EUROPEAN SOCIETY OF CARDIOLOGY-CONGRESS 2010
Objectives/Outline

- Provide an overview of the evidence supporting prevention of CVD beginning early in life
- Review current evidence-based guidelines for CVD prevention in children & youth
- Discuss implications for research, practice & policy initiatives
“Take Home” Messages

- Cardiovascular health promotion (primordial prevention) & risk reduction (primary prevention) must begin early in life.
- Overweight/obesity are critical components of CVD risk profile in children & youth.
- Individual/High-risk & Population- based approaches are necessary to reduce the risk and global public health burden of Obesity & CVD
- Nurses and nursing are central and essential to both approaches.
Life course approach to chronic disease

Underlying factors
- Growth patterns
- Diet
- Physical Activity
- Environment
- Genes

Metabolic Conditioning for
- Obesity
- Hypertension
- Insulin resistance

Critical or sensitive periods / temporal relationships / interactions / accumulation

Pre-pregnancy → Fetal life → Infancy → Childhood → Adulthood

Adapted From Ben-Shlomo Y, Int J Epidemiol 2002
Life Course Approach to CVD Prevention

- No longitudinal data linking absolute levels of risk factors measured in childhood with incident CVD in adult life
- No RCT data indicating that risk reduction in childhood prevents CVD in adult life
- Sufficient evidence to indicate that to do nothing is to do harm
The Evidence for Life Course Prevention

- Pathology Studies/Autopsy Data
- Sub-clinical and non-invasive assessment of atherosclerosis & vascular injury
- Tracking & Clustering of Risk Factors
- Prevalence & Trends

Evidence from Pathology Studies

- Presence & extent of atherosclerotic lesions at autopsy correlates positively & significantly with established and potentially modifiable risk factors and behaviors.

- Atherosclerotic processes accelerate as the number of risk factors increase.
Figure 3. The Effect of Multiple Risk Factors on the Extent of Atherosclerosis in the Aorta and Coronary Arteries in Children and Young Adults.

Values shown are the percentages of the intimal surface covered with lesions in subjects with 0, 1, 2, and 3 or 4 risk factors. Risk factors were elevated values for body-mass index, systolic blood pressure, and serum triglyceride and LDL cholesterol concentrations, defined as values above the 75th percentile for the study group (specific for study period, race, sex, and age). There were 52 subjects with no risk factors, 20 with one, 14 with two, and 7 with three or four. The P value is based on the analysis of trend. A marked increase in the percentage of the intimal surface covered by fibrous plaques is evident in the coronary vessels of subjects with multiple risk factors.
Multiple CVRFs & Atherosclerosis in Youth

The Bogalusa Heart Study
1972 – 2007

Aorta: Sudan III stain
L: Smoke, high chol
R: Low Risk

Berenson, NEJM 1998; N=204, age 2-39 years; *P<0.01 for trend
Common Carotid Artery Intima-Media Thickness (IMT) in 1170 Adults Aged 33 to 39 Years, by Number of Current and Childhood Risk Factors Measured 21 Years Earlier at Ages 12 to 18 Years (Raitakari, *JAMA*, 2003)
**Increased Carotid IMT With Obesity & Type 2 Diabetes in Youth**

- For all carotid segments, T2DM had the thickest cIMT.
- But for Internal, graded increase from lean to obese to T2DM.
- CVRF profile more adverse from L (n=182) to O (n=136) to T2DM (n=128); presence of obesity or T2DM was independent determinant of cIMT.

*P<0.05 Lean & Obese < T2DM; †P<0.05; Lean < Obese & T2DM. Urbina, Circulation, 2009
Cross sectional regression of cIMT on age suggests progression rates will be more rapid in high risk youth.

