Insulin resistance: targeting dyslipidemia beyond the LDL-cholesterol

Rocky Mountain Metabolic Syndrome Symposium
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Director of CV Prevention Programs, CPC
Staff Cardiologist, Denver Health

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• Speaking and grant support: GSK, Pfizer
• Major stock holder: none

Presentation outline
• Describe all components of the metabolic syndrome
  – How common is this syndrome?
  – Understand pathogenesis of insulin resistance & atherogenic dyslipidemia
• What is our principal focus to reduce CVD in DM?
  – Lipids vs. Glycemic control
• Treatment of LDL cholesterol
• Beyond LDL cholesterol
  – Are there better predictors of CVD risk than LDL-C ?
  – Review the concept of "residual risk"
  – Atherogenic dyslipidemia defined: lipid particles made simple
    – Does size matter?
    – Are Triglycerides (TG) an independent CVD risk factor?
  – Non-HDL-C, ApoB, and the TC/HDL ratio
• What are the therapeutic strategies for atherogenic dyslipidemia?
  – Fibrates, Omega-3 fatty acids, Niacin, Diet, Exercise
• Treatment targets
• Q & A
Components of the metabolic syndrome (a precursor to diabetes)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Defining Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference</td>
<td>&gt;40 &amp; 35 inches (men/women)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&lt;150 mg/dl</td>
</tr>
<tr>
<td>HDL-C</td>
<td>&lt;40 mg/dl men; &lt;50 mg/dl women</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>&lt;130/85 mm Hg</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>&lt;100 mg/dl</td>
</tr>
</tbody>
</table>


The evolution of insulin resistance and the metabolic syndrome

The Economist, December 11, 2003

Obesity & diabetes track in US adults

Incidence of CVD by the number of components of the Metabolic Syndrome

<table>
<thead>
<tr>
<th>No. of Components</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>1.95</td>
</tr>
<tr>
<td>2</td>
<td>2.05</td>
</tr>
<tr>
<td>3</td>
<td>2.7</td>
</tr>
<tr>
<td>4</td>
<td>5.86</td>
</tr>
</tbody>
</table>

Diabetes Care 25-1750, 2002

Over half of patients referred to cardiologists have insulin resistance

<table>
<thead>
<tr>
<th>Cardiac rehabilitation</th>
<th>Acute MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with insulin resistance syndrome (%)</td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>58</td>
</tr>
</tbody>
</table>


Insulin Resistance Etiology: Central Adiposity (not inert but metabolically active)

Atherogenic Dyslipidemia: the hallmark of metabolic syndrome

- Elevated Triglycerides
  - (>150 mg/dL)
- Reduced HDL-C
  - (<40 mg/dL in men; <50 mg/dL in women)
- Elevated small dense LDL particles
  - Highly likely in the setting of elevated TG, reduced HDL-c and borderline elevated LDL-c
- Elevated non-HDL-c and/or Apo B

NHANES: Room for improvement

< 50% of Diabetics Achieve Risk-Factor Goals

Adults With Diabetes (%)

<table>
<thead>
<tr>
<th>HbA1c &lt; 7%</th>
<th>BP &lt; 130/80 mmHg</th>
<th>TC &lt; 200 mg/dL</th>
<th>Good Control</th>
</tr>
</thead>
</table>
| Good Control indicates HbA1c, BP, and TC were at recommended levels.

National Health and Nutrition Examination Study (NHANES): cross-sectional survey of a nationally representative sample of the noninstitutionalized civilian US population, aged 20 years and older, with previously diagnosed diabetes.


We’ve gotten worse in terms of glycemic control and better with regard to lipids.

Should I focus on lipids or blood sugar?
ACCORD: Study design

N = 10,251 with T2DM and existing CVD or additional CV risk factors

<table>
<thead>
<tr>
<th>Glycemia trial</th>
<th>Lipid trial (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1C &lt;6%</td>
<td>Group A</td>
</tr>
<tr>
<td>2362</td>
<td>1178</td>
</tr>
<tr>
<td>2371</td>
<td>1178</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A1C 7.0%-7.9%</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>4733</td>
<td>1383</td>
</tr>
<tr>
<td>5518</td>
<td>1391</td>
</tr>
</tbody>
</table>

SBP <120 mg Hg

SBP <140 mg Hg

Primary outcome: CV death, MI, stroke

ACCORD: Treatment effects on glucose control

ACCORD: significant increase in death with intensive therapy
**ADVANCE: Study design**

