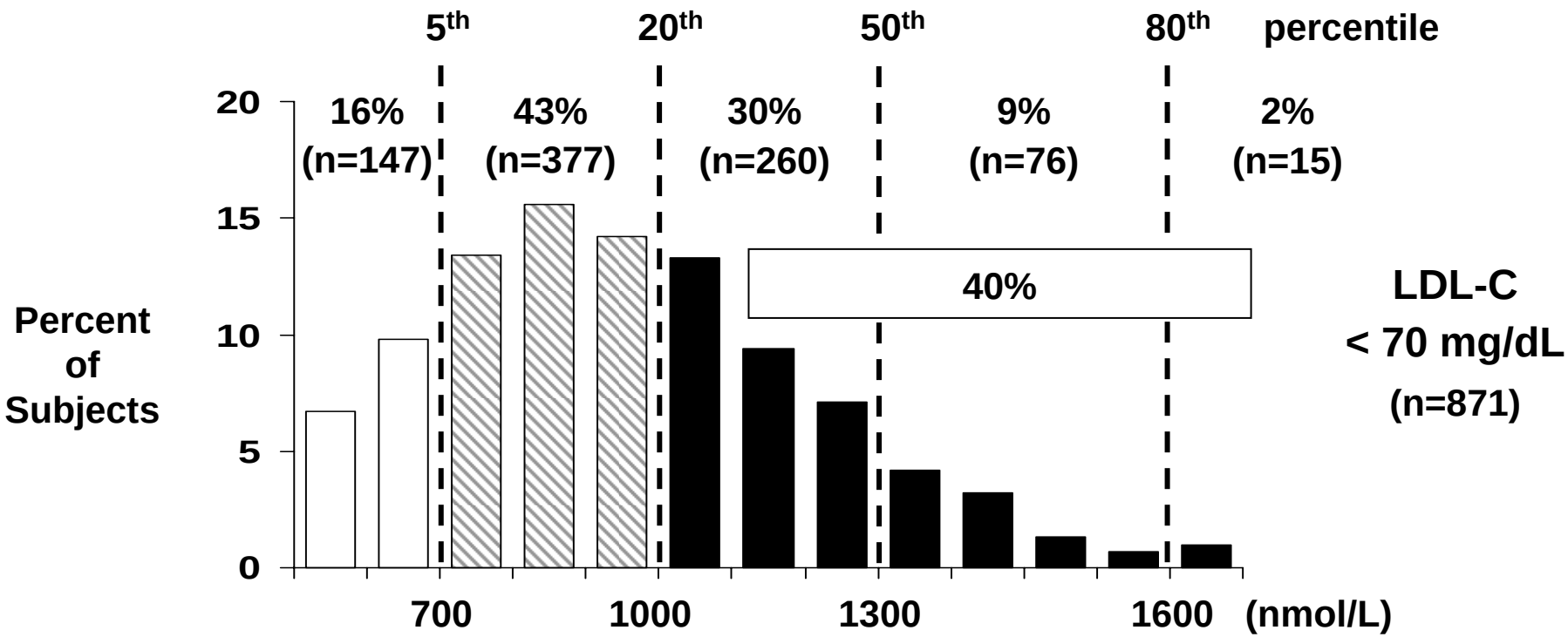

Otvos JD, Cromwell WC, et al. AHA Scientific Sessions 2003

# Characteristics of T2DM Subjects with LDL-C < 100 mg/dL (n=2,355)

| | Male | Female |
|---|---|---|
| Number | 1295 | 1060 |
| Mean Age | 65 | 66 |
| Total-C (SD) mg/dL | 144 (23.5) | 153 (24.0) |
| Trig (SD) mg/dL | 153 (81.2) | 157 (78.4) |
| HDL-C (SD) mg/dL | 40.2 (10.8) | 46.9 (12.7) |
| LDL-C (SD) mg/dL | 72.9 (18.4) | 74.9 (17.8) |
| LDL-P (SD) nmol/L | 1120 (315) | 1110 (319) |