P for slope not equal to 0 was <0.002 for Obese and T2DM, NS for Lean group. Urbina Circulation 2009
Impaired Endothelial Function in Children
Related to Risk Factors

P<0.05 between Normal & Elevated CV risk factor level.
Tracking BMI-for-Age from Birth to 18 Years with Percent of Overweight Children who Are Obese at Age 25

Whitaker et al. *NEJM*: 1997;337:869-873
Adolescent Overweight and Future Adult Coronary Heart Disease

- Modeling/simulation study designed to estimate the prevalence of obese 35-year-olds in 2020 on basis of adolescent overweight in 2000 & trend data.

- 2020 Projections: 30-37% in men and 34-44% in women

Estimated Prevalence of Cardiovascular Risk Factors among 35-Year-Old Men and Women in 2020, According to the Presence or Absence of a Projected Increase in Adult Obesity Associated with Adolescent Overweight

<table>
<thead>
<tr>
<th>Variable</th>
<th>Proportion with Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Projected Increase in Future Obesity</td>
</tr>
<tr>
<td></td>
<td>Men</td>
</tr>
<tr>
<td>Body-mass index $\geq 30$</td>
<td>25</td>
</tr>
<tr>
<td>Diastolic blood pressure $\geq 90$ mm Hg</td>
<td>7</td>
</tr>
<tr>
<td>Cholesterol</td>
<td></td>
</tr>
<tr>
<td>Low-density lipoprotein $\geq 130$ mg/dl</td>
<td>42</td>
</tr>
<tr>
<td>High-density lipoprotein $&lt;35$ mg/dl</td>
<td>20</td>
</tr>
<tr>
<td>Diabetes</td>
<td>3.1</td>
</tr>
</tbody>
</table>

Bibbins-Domingo K et al. N Engl J Med 2007;357:2371-2379
Prevalence of Coronary Heart Disease (CHD) Associated with Three Projections of Future Adult Obesity

Bibbins-Domingo K et al. N Engl J Med 2007;357:2371-2379
Adolescent Overweight and Future Adult Coronary Heart Disease

- High rates of current adolescent overweight are expected to increase the excess prevalence of CHD and to increase the population prevalence of CHD:
  - Projected increase in prevalence by 2035: range of 5-16%
  - > 100,000 excess cases of CHD attributable to increase in obesity
Clustering of Risk Factors for CVD

- Begins early in life
- Aggregates in families (shared genes & shared (common) family environment)
- Tracks from childhood to adulthood

Childhood Obesity & Cardiovascular-Related Co-Morbidities

- Dyslipidemia
- Hypertension
- Chronic Inflammation
- Endothelial Dysfunction
- Insulin resistance > Cardiometabolic risk factor clustering
- T2DM
- Left Ventricular Hypertrophy
- Sleep Apnea

## Harmonizing the Metabolic Syndrome: A Joint Interim Statement+
### Criteria for Clinical Diagnosis of the Metabolic Syndrome

<table>
<thead>
<tr>
<th>Measure</th>
<th>Categorical Cut Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevated waist circumference*</td>
<td>Population- and country-specific definitions</td>
</tr>
<tr>
<td>Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator)**</td>
<td>150 mg/dL (1.7 mmol/L)</td>
</tr>
<tr>
<td>Reduced HDL-C (drug treatment for reduced HDL-C is an alternate indicator)**</td>
<td>&lt;40 mg/dL (1.0 mmol/L) in males; &lt;50 mg/dL (1.3 mmol/L) in females</td>
</tr>
<tr>
<td>Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)</td>
<td>Systolic &gt;/= 130 and/or diastolic &gt;/= 85 mm Hg</td>
</tr>
<tr>
<td>Elevated fasting glucose (drug treatment of elevated glucose is an alternate indicator)**</td>
<td>&gt;/=100 mg/dL</td>
</tr>
</tbody>
</table>

*It is recommended that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available.

**The most commonly used drugs for elevated triglycerides and reduced HDL-C are fibrates and nicotinic acid. A patient taking 1 of these drugs can be presumed to have high triglycerides and low HDL-C. High-dose, omega-3 fatty acids presumes high triglycerides.

