



Population-Based Lipid Screening in the Era of a Childhood Obesity Epidemic: The Importance of Non-HDL Cholesterol Assessment

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Disclosures

- No disclosures

Background

- Lipid abnormalities contribute to accelerated atherosclerosis in youth.
- Original guidelines were aimed primarily at detecting familial dyslipidemias through screening based on family history.

Anonymous: Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. Pediatrics 1992; 89:525-584

Background

- Newer lipid guidelines have attempted to address the impact of the childhood obesity epidemic and to acknowledge pediatric clinical trials of more effective medications for treatment.

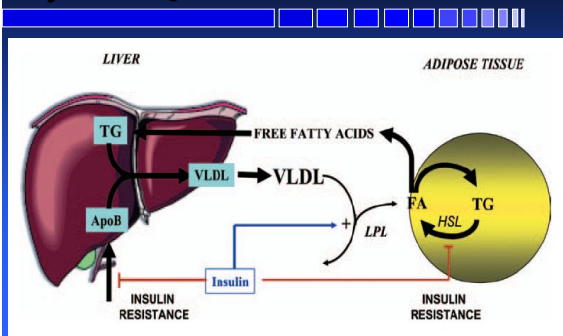
Daniels SR, Greer FR, Committee on Nutrition, AAP: Lipid screening and cardiovascular health in childhood. *Pediatrics* 2008; 122:198-208

McGrindle BW, Urbina EM, Dennison BA, Jacobson MS, Steinberger J, Rocchini AP, Hayman LL, Daniels SR: Drug therapy of high-risk lipid abnormalities in children and adolescents. *AHA Scientific Statement. Circulation* 2007; 115:1948-1967

Background

- Obesity-related lipid abnormalities consist of a lipid triad:
 - High triglycerides
 - Low HDL
 - Small, dense LDL
 - (High non-HDL, apolipoprotein B)

Alterations in plasma and tissue lipids associated with obesity and the metabolic syndrome. Aguilera et al. *Clin Sci* 2008; 114:183-193

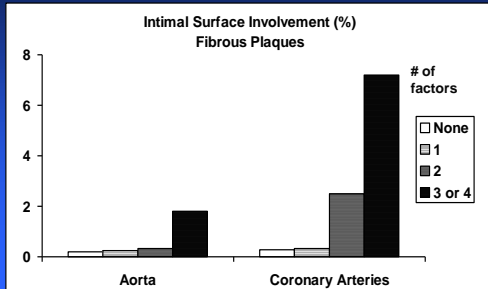


Background

Cardiometabolic Syndrome

↓
Dyslipidemia
Insulin resistance
Type 2 diabetes
Hypertension
Inflammation

Association Between Multiple Cardiovascular Risk Factors and Atherosclerosis in Children and Young Adults. Berenson et al. NEJM 1998



Background

- An imperative exists for universal lipid screening.
- Clinical practice-based screening with fasting lipid profiles may not be feasible or cost-effective.
- Non-fasting assessment does not allow accurate calculation of LDL due to post-prandial hypertriglyceridemia.

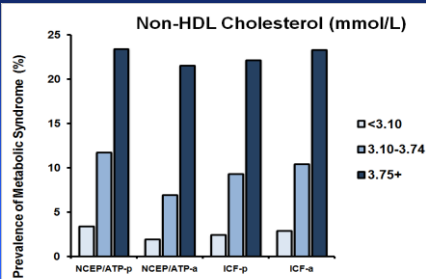
Background

- School-based screening is more likely to achieve universal assessment.
- Non-fasting fingerstick (capillary) assessment of total cholesterol and HDL allows calculation of non-HDL levels.
- Non-HDL = Total cholesterol - HDL

Background

- Non-HDL levels accurately reflect levels of both LDL and VLDL (apolipoprotein B containing particles).
- Non-HDL is elevated in both familial and obesity-related dyslipidemias, and has been shown to be an important correlate with cardiometabolic risk and accelerated atherosclerosis.

