“Aggressive Lipid Management for Diabetes”

‘Practical Ways to Achieve Targets in Diabetes Care’
Keystone, CO
July 16, 2011

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Professor of Physiology and Biophysics
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University of Colorado Anschutz Medical Campus
Duality of Interests

- Advisory Boards, Consultant
  - Amylin
  - Esperion
  - Genentech
  - Genfit
  - GTC Nutrition
  - Johnson & Johnson
  - Lilly
  - Merck
  - Pfizer
  - Regulus
  - sanofi-aventis

- Grants/Research Fellowships
  - Diadexus
  - GSK
  - sanofi-aventis

- Educational Venues
  - AccelMed
  - Cardiometabolic Health Congress
  - Vindico
Influence of Multiple Risk Factors on CVD Death

Multiple Risk Factor Intervention Trial

RFs:
- Smoking
- Hyperlipidemia
- Hypertension

Age-Adjusted CVD Death Rate per 10,000 py

No Diabetes
Diabetes

Pathogenesis of Increased Atherosclerosis in Diabetes

- Metabolic factors
  - Glucose
  - Fatty acids
  - Lipoproteins
- ↑ Inflammation
- ↑ Oxidation/Glycooxidation
- ↑ Endothelial dysfunction
- Pro-thrombotic state
  - ↑ thrombosis
  - ↓ fibrinolysis
What Are the Risk Factors for CVD in Patients with Type 2 Diabetes?

- Hypertension
- Dyslipidemia
- Glycemia
- Inflammation
- Thrombosis
What Are the Risk Factors for CVD in Patients with Type 2 Diabetes?

- Hypertension
- Dyslipidemia
- Glycemia
- Inflammation
- Thrombosis
Let’s start with Type 2 Diabetes
UKPDS CHD (n=280)
Stepwise Selection of Risk Factors
Adjusted for Age and Sex

<table>
<thead>
<tr>
<th>Position in Model</th>
<th>Variable</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>LDL-C</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Second</td>
<td>HDL-C</td>
<td>0.0001</td>
</tr>
<tr>
<td>Third</td>
<td>Hb A1c</td>
<td>0.0022</td>
</tr>
<tr>
<td>Fourth</td>
<td>SBP</td>
<td>0.0065</td>
</tr>
<tr>
<td>Fifth</td>
<td>Smoking</td>
<td>0.056</td>
</tr>
</tbody>
</table>
UKPDS: CHD Hazard Ratios and LDL Cholesterol

LDL Cholesterol (mg/dl)

<117 117-150 >150

CHD Hazard Ratios

CHD
MI

BMJ 316:823, 1998
UKPDS: CHD Hazard Ratios and Triglycerides

CHD Hazard Ratios

- <110
- 110-168
- >168

Triglycerides (mg/dl)

CHD

MI

BMJ 316:823, 1998
Fasting TGs and Risk for CHD Death
The Paris Prospective Study

Mean Annual CHD Mortality Rate/1000

<table>
<thead>
<tr>
<th>Cholesterol (mg/dL)</th>
<th>TG≤123 mg/dL</th>
<th>TG&gt;123 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤220</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>&gt;220</td>
<td>1.5</td>
<td>6</td>
</tr>
</tbody>
</table>

Adapted from Fontbonne A et al. Diabetologia 32:300, 1989
UKPDS: CHD Hazard Ratios and HDL Cholesterol

CHD Hazard Ratios

<37 37-44 >44

HDL Cholesterol (mg/dl)

CHD
MI

BMJ 316:823-29, 1998
LDL vs. Non-HDL Cholesterol in Patients with T2DM: FCS, FOS, LRCF, and MRFIT


N = 12,660 men & 6,721 women
Lipoproteins in Patients with Type 2 Diabetes

‘Metabolic Syndrome-Like’

- ↑ TG
- ↑ VLDL-C
- ↑ remnant/IDL-C
- ↓ HDL-C
- ↓ apo A-1
- ± ↑ LDL-C

- ± ↑ apo B
- ↑ Lipoprotein (a)
- renal disease
- ↑ Lipoprotein density
- LDL
- HDL
High Incidence of Dyslipidaemia in Patients with Diabetes