***Most patients with type 2 diabetes mellitus will have the metabolic syndrome by the proposed criteria.

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Prevalence and Trends
The Global Burden of CVD

- Major cause of morbidity and premature mortality in men and women in the US, most of the developed world & many developing countries
- CVD is leading cause of mortality in 5 of the 6 World Health Organization worldwide regions
- For CHD, potentially modifiable risk factors account for 90% of PAR in men & ~ 95% in women

• Yusuf & the INTERHEART Investigators, *Lancet*, 2004
<table>
<thead>
<tr>
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<td>17.5</td>
<td>17.3</td>
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<td>23.2</td>
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<tr>
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<td>30.6</td>
<td>31.3</td>
<td>32.3</td>
<td>33.7</td>
<td>34.3</td>
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The next generation

<table>
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<tr>
<th>Name</th>
<th>Malri Twalib</th>
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<tr>
<td>Age</td>
<td>5</td>
</tr>
<tr>
<td>Country</td>
<td>United Republic of Tanzania</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Obesity</td>
</tr>
</tbody>
</table>
Childhood Obesity: A Worldwide Epidemic

- 2005: ~20 million children under age of 5 were overweight
- By end of 2010, an estimated 43 million children under five will be overweight: 35 million in developing countries

Healthy Lifestyle Behaviors and Therapeutic Lifestyle Change

- Cornerstone of Cardiovascular Health Promotion and Risk Reduction

- Kavey et al., Circ., 2003; Williams et al., Circ., 2002; Daniels et al., Circ., 2005; Daniels et al., Pediatr., 2008; McCrindle et al., Circ., 2007; Kavey et al., Circ., 2006; Hayman et al., Circ., 2007; Graham et al, European Heart Journal, 2007
Eat Healthy and Exercise
AHA Pediatric Dietary Strategies
For Individuals Aged > 2 Years*

- Balance dietary calories with physical activity to maintain normal growth
- Engage in 60 mins of moderate to vigorous play or physical activity daily
- Eat vegetables & fruits daily; limit juice intake
- Use vegetable oils & soft margarines low in saturated fat & trans fatty acids
- Eat whole grain cereals and bread rather than refined grain products
- Use non-fat/skim or low-fat milk and dairy products daily
- Eat more fish, especially oily fish, broiled or baked
- Reduce salt intake including from processed foods

*Gidding et al., Pediatrics, 2006;117:544-559; Gidding et al., Circulation, 2009;119:1161-1175
2008 Physical Activity Guidelines*

- School-aged children and adolescents (6 to 17 years of age):
  - 60 minutes or more per day of moderate-to-vigorous physical activity (MVPA)
  - Vigorous activity on at least 3 days of the week
  - Muscle strengthening & Bone strengthening activities on at least 3 days per week

Sweden Known Throughout the World

Athletes and Active Life Styles
Schematic representation of candidate CVD risk factors and associated influences in children European Youth Heart Study (Riddoch et al., *J of Physical Activity & Health*, 2005).
European Youth Heart Study (EYHS)– Age and gender distribution of time engaged in physical activity of at least moderate intensity by country (columns are means ±SD). (Riddoch et al., MSSE, 2004).
YOU can EXCEL!
The EXCEL Study*

Childhood obesity is an increasingly common risk factor for diabetes and CVD. Research suggests exercise reduces cardiometabolic risk.

Purpose: determine if an “exer-game” intervention improves levels of moderate or vigorous physical activity, CVD risk factors, fitness, and self-efficacy/competence in Boston Public School elementary children, compared to an Advice-Only condition. A Children’s Hospital Boston sub-study is examining effects of exergaming on lipids, insulin resistance, vascular reactivity and body composition.