Non-HDL cholesterol concentration is associated with the metabolic syndrome among US youth aged 12-19 years. Li et al. J Pediatr 2011; 158:201-7



Background



- New NIH Integrated Pediatric CV Risk Guidelines will recommend universal lipid screening, which may include non-fasting non-HDL assessment.
- These guidelines will specify the contribution of other risk factors / risk conditions to decision-making regarding interventions, including use of lipid-lowering medication.

Objectives



- To determine:
 - The prevalence of lipid abnormalities in a population-based universal screening of adolescents.
 - To determine associations of lipid values with measures of adiposity, family history and blood pressure.
 - To determine the proportion of adolescents who would meet criteria for lipid-lowering drug therapy.

Methods



- Heart Niagara Inc. Heart Healthy Schools' Program:
 - Curriculum enrichment program that targets the entire population of adolescents in grade 9 physical education class in Niagara Region, Ontario.
 - Provides personalized information regarding cardiometabolic risk and lifestyle.
 - Identifies adolescents and their families at increased risk for premature CV disease.

Methods



- Measurements:
 - Standardized questionnaire
 - Height, weight, waist circumference:
 - BMI (WHO) – %ile class, z score
 - WC (NHANES) – %ile class, WC / height
 - Blood pressure – 4th Report classification
 - Fingertick (capillary) total cholesterol and HDL
 - Non-HDL
 - Total cholesterol / HDL

Methods



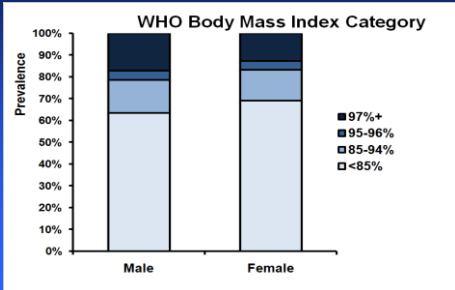
- Data analysis:
 - Means with standard deviations, frequencies
 - General linear regression modeling

Results Participants



- 4104 (84%) of 4884 Grade 9 students participated in the 2009-2010 school year
 - 51% males
 - Mean age 14.6 ± 0.5 years
 - Positive family history of premature CV disease in 33%
 - Diabetes in 0.4%
 - Current smoker in 2.8%

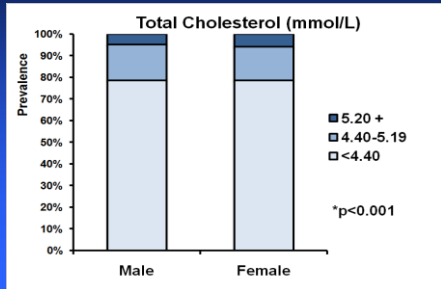
Results Adiposity



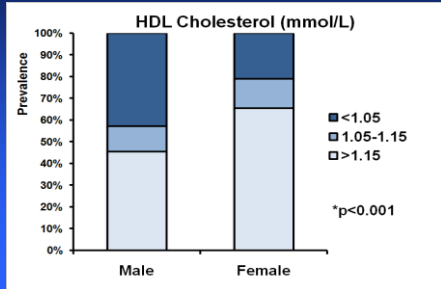
Results Lipid values

- 3283 (80%) of 4104 participants had lipids assessed.
- Total cholesterol 3.86 ± 0.75 mmol/L
- HDL cholesterol 1.22 ± 0.33 mmol/L
- Non-HDL cholesterol 2.64 ± 0.73 mmol/L
- Total / non-HDL ratio 3.38 ± 1.21
- No relation to age
- Significant gender differences

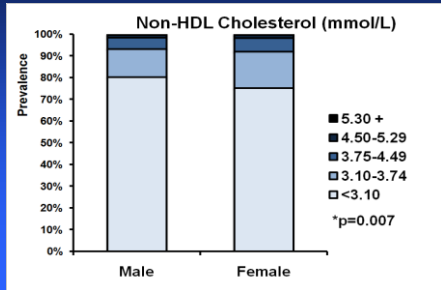
Results Lipid abnormalities



Results Lipid abnormalities



Results Lipid abnormalities



Results Lipid values

- Total cholesterol: HDL ratio:
 - Males 3.50 ± 1.30
 - Females 3.25 ± 1.09 p<0.001