*245 men with diabetes and 253 women with diabetes aged ≥18 years from NHANES 1999-2000.
Can CVD Risk be Reduced in Patients with T2DM?
# CVD ‘Primary Prevention’ with Statins in T2DM

<table>
<thead>
<tr>
<th>Study</th>
<th>Drug</th>
<th>n</th>
<th>LDL-C</th>
<th>LDL-C % ↓</th>
<th>MI %</th>
<th>CVD Mort%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CARDS</td>
<td>Atorva 10 mg</td>
<td>2838</td>
<td>118 mg/dl</td>
<td>40</td>
<td>RRR 35*</td>
<td>RRR 38*</td>
</tr>
<tr>
<td>ASPEN</td>
<td>Atorva 10 mg</td>
<td>1905</td>
<td>114 mg/dl</td>
<td>30</td>
<td>RRR 19*</td>
<td>RRI 25↑</td>
</tr>
<tr>
<td>HPS</td>
<td>Simva 40 mg</td>
<td>5963</td>
<td>124 mg/dl</td>
<td>31</td>
<td>RRR 25*</td>
<td>RRR 20*</td>
</tr>
<tr>
<td>ASCOT-LLA</td>
<td>Atorva 10 mg</td>
<td>2532</td>
<td>127 mg/dl</td>
<td>29</td>
<td>RRR 16</td>
<td>RRI 24↑</td>
</tr>
</tbody>
</table>
TNT: Substantial Risk Persists Despite Maximal Dose Statin in Patients With CHD

- Patients with Major Cardiovascular Event (%)

- Time to First Major Cardiovascular Event (years)

- All Metabolic Syndrome
  - Atorvastatin 10 mg (N=2820)
  - P<0.0001
  - Atorvastatin 80 mg (N=2764)
- All Metabolic Syndrome, No Diabetes
  - Atorvastatin 10 mg (N=2191)
  - P=0.0002
  - Atorvastatin 80 mg (N=2162)

TNT=Treating to New Targets; CHD=coronary heart disease

## Fibrate CVD Trials in T2DM

<table>
<thead>
<tr>
<th>Study</th>
<th>Drug</th>
<th>n</th>
<th>TG (Criteria)</th>
<th>TG ↓</th>
<th>Primary Endpoint ↓</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA-HIT (DM)</td>
<td>Gemf</td>
<td>2531 (550)</td>
<td>160 mg/dl (&lt;300)</td>
<td>31%</td>
<td>24%*</td>
</tr>
<tr>
<td>BIP (DM)</td>
<td>Beza</td>
<td>3090 (330)</td>
<td>145 mg/dl (&lt;300)</td>
<td>21%</td>
<td>7%</td>
</tr>
<tr>
<td>FIELD (DM)</td>
<td>Feno</td>
<td>9795</td>
<td>156 mg/dl (90-450)</td>
<td>29%</td>
<td>11%</td>
</tr>
<tr>
<td>ACCORD-LIPID (DM)</td>
<td>Feno</td>
<td>2532</td>
<td>162 mg/dl (&lt;400)</td>
<td>20%</td>
<td>8%</td>
</tr>
</tbody>
</table>
Hypertriglycerideridemia: The Problems

- The genetic disorders are largely without genes.
- The acquired disorders are almost infinite in number.
- The clinical trials with TG lowering drugs have suffered:
  - design
  - number
  - results are hypothesis-generating at best
- Is it the TG-rich particles that confer risk for atherosclerotic CVD and/or the company they keep?

Goldberg IJ et al, ATVB April 2011 Epub
FIELD Study: Fenofibrate and the Metabolic Syndrome and CVD Event Risk

Adjusted for age, gender, and A1c

Scott R et al, *Diabetes Care* 32:493, 2009
Lipoprotein Classes

- Chylomicrons
- Remnants
- VLDL
- IDL
- HDL
- LDL

Diameter (nm) vs. Density (g/ml)

Apo B Containing

HDL

HDL$_2$

HDL$_3$

LDL

IDL

VLDL

Chylomicrons Remnants

Density (g/ml)