*DeFerranti, Hayman, Osganian, Crouter, Whiteley (Harvard Catalyst/The Harvard Clinical & Translational Science Center-NIH #1 UL1 RR 025758-02)
Guidelines for Cardiovascular Health Promotion & Risk Reduction in Children & Youth

- National Cholesterol Education Program, 1991
- Integrated Cardiovascular Health Promotion AHA, 2002
- Primary Prevention of CVD, AHA, 2003
- Cardiovascular Health Promotion in Schools, AHA, 2004
- Cardiovascular Risk Reduction In High-Risk Pediatric Populations, AHA, 2006
- Drug Therapy of High-Risk Lipid Abnormalities in Children, AHA, 2007
- Lipid Screening & Cardiovascular Health in Childhood, AAP, 2008
- NHLBI Integrated Pediatric Guideline for Cardiovascular Health & Risk Reduction- Forthcoming
Guidelines for Identification of Children & Adolescents at High Risk of CVD

General Assessment:

Goals for Pediatric Care Providers:
- Timed targeted risk factor assessment
- Appropriate interpretation of results and communication to families

Goals for Parents:
- Recognition of risk factor significance for development of cardiovascular disease, especially family history

Recommendations:
- Family history: Regular update (parents, grandparents, aunts, and uncles): obesity, hypertension, dyslipidemia, diabetes, cigarette smoking, cardiovascular disease
- Height, weight, BMI: Assessment at every examination
- BP measurement: At every examination after age 3 years; charted for age/sex/height
- Diet and physical activity: Assessment at every visit
- Cigarette smoking: Evaluation starting at 9-10 years of age
Specific Risk Assessment:

Lipids and Lipoproteins:
- Total cholesterol >170 mg/dL (~4.25 mmol/L) is borderline, > 200 mg/dL is elevated (~5 mmol/L)
- LDL-C > 110 mg/dL (~2.75 mmol/L) is borderline, > 130 mg/dL (~3.25 mmol/L) is elevated
- Triglycerides > 150 mg/dL (~1.7 mmol/L)
- HDL-C < 40 mg/dL (~<1.0 mmol/L)

Recommendations:

Targeted screening of fasting lipids in children > 2 yrs. with family history of dyslipidemia or premature CVD

For children in which family history is unknown and other risk factors are present, lipids and lipoproteins should be assessed.
Guidelines for Identification of Children & Adolescents at High Risk of CVD (Cont’d)

Specific Risk Assessment:

Blood Pressure:
- Systolic and diastolic blood pressure > 90th percentile for age, sex, and height
- Pre-HTN: >/= 90th-95th percentile for age, sex, and height

Recommendations:

Know appropriate blood pressure measurement techniques, including appropriate cuff size
- Interpret blood pressure measurements based on age, sex, and height (BP percentiles available at http://www.nhlbi.nih.gov/health-prof/heart/hbp/hbp_ped.htm)
Specific Risk Assessment:

Body Size:
- BMI > 85\textsuperscript{th} percentile is overweight; > 95\textsuperscript{th} percentile is obese

Recommendations:
- Body size should be charted by BMI. (Norms for BMI \% iles are available at: http://www.cdc.gov/nchs/about/major/nhanes/growthcharts/char ts.htm)
Primary Prevention: Risk Factor Management

- Adequate Trial of therapeutic lifestyle change

- Individually tailored:
  - Age/developmental level of child, presence & extent of co-morbidities
  - Emphasis on normalization of body weight
## Treatment Goals - Weight Loss Targets