Results Blood pressure



- 3968 (97%) of 4104 participants had blood pressure assessed.
- Blood pressure category:
 - Normal <90%ile 91.4%
 - Pre-HTN 90-94%ile 5.1%
 - Stage 1 HTN 95-98%ile 2.8%
 - Stage 2 HTN >99%ile 0.7%
- No significant gender differences

Results: Relation to family history



- There was no significant relationship between a positive family history of premature CV disease and any lipid variable.

Results Relation to blood pressure

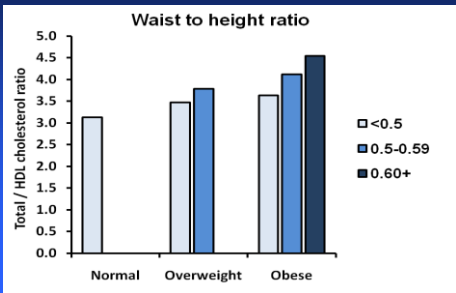


- Overall, significant though weak relationships (R^2 0.0035 to 0.0154) between blood pressure category and lipid variables.
- Strongest relationship was with non-HDL > TChol/HDL ratio > TChol > HDL; stronger for systolic vs. diastolic BP.
- Blood pressure category: non-HDL
 - Normal <90%ile 3.84 mmol/L
 - Pre-HTN 90-94%ile 4.03 mmol/L
 - Stage 1+2 HTN 95%ile + 4.15 mmol/L

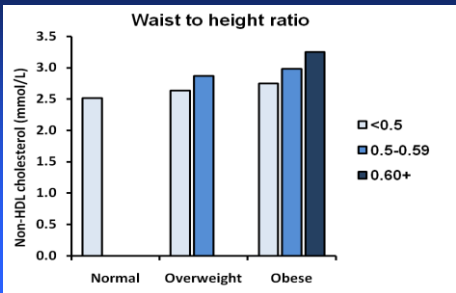
Results Relation to adiposity

- Overall, significant though weak relationships between adiposity variables and lipid variables.
- TChol R^2 0.0124 to 0.0283
- HDL R^2 0.0538 to 0.0880
- Non-HDL R^2 0.0565 to 0.0794
- TC/HDL R^2 0.0969 to 0.1195
- Relationships with adiposity
 - TC/HDL > non-HDL > HDL > TChol
 - Waist measures > BMI

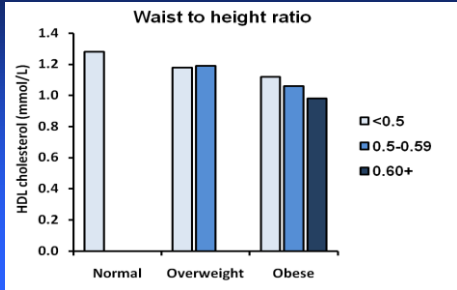
Results Relation to adiposity



Results Relation to adiposity



Results Relation to adiposity



Results Screening utility

- Application of NIH Integrated CV Risk Guidelines (not yet released)
- Explicit mechanisms for simultaneously considering multiple risk factors and risk conditions in clinical decision-making.
- Will recommend universal lipid screening at age 9-11 years.

Guidelines for Medication Use in Childhood and Adolescent Obesity

Risk Factors

Positive Family History

Premature CV disease in parent / grandparent:

<55 yrs males, <65 years females

Events: sudden cardiac death, angina, MI, stroke

Objectively diagnosed CV disease

Related procedures: angioplasty or stent, CABG

Guidelines for Medication Use in Childhood and Adolescent Obesity



Risk Factors

High Risk

- HTN requiring drug therapy (BP $\geq 99^{\text{th}}$ percentile + 5 mmHg)
- Current smoker
- BMI $\geq 97^{\text{th}}$ percentile