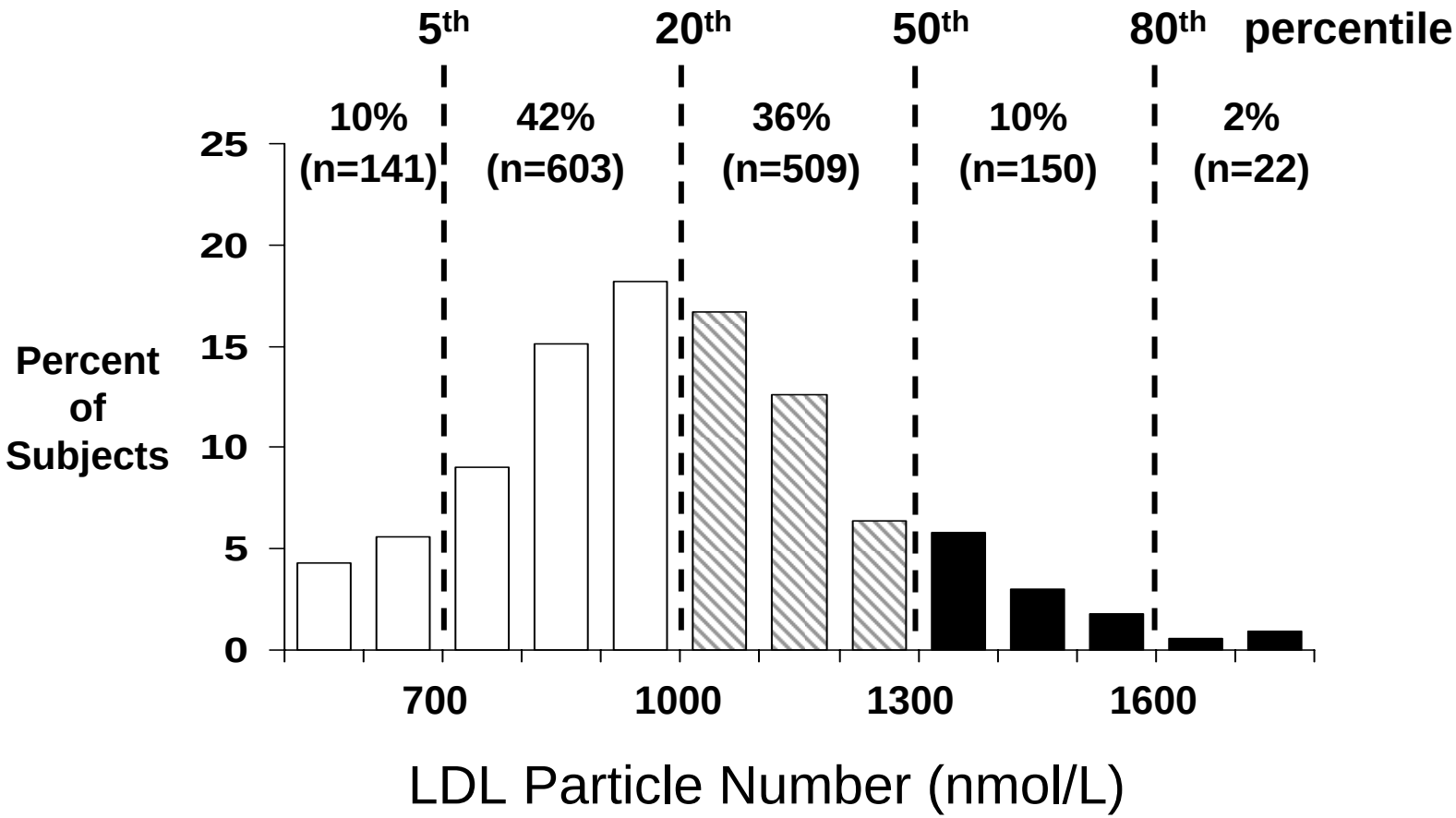
Cromwell WC, Otvos JD. *Am J Cardiol* 2006;98:1599-1602