Diameter (nm)
## Coronary Drug Project: 15-Year Mortality Results

<table>
<thead>
<tr>
<th></th>
<th>Niacin n=1,119</th>
<th>Placebo n=2,789</th>
<th>Risk Reduction</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Mortality</td>
<td>52%</td>
<td>58%</td>
<td>-11%</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>FBG &lt; 100 mg/dL</td>
<td>48%</td>
<td>53%</td>
<td>-9%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>FBG ≥ 100 mg/dL</td>
<td>56%</td>
<td>63%</td>
<td>-12%</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>CHD Mortality</td>
<td>36%</td>
<td>41%</td>
<td>-12%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Coronary Drug Project: Niacin in patients with diabetes
– post hoc analysis at 15 yr demonstrates benefit.
Is it secondary to ↑HDL?
What about Lipids and Type 1 Diabetes?
Determine the *prevalence* of coronary calcification in Type 1 Diabetes

Identify *risk factors* for coronary calcification in Type 1 Diabetes

Measure *progression* of coronary calcification in Type 1 Diabetes
Lipid Levels Adjusted for Age and Waist/Hip Ratio in Women with T1DM: CACTI

<table>
<thead>
<tr>
<th>Lipids (mg/dl)</th>
<th>Non-DM</th>
<th>T1-DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trig</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Wadwa RP et al, Diabetes Care, 28:1051, 2005

* p < 0.01 for all

(n=354) (n=382)
Lipid Levels Adjusted for Age and Waist/Hip Ratio in *Men* with T1DM: CACTI

Wadwa RP et al, Diabetes Care, 28:1051, 2005
Serum Lipids and Glucose Control

The SEARCH for Diabetes in Youth Study

Diana B. Petitti, MD, MPH; Giuseppina Imperatore, MD, PhD; Shana L. Palla, MS; Stephen R. Daniels, MD, PhD; Lawrence M. Dolan, MD; Ann K. Kershner, MD; Santica Marcovina, PhD, ScD; David J. Pettitt, MD; Catherine Pihoker, MD; for the SEARCH for Diabetes in Youth Study Group

Objective: To assess the relationship of serum lipid concentrations with glucose control in youth with diabetes mellitus.

Design: Cross-sectional analyses of data from the SEARCH for Diabetes in Youth study.

Setting: Multicenter study of youth with diabetes onset at younger than 20 years.

Patients/Participants: Nineteen hundred seventy-three SEARCH participants aged 10 years or older with hemoglobin A1c and fasting total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides measured at the SEARCH study examination.

Main Exposure: Hemoglobin A1c.

Outcome Measure: Lipid concentrations.

Results: There were significant trends of higher levels of TC, LDL-C, triglyceride, and non-HDL-C (but not HDL-C) with higher hemoglobin A1c concentrations for both diabetes types. The slopes of TC increase were 7.8 mg/dL (0.20 mmol/L) per unit increase in hemoglobin A1c for type 1 and 8.1 mg/dL (0.21 mmol/L) for type 2. Levels of TC, LDL-C, triglyceride, and non-HDL-C were all significantly higher (all P values < .001) in type 2 than in type 1 diabetes (mean differences in milligrams per deciliter [millimoles per liter], +13.6 [+0.35] for TC; +8.3 [+0.22] for LDL-C; +66.3 [+0.75] for triglyceride; +25.5 [+0.66] for non-HDL-C). Levels of HDL-C were lower in youth with type 2 diabetes (mean difference, –11.9 mg/dL [-0.31 mmol/L]). Among those with type 1 diabetes in poor glycemic control, 35%, 27%, and 12% had high concentrations of TC (≥200 mg/dL [5.17 mmol/L]), LDL-C (≥130 mg/dL [3.36 mmol/L]), and triglycerides (≥200 mg/dL [2.26 mmol/L]), respectively. In youth with type 2 diabetes in poor glycemic control, percentages with high levels of TC, LDL-C, and triglycerides were 65%, 43%, and 40%, respectively.

Conclusions: Glycemic control and lipid levels are independently associated in youth with both type 1 and type 2 diabetes.