<table>
<thead>
<tr>
<th>Age Group</th>
<th>BMI 85-94% No Risks</th>
<th>BMI 85-94% With Risks</th>
<th>BMI 95-98%</th>
<th>BMI &gt;= 99%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 2-5 Years</td>
<td>Maintain weight velocity</td>
<td>Decrease weight velocity or weight maintenance</td>
<td>Weight maintenance</td>
<td>Gradual weight loss of up to 1 pound a month if BMI is very high (&gt;21 or 22 kg/m²)</td>
</tr>
<tr>
<td>Age 6-11 Years</td>
<td>Maintain weight velocity</td>
<td>Decrease weight velocity or weight maintenance</td>
<td>Weight maintenance or gradual loss (1 lb per month)</td>
<td>Weight loss (maximum is 2 pounds per week)</td>
</tr>
<tr>
<td>Age 12-18 Years</td>
<td>Maintain weight velocity. After linear growth is complete, maintain weight</td>
<td>Decrease weight velocity or weight maintenance</td>
<td>Weight loss (maximum is 2 pounds per week)</td>
<td>Weight loss (maximum is 2 pounds per week)</td>
</tr>
</tbody>
</table>

What works? CVD Prevention

- Components of effective models
  - Evidence-based, algorithm driven protocols
  - Individually-tailored lifestyle management
  - Regular follow-up to monitor compliance
  - Information systems: feedback to providers & reminders to consumers/patients
  - Coordination of multidisciplinary services by advanced practice nurse with specialized knowledge & skill
  - Individual & family-focused method of behavior change

Prevention -to -treatment continuum

An Ecological Framework Depicting Multiple Influences on Physical Activity and Eating Behaviors

- Individual Factors (personal)
  - Skills and behaviors
  - Cognitions (e.g. attitudes, preferences, knowledge, values)
  - Lifestyle
  - Biological (e.g. genes, gender, age)
  - Demographics (e.g. income, race/ethnicity)

- Social Environment (networks)
  - Role modeling
  - Social support
  - Social norms
  - Family
  - Friends
  - Peers

- Physical Environments (settings)
  - Availability
  - Access
  - Barriers
  - Opportunities

- Macro-level Environments (sectors)
  - Practices
  - Legislative, regulatory, or policy actions

- Physical Environments (settings)
- Social Environment (networks)
- Macro-level Environments (sectors)

- Macro-level Environments (sectors)
  - Societal and cultural norms and values
  - Food and beverage industry
  - Food marketing and media
  - Food and agriculture policies
  - Economic systems
  - Food production & distribution systems
  - Government & political structures and policies
  - Food assistance programs
  - Health care systems
  - Land use and transportation, zoning

- Environments (settings)
  - Home
  - School, Afterschool
  - Child-care
  - Neighborhoods & Communities
  - Restaurants & fast food outlets
  - Supermarkets, Convenience & corner stores
  - Parks, bike lanes, footpaths

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  - Food assistance programs
  - Health care systems
  - Land use and transportation, zoning
Meeting the Challenge

- “WE HAVE THE SCIENTIFIC KNOWLEDGE TO CREATE A WORLD IN WHICH MOST CVD COULD BE ELIMINATED…IN SUCH A WORLD, PREVENTION PRACTICES WOULD BE INCORPORATED EARLY IN LIFE…EVERYONE WOULD HAVE ACCESS TO POSITIVE HEALTHY LIVING, GOOD NUTRITION, REGULAR PHYSICAL ACTIVITY AND SUPPORTIVE LIVING & WORKING ENVIRONMENTS”

- Victorian Declaration on Health
Better Health for
All the Children of the World
A child's life is like a piece of paper on which every person leaves a mark.