# LDL Particle Number Distribution in T2DM Subjects




Cromwell WC, Otvos JD. *Am J Cardiol* 2006;98:1599-1602

# LDL Particle Number Distribution in MESA
# Quartile1: LDL-C <100 mg/dL (n=1,425)

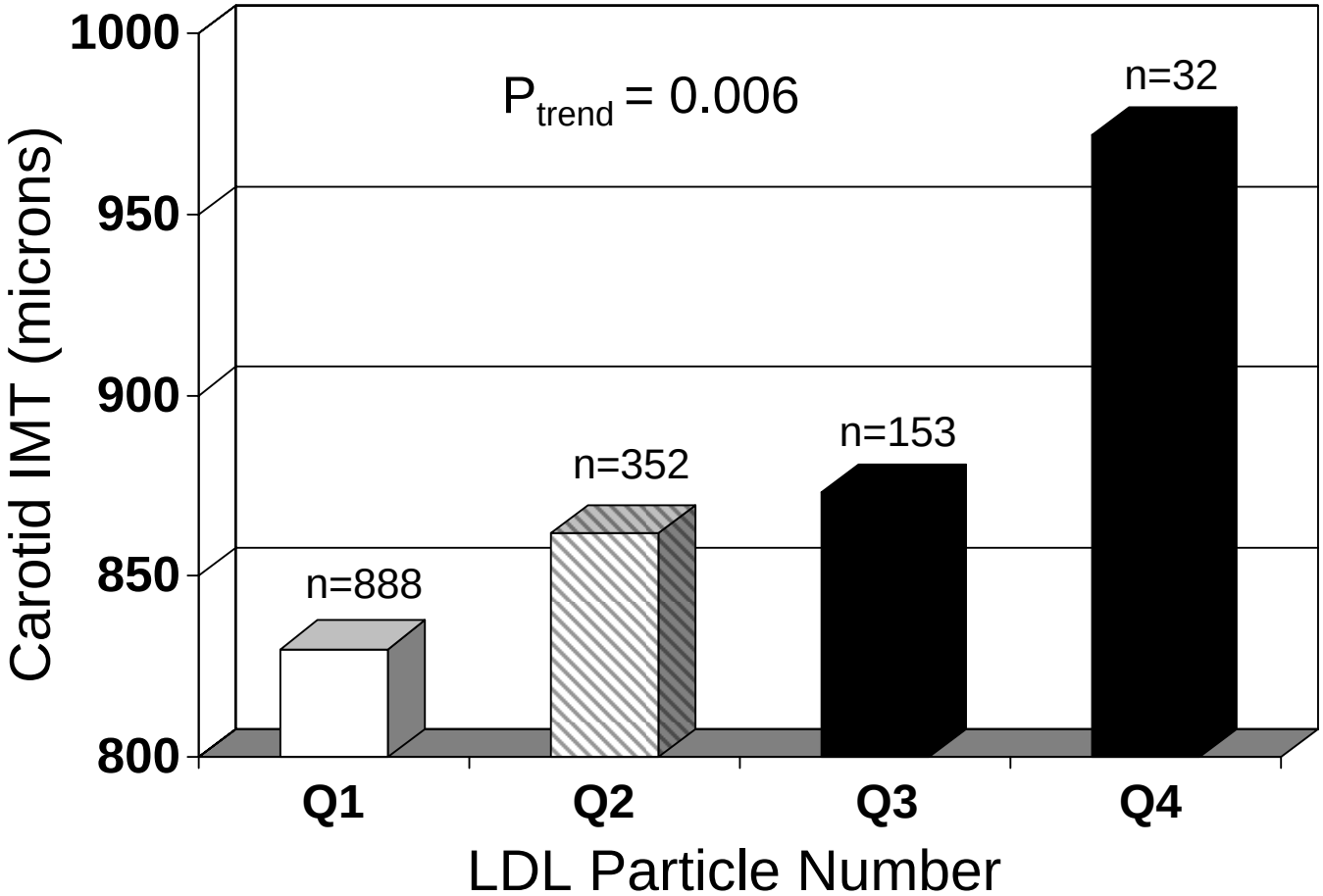



Mora et al, AHA/ADA Metabolic Syndrome meeting, May 2006

# Carotid Atherosclerosis in MESA

(adjusted for age, sex, race, smoking, diabetes, TG, and HDL-C)

Quartile1: LDL-C <100 mg/dL (n=1,425)