N = 11,140 with T2DM and high risk for CV events

- Intensive glucose control
  - Perindopril/Indapamide
  - Placebo
- Standard glucose control
  - Perindopril/Indapamide
  - Placebo

Primary outcomes: Macro (CV death, MI, stroke), micro (new/worsening nephropathy, retinopathy)


**ADVANCE: Treatment effect on glucose control**

<table>
<thead>
<tr>
<th>Follow-up (months)</th>
<th>Standard control Mean A1C (%)</th>
<th>Intensive control Mean A1C (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>7.0</td>
<td>6.0</td>
</tr>
<tr>
<td>12</td>
<td>6.0</td>
<td>5.5</td>
</tr>
<tr>
<td>18</td>
<td>5.5</td>
<td>5.0</td>
</tr>
<tr>
<td>24</td>
<td>5.0</td>
<td>4.5</td>
</tr>
<tr>
<td>30</td>
<td>4.5</td>
<td>4.0</td>
</tr>
<tr>
<td>36</td>
<td>4.0</td>
<td>3.5</td>
</tr>
<tr>
<td>42</td>
<td>3.5</td>
<td>3.0</td>
</tr>
<tr>
<td>48</td>
<td>3.0</td>
<td>2.5</td>
</tr>
<tr>
<td>54</td>
<td>2.5</td>
<td>2.0</td>
</tr>
<tr>
<td>60</td>
<td>2.0</td>
<td>1.5</td>
</tr>
<tr>
<td>66</td>
<td>1.5</td>
<td>1.0</td>
</tr>
</tbody>
</table>

P < 0.001


**ADVANCE: Effect on macrovascular outcomes**

<table>
<thead>
<tr>
<th>Follow-up (months)</th>
<th>Standard control Cumulative incidence (%)</th>
<th>Intensive control Cumulative incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>0.34 (0.24) HR 0.94 (0.84-1.06) P = 0.32</td>
<td>HR 0.99 (0.80-1.20) P = 0.86</td>
</tr>
<tr>
<td>20</td>
<td>HR 0.99 (0.80-1.20) P = 0.86</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>HR 0.99 (0.80-1.20) P = 0.86</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>HR 0.99 (0.80-1.20) P = 0.86</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>HR 0.99 (0.80-1.20) P = 0.86</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>HR 0.99 (0.80-1.20) P = 0.86</td>
<td></td>
</tr>
</tbody>
</table>

NCEP: approach to lipids

Step one - No surprise - lower LDL-C

HPS and CARDS: Benefits of lowering LDL-C in diabetes

<table>
<thead>
<tr>
<th>Event rate (%)</th>
<th>Statin better</th>
<th>Placebo better</th>
<th>P</th>
<th>LDL-C (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPS All diabetes</td>
<td>9.4</td>
<td>12.6</td>
<td>0.73</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes, no CVD</td>
<td>9.3</td>
<td>13.5</td>
<td>0.87</td>
<td>0.0003</td>
</tr>
<tr>
<td>CARDS</td>
<td>5.8</td>
<td>9.0</td>
<td>0.83</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Relative risk

*Statin vs placebo
HPS = Heart Protection Study
CARDS = Collaborative Atorvastatin Diabetes Study

ASCOT-LLA: Statin reduces CV events in DM & HTN

N = 2532, baseline LDL-C 128 mg/dL

23% Risk reduction
P = 0.006

NCEP approach: Step 2, beyond LDL

The concept of "residual dyslipidemia risk"

Residual Risk in Patients Treated With Intensive Statin Therapy

Heart Protection Study

Among Simvastatin-treated patients who entered the trial with LDL-C levels < 116 mg/dL, and who had mean LDL-C levels of ~ 70 mg/dL during the study:

The 5-year risk of a major vascular event was still 18%.
This would equate to a 10-year risk of 35%.
Patients at LDL-C Targets May Benefit From Further Treatment


![Graph showing reduction in major coronary events vs. placebo (%)](image)

**Shortcomings of LDL:** both calculated and measured

- Friedewald equation (LDL-C = TC – HDL-C - TG/5)
  - Cholesterol content in LDL varies between individuals
  - Influenced by metabolic factors (insulin resistance)
  - Changes with statin treatment
  - Less accurate at LDL < 100 mg/dL
  - Less accurate as triglycerides >150 mg/dL
  - Does not represent all atherogenic ApoB-lipoproteins
  - Does not accurately represent the number of LDL particles
- Direct LDL cholesterol measures
  - Poor standardization
  - Less accurate at LDL < 100 mg/dL