Thank you!
### Table 2. Definition of Ideal Cardiovascular Health

<table>
<thead>
<tr>
<th>Goal/Metric</th>
<th>Ideal Cardiovascular Health Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smoking</td>
<td>Never or quit &gt;12 mo ago&lt;br&gt;Never tried; never smoked whole cigarette</td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>&lt;25 kg/m²&lt;br&gt;&lt;85th Percentile</td>
</tr>
<tr>
<td>Children 12–19 y of age</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>&gt;/=150 min/wk moderate intensity or &gt;/= 75 min/wk vigorous intensity or combination</td>
</tr>
<tr>
<td>Children 2–19 y of age</td>
<td>&gt;/=60 min of moderate- or vigorous-intensity activity every day</td>
</tr>
<tr>
<td>Physical activity</td>
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</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>4–5 Components*</td>
</tr>
<tr>
<td>Children 12–19 y of age</td>
<td>4–5 Components*</td>
</tr>
<tr>
<td>Healthy diet score*</td>
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<tr>
<td>Adults &gt;20 y of age</td>
<td>4–5 Components*</td>
</tr>
<tr>
<td>Children 5–19 y of age</td>
<td>4–5 Components*</td>
</tr>
<tr>
<td>Total cholesterol</td>
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<tr>
<td>Adults &gt;20 y of age</td>
<td>&lt;200 mg/dL**</td>
</tr>
<tr>
<td>Children 6–19 y of age</td>
<td>&lt;170 mg/dL**</td>
</tr>
<tr>
<td>Blood pressure</td>
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</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>&lt;120/&lt;80 mm Hg**</td>
</tr>
<tr>
<td>Children 8–19 y of age</td>
<td>&lt;90th Percentile**</td>
</tr>
<tr>
<td>Fasting plasma glucose</td>
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</tr>
<tr>
<td>Adults &gt;20 y of age</td>
<td>&lt;100 mg/dL**</td>
</tr>
<tr>
<td>Children 12–19 y of age</td>
<td>&lt;100 mg/dL**</td>
</tr>
</tbody>
</table>

*The committee selected 5 aspects of diet to define a healthy dietary score. The score is not intended to be comprehensive. Rather, it is a practical approach that provides individuals with a set of potential concrete actions. A comprehensive rationale is set forth in the text of this document, and a comprehensive set of nutrition recommendations is provided by Lichtenstein, AH, et al. Circulation, 2006;114:82-96; Johnson, RK, et al. Circulation. 2009;120:1011-1020; Appel, LJ, et al. Hypertension. 2006;47:296-308. **Untreated values.
Recommendations: Pharmacologic Therapy of High Risk Dyslipidemia for Children and Adolescents (McCrindle et al., Circ., 2007)

Current Modifications: Risk factors and high risk conditions:
- Male gender
- Strong family history of premature cardiovascular disease or events
- Presence of associated low HDL cholesterol, high triglycerides, small dense LDL particles
- Presence of overweight or obesity and aspects of the metabolic syndrome
- Presence of other medical conditions associated with an increased atherosclerotic risk
- Presence of hypertension
- Current smoking and passive smoke exposure
- Presence of novel and emerging risk factors
Patient Selection

1. Use the present criteria of the NCEP Expert Panel and the subsequent modifications.

2. The age and LDL cholesterol level at which statin therapy is initiated may be influenced by the presence, magnitude and number of other cardiovascular risk factors, as well as by the presence of cutaneous xanthomas.

3. Include the preferences of the patient and family in decision-making.

4. Ensure that there are no contraindications for statin therapy.
Recommendations for the Use of HMG CoA Reductase Inhibitors (Statins): Initiation & Titration (McCrindle et al., Circ., 2007)

1. Start with lowest dose (1X/daily); Measure baseline CK, ALT, AST
2. Encourage reporting & monitoring of side effects; if myopathy, assess recent physical activity; assess CK
3. Consider restarting medication after symptoms & Lab abnormalities resolve.
4. Advise females: pregnancy & (if appropriate) need for contraception
5. After 4 weeks: fasting lipoprotein profile, CK, ALT, AST & compare with lab-specific normal values
   Levels of concern: CK: 10x upper limit of reported normal ALT & AST: 3X upper limit of reported normal
   If target levels achieved, continue therapy & recheck in 8 wks. & then 3 months
   If targets not achieved, double dose, repeat labs in 4 wks.
AHA Scientific Statement

Cardiovascular Risk Reduction in High-Risk Pediatric Patients

A Scientific Statement From the American Heart Association Expert Panel on Population and Prevention Science; the Councils on Cardiovascular Disease in the Young, Epidemiology and Prevention, Nutrition, Physical Activity and Metabolism, High Blood Pressure Research, Cardiovascular Nursing, and the Kidney in Heart Disease; and the Interdisciplinary Working Group on Quality of Care and Outcomes Research