Arch Pediatr Adolesc Med. 2007;161:159-163

In adults with diabetes, the risk of atherosclerotic cardiovascular disease morbidity and mortality is greatly increased. Diabetes melliticaemic control extended to adolescents with type 1 diabetes. The benefits were long-lasting. Glycemic control also reduces the likelihood of microvascular complications.
Serum Lipids and HbA1c: Search of Diabetes in Youth Study

Lipid-Related Risk Factors for CHD in Type 1 Diabetes: EDC

<table>
<thead>
<tr>
<th></th>
<th>No CHD (n=59)</th>
<th>CHD (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>35.0 (6.0)</td>
<td>34.5 (6.0)</td>
</tr>
<tr>
<td>A1c (%)</td>
<td>10.5 (1.5)</td>
<td>10.7 (1.8)</td>
</tr>
<tr>
<td>Total Cholesterol (mM)</td>
<td>4.87 (0.83)</td>
<td>5.17 (1.18)</td>
</tr>
<tr>
<td>Triglycerides (mM)</td>
<td>0.72 (0.51-0.90)</td>
<td>1.17 (0.81-1.57) ***</td>
</tr>
<tr>
<td>HDL Cholesterol (mM)</td>
<td>1.51 (0.33)</td>
<td>1.26 (0.32) ***</td>
</tr>
<tr>
<td>LDL Cholesterol (mM)</td>
<td>2.96 (0.78)</td>
<td>3.26 (1.03)</td>
</tr>
<tr>
<td>Non-HDL Cholesterol (mM)</td>
<td>3.36 (0.89)</td>
<td>3.91 (1.22) **</td>
</tr>
<tr>
<td>Apo B (mg/DL)</td>
<td>95 (19)</td>
<td>112 (31) ***</td>
</tr>
<tr>
<td>Apo A-1/Apo B</td>
<td>2.49 (0.59)</td>
<td>2.90 (0.67) ***</td>
</tr>
</tbody>
</table>

Metabolic Phenotypes and Risk of Premature Death: FinnDiane

(n = 4197)

What is it about the metabolic syndrome in patients with T1DM that confers the increased risk for CHD?
Effect of Excessive Weight Gain With Intensive Therapy of Type 1 Diabetes on Lipid Levels and Blood Pressure

Results From the DCCT

Jonathan O. Purnell, MD; John E. Hokanson, MPH, PhD; Santica M. Marcovina, PhD; Michael W. Steffes, MD, PhD; Patricia A. Cleary, MS; John D. Brunzell, MD

Context.—Intensive treatment of type 1 diabetes results in greater weight gain than conventional treatment.

Objective.—To determine the effect of this weight gain on lipid levels and blood pressure.

Design.—Randomized controlled trial; ancillary study of the Diabetes Control and Complications Trial (DCCT).

Setting.—Twenty-one clinical centers.

Participants.—The 1168 subjects enrolled in DCCT with type 1 diabetes who were aged 18 years or older at baseline.

Intervention.—Randomized to receive either intensive (n = 586) or conventional (n = 582) diabetes treatment with a mean follow-up of 6.1 years.

Main Outcome Measures.—Plasma lipid levels and blood pressure in each treatment group categorized by quartile of weight gain.

Results.—With intensive treatment, subjects in the fourth quartile of weight gain had the highest body mass index (BMI) (a measure of weight adjusted for height), blood pressure, and levels of triglyceride, total cholesterol, low-density lipoprotein cholesterol (LDL-C), and apolipoprotein B compared with the other weight gain quartiles with the greatest difference seen when compared with the first quartile (mean values for the highest and lowest quartiles: BMI, 31 vs 24 kg/m²; blood pressure, 120/77 mm Hg vs 113/73 mm Hg; triglyceride, 0.99 mmol/L vs 0.79 mmol/L; [88 mg/dl vs 70 mg/dl]; LDL-C, 3.15 mmol/L vs 2.74 mmol/L [122 mg/dL vs 106 mg/dL]; and apolipoprotein B, 0.89 g/L vs 0.78 g/L; all P<.001). In addition, the fourth quartile group had a higher waist-to-hip ratio; more cholesterol in the very low density lipoprotein, intermediate density lipoprotein, and dense LDL fractions; and lower high-density lipoprotein cholesterol and apolipoprotein A-I levels compared with the first quartile. Baseline characteristics were not different between the first and fourth quartiles of weight gain with intensive therapy except for a higher hemoglobin A₁c in the fourth quartile. Weight gain with conventional therapy resulted in smaller increases in BMI, lipids, and systolic blood pressure.