**Atherogenic lipoproteins: “non-HDL-C”**

- Very low-density lipoprotein (VLDL)
  - Made in the liver
  - TG-rich
  - Atherogenic
- Intermediate-density lipoprotein (IDL)
  - Formed from VLDL by TG lipolysis
  - Also known as a VLDL remnant particle
  - Atherogenic
- Low-density lipoprotein (LDL)
  - Formed from IDL due to further TG lipolysis
  - Taken up by the liver and other organs via the LDL receptor
  - Major atherogenic particle
- High-density lipoprotein (HDL)
  - Anti-atherogenic, carries cholesterol away from artery wall for metabolism or excretion
  - Other possible antiatherogenic effects include anti-inflammatory and antioxidant actions, and improvement in endothelial function

*Formed in the liver and cleared by LDL receptor.
*Other possible antiatherogenic effects include anti-inflammatory and antioxidant actions, and improvement in endothelial function.

*Formed in the liver and cleared by LDL receptor.*

*Formed in the liver and cleared by LDL receptor.*

*Formed in the liver and cleared by LDL receptor.*

*Formed in the liver and cleared by LDL receptor.*
Are there stronger CVD risk predictors beyond LDL-C?

LDL-C a weaker predictor of CVD vs. non-HDL or ApoB
Combined Analysis of >18,000 patients in TNT & IDEAL trials

<table>
<thead>
<tr>
<th>Measure</th>
<th>Hazard Ratio Model 1*</th>
<th>Hazard Ratio Model 1 + LDL-C</th>
<th>Hazard Ratio Model 1 + Non-HDL</th>
<th>Hazard Ratio Model 1 + ApoB</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>1.15 (1.10-1.20) P = &lt;0.001</td>
<td>0.99 (0.92-0.96) P = 0.002</td>
<td>0.99 (0.97-1.00) P = 0.63</td>
<td></td>
</tr>
<tr>
<td>Non-HDL-C</td>
<td>1.29 (1.15-1.45) P = 0.001</td>
<td>1.31 (1.25-1.40) P = 0.001</td>
<td>1.36 (1.30-1.43) P = 0.002</td>
<td></td>
</tr>
<tr>
<td>ApoB</td>
<td>1.19 (1.14-1.24) P = &lt;0.001</td>
<td>1.24 (1.14-1.36) P = &lt;0.001</td>
<td>1.05 (0.92-1.20) P = 0.47</td>
<td></td>
</tr>
</tbody>
</table>

*Model 1: age, sex and study (TNT / IDEAL)
**Value of the Ration: INTERHEART Study**

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio (90% CI)</th>
<th>1st MI</th>
<th>2nd MI</th>
<th>All MI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>2.9</td>
<td>2.9</td>
<td>2.9</td>
<td>2.9</td>
</tr>
<tr>
<td>4</td>
<td>4.9</td>
<td>4.9</td>
<td>4.9</td>
<td>4.9</td>
</tr>
<tr>
<td>12</td>
<td>12.9</td>
<td>12.9</td>
<td>12.9</td>
<td>12.9</td>
</tr>
</tbody>
</table>

Case-control trial of 30,000 in 52 countries

---

**Do I need to measure ApoB/Apo A ratio or is TC/HDL adequate?**

Answer: minimal incremental predictive value in measuring Apolipoproteins, but huge economic cost

---

**What is perhaps the most common metabolic manifestations of obesity?**
Hypertriglyceridemia Prevalence

US Adult Population
Total = 217 million

TG > 500 mg/dL
2% - 3%
5 - 6 MM Patients

TG 200 - 499 mg/dL
~13%
25 - 27 MM Patients

*This census is outdated as there are roughly 305 million in the US
*Numbers exceeding metabolic syndrome cut-point (>150 mg/dl) are much greater

Estimated from NCEP ATPIII guidelines data; US Census 2003

Clinical Relevance
• Risk for pancreatitis
• Risk for CVD

Clinical Relevance
• Risk for pancreatitis
• Risk for CVD

Does high TG matter or just LDL-C?

Incidence of CHD Events According to Serum LDL-C and TG Concentration*

Baseline LDL-C (mg/dL)

Baseline TG < 200 mg/dL
Baseline TG ≥ 200 mg/dL

<130 130-159 160-189 190

Baseline TG < 200 mg/dL
Baseline TG ≥ 200 mg/dL

* Lipids from 4849 middle-aged men who were followed up for 8 years to record incidence of CHD. Study demonstrated that fasting levels of TGs were an independent risk factor for CHD events, irrespective of serum levels of LDL-C.

CHD = coronary heart disease; LDL-C = low-density lipoprotein cholesterol; TG = triglyceride.