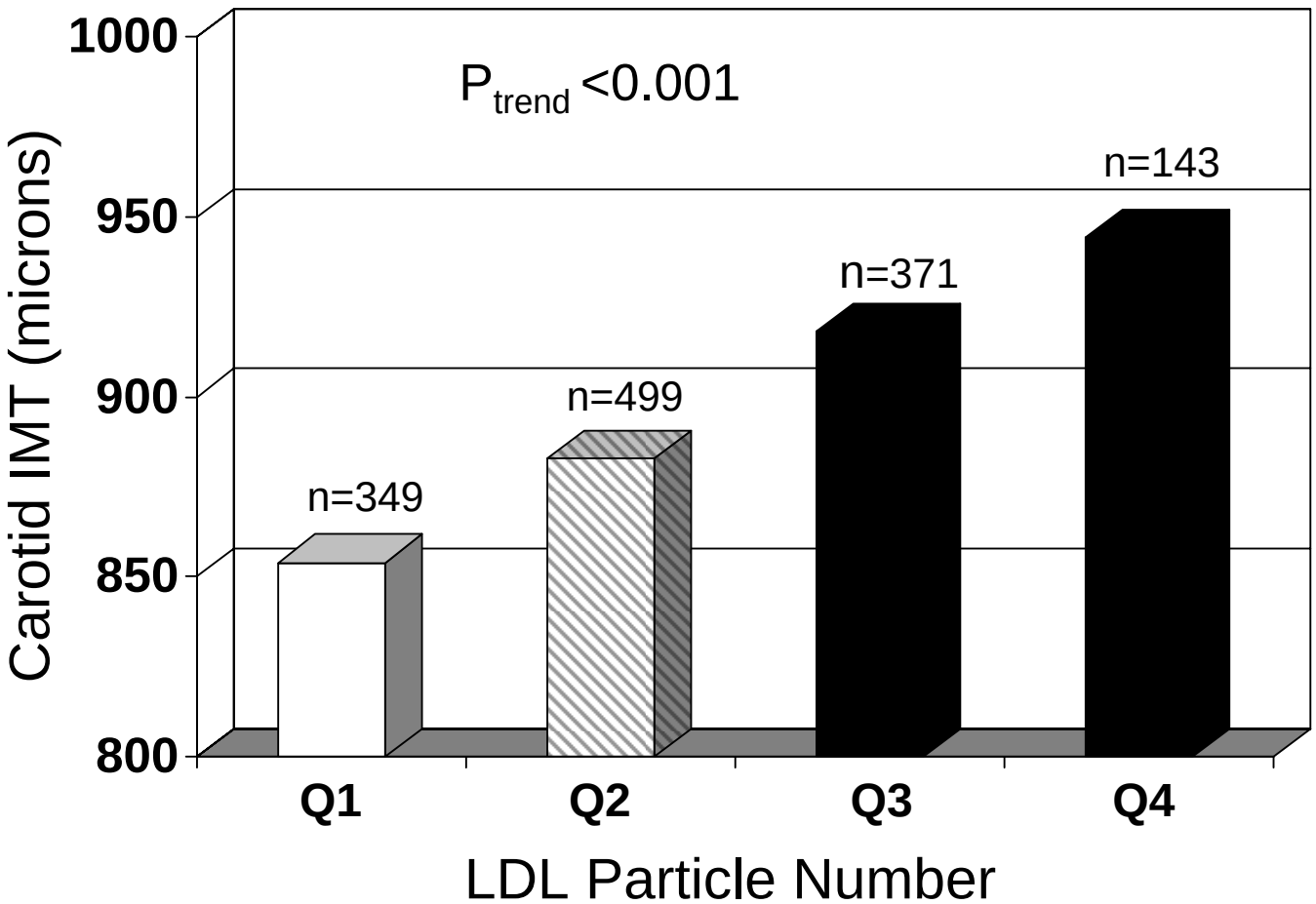



Mora et al, AHA/ADA Metabolic Syndrome meeting, May 2006

# Carotid Atherosclerosis in MESA

(adjusted for age, sex, race, smoking, diabetes, TG, and HDL-C)

Quartile 2: LDL-C = 100-118 mg/dL (n=1,362)

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# Case CG

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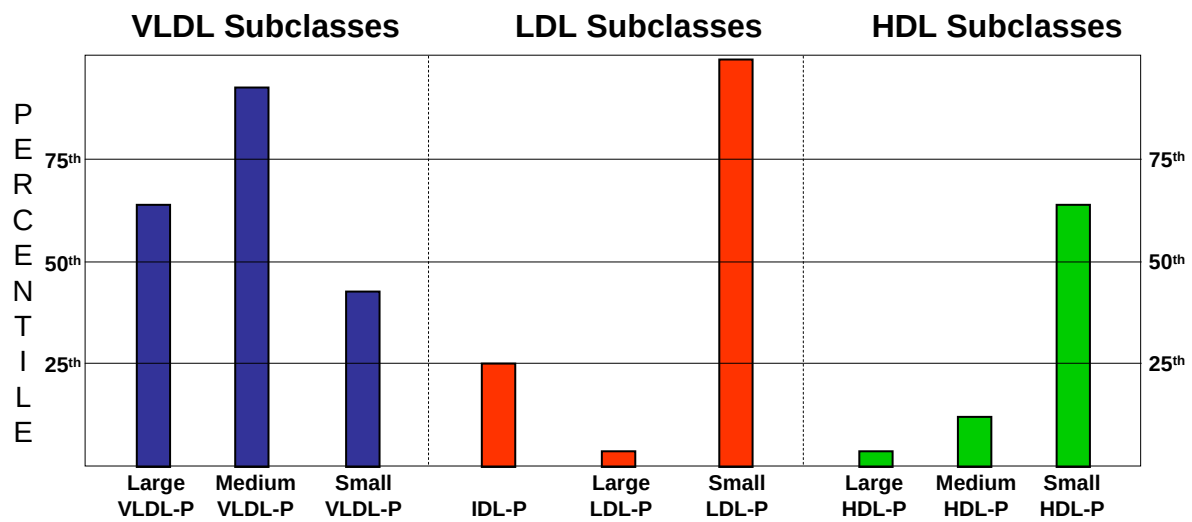
**LDL Particle Numbers**

| | nmol/L | Optimal | Near or above optimal | Borderline-high | High | Very High |
|---|---|---|---|---|---|---|
| **LDL-P** | **1809** | <1000 | 1000 - 1299 | 1300 - 1599 | 1600 - 2000 | >2000 |

| | nmol/L | Optimal | Moderate | Borderline-high | High |
|---|---|---|---|---|---|
| **Small LDL-P** | **1650** | <600 | 600 - 849 | 850 - 1200 | <1200 |

**Subclass Particle Numbers**