Endorsed by the American Academy of Pediatrics

Rae-Ellen W. Kavey, MD, MPH, FAHA, Chair; Vivek Allada, MD; Stephen R. Daniels, MD, PhD, FAHA; Laura L. Hayman, PhD, RN, FAHA; Brian W. McCrindle, MD, MPH; Jane W. Newburger, MD, MPH, FAHA; Rulan S. Parekh, MD, MS; Julia Steinberger, MD, MS
# Primary Prevention

## Disease Stratification by Risk

<table>
<thead>
<tr>
<th>Tier</th>
<th>Risk Category</th>
<th>Rationale</th>
<th>Disease Process/Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier I</td>
<td>High Risk</td>
<td>Manifest CAD &lt;30 yrs of age: Clinical/Pathologic Evidence</td>
<td>Homozygous familial hypercholesterolemia, Diabetes mellitus, Type 1, Chronic kidney disease, Post orthotopic heart transplant, Kawasaki disease with current coronary aneurysms</td>
</tr>
<tr>
<td>Tier II</td>
<td>Moderate Risk</td>
<td>Accelerated Atherosclerosis: Pathophysiologic Evidence</td>
<td>Heterozygous familial hypercholesterolemia, Kawasaki disease with regressed coronary aneurysms, Diabetes mellitus, Type 2, Chronic Inflammatory Disease</td>
</tr>
<tr>
<td>Tier III</td>
<td>At Risk</td>
<td>High Risk Setting for Accelerated Atherosclerosis: Epidemiologic Evidence</td>
<td>Post cancer treatment survivors, Congenital heart disease, Kawasaki disease without detected coronary involvement</td>
</tr>
</tbody>
</table>
HIGH-RISK PEDIATRIC POPULATIONS: RISK STRATIFICATION AND TREATMENT

**Step 1. RISK STRATIFICATION BY DISEASE PROCESS**

**Tier 1: High Risk**
- Homozygous FH
- Diabetes mellitus type I
- Chronic kidney disease/ESRD
- After orthotopic heart transplantation
- Kawasaki disease with current coronary artery aneurysms

**Tier II: Moderate Risk**
- Heterozygous FH
- Chronic inflammatory disease
- Kawasaki disease with regressed coronary aneurysms
- Type 2 diabetes mellitus

**Tier III: At Risk**
- Congenital heart disease
- Kawasaki disease without detected coronary involvement
- Cancer treatment survivors

**Step 2. ASSESS ALL CV RISK FACTORS**
If > additional comorbidities: Advance to next higher risk tier

**Step 3. TIER-SPECIFIC CUTPOINTS/TREATMENT GOALS**

**Step 4. LIFESTYLE CHANGE**

**Step 5. DRUG THERAPY**

**CARDIOVASCULAR RISK FACTORS/COMORBIDITIES**
- Fasting lipid profile
- Smoking history
- Family history of early CAD in expanded 1st-degree pedigree (M<55y; F<65 y)
- Blood pressure (3 separate occasions), interpreted for age/sex/height
- BMI
- Fasting glucose
- Physical activity history

**Tier I: High Risk**
- BMI <85%ile for age/sex
- BP<90%ile for age/sex
- LDL cholesterol <100 mg/dL
- FG,100 mg/dL, HgbA1c <7%

**Tier II: Moderate Risk**
- BMI <90%ile for age/sex
- BP <95%ile for age/sex/ht%ile
- LDL cholesterol <100 mg/dL
- FG < 100mg/dL, HgbA1c <7%

**Tier III: At Risk**
- BMI <95%ile for age/sex
- BP <95%ile+5mm Hg for age/sex/ht%ile
- LDL cholesterol <160 mg/dL
- FG < 100mg/dL, HgbA1c <7%