Hypertriglyceridemia Increases CHD Risk
In Patients with good versus bad "Ratios"

Prospective Cardiovascular Multiniter Study PROCAM

Prospective Cardiovascular Multiniter Study PROCAM

CHD events/1000 person-years in 4 years

Baseline TG < 200 mg/dL
Baseline TG ≥ 200 mg/dL

* Bar represents 5% of subjects in which 25% of CHD events occurred
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Do high triglycerides matter? Independent predictor in post-ACS patients


Triglycerides summary
Independent Risk Factor for CHD

- Meta-analysis of 17 prospective studies that evaluated fasting TG levels and CVD endpoints
- 8 studies adjusted for HDL-C
- Results when adjusting for HDL-C
  - Relative risk (RR) = 1.14 for men, RR = 1.37 for women
  - Higher CVD risk for women
- Conclusion: elevated TG is a risk factor for CVD independent of HDL-C and the risk is greater for women
- Note: Triglyceride goals (< 150 mg/dl) are rarely achieved


Impact of LDL Size Differences
At the Same LDL Cholesterol Concentration

Up to 70% More Particles
**High TG lead to a decrease in Particle Size & an increase in Particle Number**

- Fewer Particles
- More Particles

![Diagram showing decrease in particle size and increase in particle number.

**High Triglycerides Are Associated With LDL Subclass Pattern B**

- Pattern A (large, fluffy)
- Pattern B (small, dense)

![Graph showing cumulative percent of triglycerides (TGs) associated with different LDL subclass patterns.

**Small, Dense LDL**

- ↑ susceptibility to oxidation
- ↑ vascular permeability
- Conformational change in ApoB component
- ↓ affinity for LDL receptor for hepatic clearance
- Association with insulin resistance syndrome
- Association with high TG and low HDL-C (atherogenic dyslipidemia phenotype)

![List of characteristics of small, dense LDL.

**Correlates with:**

- TC 198 mg/dL
- LDL-C 130 mg/dL
- TG 90 mg/dL
- HDL-C 50 mg/dL
- Non-HDL-C 148 mg/dL

**Correlates with:**

- TC 210 mg/dL
- LDL-C 130 mg/dL
- TG 250 mg/dL
- HDL-C 30 mg/dL
- Non-HDL-C 180 mg/dL

Otvos JD et al. *Am J Cardiol*. 2002;90:22i-29i.


Outcomes: Technically, Size doesn’t matter
particle number does

• The relationship between small LDL particle size and CHD is intertwined with a complex physiologic syndrome “atherogenic dyslipidemia” which includes high TG, low HDL-C, and increased LDL particle number

• Following multivariate analysis that includes TGs, HDL-C, and LDL-particle number among 17 cross-sectional, 8 prospective and 6 interventional trials:
  – LDL particle size is rarely a significant, independent predictor of CHD events


Women’s Health Study
CVD Relative Risk* and Lipid Quartiles

*Adjusted for aspirin or vitamin E use

Why use Non-HDL-C Goals?
Treatment approach case 1 vs. case 2

<table>
<thead>
<tr>
<th>chol (mg/dL)</th>
<th>Case 1</th>
<th>Case 2</th>
<th>TC= 209 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG=120 mg/dL</td>
<td>400 mg/dL</td>
<td>24 mg/dL</td>
<td>VLDL</td>
</tr>
<tr>
<td>VLDL-C=24 mg/dL</td>
<td>145 mg/dL</td>
<td>LDL-C=89 mg/dL (may not trigger Rx)</td>
<td></td>
</tr>
<tr>
<td>LDL-C=145 mg/dL</td>
<td>40 mg/dL</td>
<td>HDL-C=32 mg/dL</td>
<td></td>
</tr>
<tr>
<td>HDL-C=40 mg/dL</td>
<td>169 mg/dL</td>
<td>Non-HDL-C=177 mg/dL (should trigger Rx)</td>
<td></td>
</tr>
<tr>
<td>Non-HDL-C=169 mg/dL</td>
<td>3.0</td>
<td>TG/HDL-C ratio</td>
<td></td>
</tr>
<tr>
<td>TG/HDL-C ratio=3.0</td>
<td>6.5</td>
<td>TCHDL-C ratio</td>
<td></td>
</tr>
<tr>
<td>TCHDL-C ratio=6.5</td>
<td>209 mg/dL</td>
<td>TC=209 mg/dL</td>
<td></td>
</tr>
</tbody>
</table>

HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; TC=total cholesterol; VLDL=very low-density lipoprotein.
Because Non-HDL contains Apo-B, all of these particles are involved in Atherogenesis

All ApoB lipoproteins: LDL, IDL, VLDL, RLP

- IDA enters via through receptor-mediated uptake
- IDA 
  - LDL: enhances uptake and removal of IDA
  - IDL: enables other cholesterol uptake
  - HDL: preferentially carries cholesterol and the cholesterol esters to liver
  - IDA uptake involves a decrease in IDA levels

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An Unmet Clinical Need for TG Reduction in Insulin resistant patients: Rx options

- Niacin
- Omega 3’s
- Fibrates
- Sirtans

Fibrates
Primary and Secondary Prevention

- Primary Prevention
- Secondary Prevention


Niacin vs. Placebo among Insulin Resistance Patients: 6-yr AMI rate by baseline FPG

<table>
<thead>
<tr>
<th>FBG, mg/dL</th>
<th>Placebo</th>
<th>Niacin</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;95</td>
<td>20</td>
<td>20</td>
<td>0.70</td>
</tr>
<tr>
<td>95-104</td>
<td>15</td>
<td>15</td>
<td>0.76</td>
</tr>
<tr>
<td>105-125</td>
<td>10</td>
<td>10</td>
<td>0.75</td>
</tr>
<tr>
<td>126+</td>
<td>5</td>
<td>5</td>
<td>0.43</td>
</tr>
</tbody>
</table>

n=1119 for niacin; n=2787 for placebo.
* z for interaction = –0.44 (p=0.66); indicates homogeneity.


Addition of Omega-3 FA esters 4 g/day in Patients Taking Simvastatin with Triglycerides 200-499 mg/dL

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Simvastatin + Omega-3 (n=122)</th>
<th>Simvastatin + Placebo (n=132)</th>
<th>Median % Chg*</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-HDL-C</td>
<td>120 116 116</td>
<td>129 116 116</td>
<td>-6.3</td>
<td>-0.0001</td>
<td></td>
</tr>
<tr>
<td>TG</td>
<td>156 146 146</td>
<td>156 146 146</td>
<td>-3.9</td>
<td>-0.0001</td>
<td></td>
</tr>
<tr>
<td>HDL-C</td>
<td>53 37 37</td>
<td>53 37 37</td>
<td>-23.2</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Apo B</td>
<td>48 48 48</td>
<td>48 48 48</td>
<td>-23.2</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>VLDL-C</td>
<td>48 48 48</td>
<td>48 48 48</td>
<td>-14.6</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>LDL-C</td>
<td>91 88 88</td>
<td>91 88 88</td>
<td>+3.5</td>
<td>&lt;0.0005</td>
<td></td>
</tr>
</tbody>
</table>

*Response to the addition of Omega-3 fatty acids, 4 g/day after 8 weeks of simvastatin 40 mg therapy during lead-in

Suggested Treatment Goals
In Dyslipidemia Patients at High Risk

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LDL-C goal (mg/dL)</th>
<th>Non-HDL-C goal (mg/dL)</th>
<th>ApoB goal (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest-risk patients:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Known CVD</td>
<td>&lt;100</td>
<td>&lt;150</td>
<td>&gt;90</td>
</tr>
<tr>
<td>• Diabetes + ≥ 1 major CVD risk factor*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-risk patients:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• No diabetes or known CVD and ≥ 2 major CVD risk factors*</td>
<td>&lt;100</td>
<td>&lt;130</td>
<td>&gt;90</td>
</tr>
<tr>
<td>• Diabetes without major CVD risk factors*</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Lipoprotein Management in Patients with Cardiometabolic Risk (Diabetes Care 2008; 31:611-622.
CVD = cardiovascular disease.
* Major CVD risk factors = smoking, HTN, family history of premature coronary artery disease.
Don’t forget Lifestyle…Lyon Heart Study

- Numbers in bars are # of events

Guess my syndrome (X)?

Conclusion

- Insulin resistance (metabolic syndrome) is a growing epidemic
- Atherogenic dyslipidemia mediates the increased risk for CVD
- The strongest predictors of CVD include:
  - TC/HDL ratio (or ApoB/Apo A ratio)
  - Non-HDL cholesterol (VLDL, LDL, IDL)
  - LDL is actually a weaker CVD risk predictor
- Nonetheless, achieving LDL goals is the first step
- Next, manage high TG and low HDL
  - Exercise
  - Dietary modification
  - Omega-3s, Niacin, Fibrates
- Though further outcome studies are warranted
Acknowledgements

- AHA Spotlight lipid group