Moderate Risk

- HTN not requiring drug therapy
- BMI $\geq 95^{\text{th}}$ percentile, $< 97^{\text{th}}$ percentile
- HDL < 1.0 mmol/L

Guidelines for Medication Use in Childhood and Adolescent Obesity



Risk Conditions

High Risk

- Kawasaki disease with current aneurysms
- Post heart transplantation
- Chronic renal disease

Diabetes

Moderate Risk

- Kawasaki disease with regressed aneurysms
- Nephrotic syndrome
- HIV
- Chronic inflammatory disease (JRA, SLE)

Guidelines for Medication Use in Childhood and Adolescent Obesity



- Measure and average 2 fasting lipid profiles.
- Decision-making to start a statin is primarily based on the LDL level, but modified by other lipid abnormalities, family history, RF / RC.
- In the setting of obesity and higher triglycerides, cutpoints for non-HDL levels are also provided to guide decision-making.

Guidelines for Medication Use in Childhood and Adolescent Obesity



BMI $\geq 97^{\text{th}}$ percentile:

- LDL ≥ 4.90 mmol/L (non-HDL ≥ 5.30)
- LDL ≥ 4.15 to 4.89 mmol/L (non-HDL 4.50-5.29)
- LDL ≥ 3.35 to 4.14 mmol/L (non-HDL 3.75-4.49)
with:
 - 1 high level RF/RC or
 - ≥ 2 or more moderate level RF/RC or
 - clinical CVD

Guidelines for Medication Use in Childhood and Adolescent Obesity



BMI $\geq 95^{\text{th}}$ and $< 97^{\text{th}}$ percentile:

- LDL ≥ 4.90 mmol/L (non-HDL ≥ 5.30)
- LDL ≥ 4.15 to 4.89 mmol/L (non-HDL 4.50-5.29)
with: positive family history or
 - 1 high or moderate level RF/RC
- LDL ≥ 3.35 to 4.14 mmol/L (non-HDL 3.75-4.49)
with: ≥ 2 high level RF/RC or
 - 1 high + 1 moderate level RF/RC or
 - clinical CVD

Guidelines for Medication Use in Childhood and Adolescent Obesity



BMI $< 95^{\text{th}}$ percentile:

- LDL ≥ 4.90 mmol/L (non-HDL ≥ 5.30)
- LDL ≥ 4.15 to 4.89 mmol/L (non-HDL 4.50-5.29)
with: positive family history or
 - 1 high or ≥ 2 moderate level RF/RC
- LDL ≥ 3.35 to 4.14 mmol/L (non-HDL 3.75-4.49)
with: ≥ 2 high level RF/RC or
 - 1 high + ≥ 2 moderate level RF/RC or
 - clinical CVD

Results

Who needs a statin?



- 35 (1.1%) of 3283 participants screened would meet criteria for lipid-lowering medication independent of adiposity.
- 56 (1.7%) would meet criteria for lipid-lowering medication when BMI is incorporated as a risk factor.
- No participant was taking lipid-lowering medication.

Results

Who needs a statin?



| BMI category | without BMI | with BMI |
|--------------|-------------|----------|
| <85%ile | 0.5% | 0.5% |
| 85-<95%ile | 1.2% | 1.2% |
| 95-<97%ile | 0% | 2.3% |
| ≥97%ile | 4.0% | 7.8% |

Limitations



- Completion and results of further diagnostic evaluation of abnormalities noted on screening were not tracked.

Conclusions



- Non-fasting lipid screening in the school setting is feasible and identifies an important proportion of adolescents with abnormalities and increased cardiometabolic risk.
- Total cholesterol screening alone is inadequate; HDL assessment is required.
- Non-HDL, HDL and total cholesterol:HDL ratio discriminate risk in screening algorithms and new guidelines.

Conclusions



- In the general population, lipid abnormalities are related to adiposity, and waist measures further discriminate risk above BMI alone.
- Few adolescents, regardless of adiposity, will meet criteria for lipid-lowering medication.

Acknowledgements



www.obesityinyouth.org



www.heartniagara.com