Conclusions.—The changes in lipid levels and blood pressure that occur with excessive weight gain with intensive therapy are similar to those seen in the insulin resistance syndrome and may increase the risk of coronary artery disease in this subset of subjects with time.
# Patients with Type 1 Diabetes in DCCT

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>Intensive</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%)</td>
<td>9.2</td>
<td>7.3</td>
<td>&lt;0.000001</td>
</tr>
<tr>
<td>TG (mg/dl))</td>
<td>87</td>
<td>80</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LDL-C</td>
<td>114</td>
<td>111</td>
<td>0.05</td>
</tr>
<tr>
<td>Apo B</td>
<td>86</td>
<td>83</td>
<td>0.01</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>12.5</td>
<td>10.7</td>
<td>0.03</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25</td>
<td>27</td>
<td>1x10⁻¹⁴</td>
</tr>
</tbody>
</table>

Clinical Characteristics: DCCT Cohort at Year 11 of EDIC

<table>
<thead>
<tr>
<th></th>
<th>INTENSIVE</th>
<th>CONVENTIONAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>45 yr</td>
<td>45 yr</td>
</tr>
<tr>
<td><strong>Duration of DM</strong></td>
<td>24 yr</td>
<td>23 yr</td>
</tr>
<tr>
<td><strong>Cigarettes</strong></td>
<td>14%</td>
<td>11%</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>28.4 kg/m²</td>
<td>27.6 kg/m²</td>
</tr>
<tr>
<td><strong>BP</strong></td>
<td>120/75</td>
<td>121/75</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>38%</td>
<td>41%</td>
</tr>
<tr>
<td><strong>Beta blockers</strong></td>
<td>3%</td>
<td>7%</td>
</tr>
<tr>
<td><strong>ACE inhibitors</strong></td>
<td>38%</td>
<td>41%</td>
</tr>
</tbody>
</table>
Clinical Characteristics: DCCT Cohort at Year 11 of EDIC

<table>
<thead>
<tr>
<th></th>
<th>INTENSIVE</th>
<th>CONVENTIONAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>112 mg/dl</td>
<td>109 mg/dl</td>
</tr>
<tr>
<td>Non-HDL-C</td>
<td>131 mg/dl</td>
<td>126 mg/dl</td>
</tr>
<tr>
<td>HDL-C</td>
<td>55 mg/dl</td>
<td>55 mg/dl</td>
</tr>
<tr>
<td>Statins</td>
<td>34%</td>
<td>33%</td>
</tr>
<tr>
<td>AER</td>
<td>54 mg/24 hr</td>
<td>116 mg/24 hr*</td>
</tr>
<tr>
<td>&gt; 300 mg/24 hr</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>Creat &gt; 2.0</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>A1c</td>
<td>7.9%</td>
<td>7.8%</td>
</tr>
</tbody>
</table>
Is Insulin Resistance in T1DM a New Concept?

- n = 51
- Insulin tolerance test - Glucose assimilation index derived from rate of glucose decrease after IV insulin
- Subjects:
  - All BMI < 30
  - Duration 15-40 years
  - 3 with TGs > 150
  - Insulin dose: 28-88 units/day
- Insulin resistance independent of glycemic control

<table>
<thead>
<tr>
<th></th>
<th>Type 1 Female</th>
<th>Non-DM Female</th>
<th>Type 1 Male</th>
<th>Non-DM Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>21</td>
<td>22</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>Age</td>
<td>44±9</td>
<td>44±8</td>
<td>47±10</td>
<td>47±6</td>
</tr>
<tr>
<td>Duration</td>
<td>22±8</td>
<td>NA</td>
<td>23±8</td>
<td>NA</td>
</tr>
<tr>
<td>BMI</td>
<td>25.8±4.3</td>
<td>25.8±4.3</td>
<td>28.3±4.3</td>
<td>27.2±3.6</td>
</tr>
<tr>
<td>TG</td>
<td>69±42*</td>
<td>99±40</td>
<td>70±22*</td>
<td>126±73</td>
</tr>
<tr>
<td>HDL-C</td>
<td>56±13</td>
<td>57±10</td>
<td>61±30*</td>
<td>45±9</td>
</tr>
<tr>
<td>LDL-C</td>
<td>66±25*</td>
<td>95±29</td>
<td>70±25*</td>
<td>101±25</td>
</tr>
<tr>
<td>Statins</td>
<td>52%*</td>
<td>9%</td>
<td>68%*</td>
<td>15%</td>
</tr>
<tr>
<td>OCP</td>
<td>86%</td>
<td>73%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>A1c</td>
<td>7.5±0.9*</td>
<td>5.4±0.3</td>
<td>7.5±0.8*</td>
<td>5.4±0.3</td>
</tr>
</tbody>
</table>
CACTI Clamp Study Results

Adjusted for age, visceral fat area, fasting glucose, final clamp glucose and insulin.  * P <0.0001; ** P<0.001 vs. same-sex controls;

Insulin Resistance is not Correlated with Glycemic Control

Clamp FFA

* p < 0.0001; §Least square means adjusted for age, BMI, gender, starting glucose concentration, and time point insulin level.

### Insulin Resistance and Clamp FFA Correlate with CAC

Spearman correlation coefficients (p-value) between measures of IR and measures of CAC:

<table>
<thead>
<tr>
<th></th>
<th>CAC volume (visit 3)</th>
<th>CAC progression (baseline to v3)</th>
<th>CAC progression (visit 2 to v3)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GIR (mg/kg/min)</strong></td>
<td>-0.45 (0.0026)</td>
<td>-0.51 (0.0007)</td>
<td>-0.41 (0.0073)</td>
</tr>
<tr>
<td><strong>Stage 1 FFA</strong></td>
<td>0.30 (0.054)</td>
<td>0.32 (0.04)</td>
<td>0.31 (0.047)</td>
</tr>
<tr>
<td><strong>Stage 2 FFA</strong></td>
<td>0.39 (0.01)</td>
<td>0.43 (0.005)</td>
<td>0.40 (0.0097)</td>
</tr>
</tbody>
</table>
Insulin Resistance in Adolescents with Type 1 Diabetes

Nadeau K et al, JCEM 95:513, 2010
IR Tertiles highest vs. lowest

Maahs DM et al, *Diabetes* 59:1, 2010
What about CVD risk reduction in T1DM by lipid management?
Effects of Simvastatin on First Major CVD Event in Diabetes: HPS

<table>
<thead>
<tr>
<th>Type of diabetes</th>
<th>Type 1</th>
<th>53/302 (17.5%)</th>
<th>0.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2</td>
<td>558/2665 (20.9%)</td>
<td>695/2683 (25.9%)</td>
<td></td>
</tr>
<tr>
<td>No diabetes</td>
<td>1432/7291 (19.6%)</td>
<td>1837/7282 (25.2%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HbA1c (%)</th>
<th>&lt;7.0</th>
<th>294/1610 (18.3%)</th>
<th>0.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥7.0</td>
<td>301/1334 (22.6%)</td>
<td>373/1355 (27.5%)</td>
<td></td>
</tr>
<tr>
<td>No diabetes</td>
<td>1432/7291 (19.6%)</td>
<td>1837/7282 (25.2%)</td>
<td></td>
</tr>
</tbody>
</table>

| All patients     | 2033/10269 (19.8%) | 2585/10267 (25.2%) | 0.76 (0.72-0.81) p<0.0001 |

What Are the Cholesterol Goals in Diabetes?

- LDL cholesterol
  - < 100 mg/dl always?
- Non-HDL cholesterol
  - < 130 mg/dl always?
- VLDL cholesterol
  - TG < 150 mg/dl?
- HDL cholesterol
  - > 40 – men?
  - > 50 – women?
### ADA/ACC Lipid Goals

<table>
<thead>
<tr>
<th>CHD or DM + 1 Risk Factor</th>
<th>LDL-C</th>
<th>Non-HDL-C</th>
<th>Apo B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 70 mg/dl</td>
<td>&lt; 100 mg/dl</td>
<td>&lt; 80 mg/dl</td>
</tr>
<tr>
<td>≥ 2 Risk Factors or DM</td>
<td>&lt; 100 mg/dl</td>
<td>&lt; 130 mg/dl</td>
<td>&lt; 90 mg/dl</td>
</tr>
</tbody>
</table>

Until ATP-IV
(Opinion)

- Type 2 Diabetes
  - Statin for all
  - Fibrate when fasting TG > 200 mg/dl

- Type 1 Diabetes
  - Statin to lower LDL-C to < 100 mg/dl

Otherwise ATP-III guidelines