American Academy of Pediatrics
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ENDORSED POLICY STATEMENT

Cardiovascular Risk Reduction in High-Risk Pediatric Populations

ON JULY 7, 2006, the American Academy of Pediatrics endorsed the following publication: Kavey REW, Allada V, Daniels SR, et al. Cardiovascular risk reduction in high-risk pediatric populations: 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. *Circulation*. 2006;114:2710–2738. Available at: http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.106.179568v1.pdf

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Executive Summary of an American Heart Association Scientific Statement: Cardiovascular Risk Reduction in High-Risk Pediatric Patients

While atherosclerosis has been clearly shown to begin in childhood, the process is usually subclinical, the rate of progression is slow, and the appropriate therapeutic approach is preventive. By contrast, certain pediatric disease states are associated with dramatically accelerated atherosclerosis, with clinical coronary events occurring in childhood or very early adult life. Intensive cardiovascular risk reduction is of critical importance in such children. This executive summary summarizes the work of an expert panel convened by the American Heart Association to develop recommendations for cardiovascular risk management in high-risk pediatric settings. The recommendations were peer reviewed and then endorsed by the American Academy of Pediatrics; the complete scientific statement was published in the December 12, 2006, issue of *Circulation* (2006;114:2710–2738).

In pediatric populations, a large and growing knowledge base documents the presence of accelerated atherosclerosis, the relationship of the atherosclerotic process to the number and intensity of defined risk factors, and the response at the clinical, pathologic, and vascular level to risk factor change. The panel reviewed all the available science regarding very early atherosclerotic disease as well as the range of approaches to risk assessment and treatment and the response to intervention. From this evidence, 8 pediatric disease settings were selected for inclusion: (1) familial hypercholesterolemia; (2) diabetes mellitus, type 1 and type 2; (3) chronic kidney disease; (4) post–heart transplantation; (5) Kawasaki disease; (6) chronic inflammatory disease; (7) congenital heart disease; and (8) childhood cancer survivors. Based on the presence of manifest atherosclerotic disease in childhood, a stratification protocol was developed, and each disease was classified (Table 1):

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TABLE 1 **Disease Stratification by Risk**

	Risk Category	Rationale	Disease Process/Condition
Tier I	High risk	Manifest CAD <30 years of age: clinical/pathologic evidence	Homozygous FH Diabetes mellitus, type 1 Chronic kidney disease/end-stage renal disease Post–orthostatic heart transplantation Kawasaki disease with current coronary aneurysms
Tier II	Moderate risk	Accelerated atherosclerosis: pathophysiological evidence	Heterozygous FH Kawasaki disease with regressed coronary aneurysms Diabetes mellitus, type 2 Chronic inflammatory disease
Tier III	At risk	High-risk setting for accelerated atherosclerosis: epidemiological evidence	Post–cancer-treatment survivors Congenital heart disease Kawasaki disease without detected coronary involvement

CAD indicates coronary artery disease; FH, familial hypercholesterolemia.

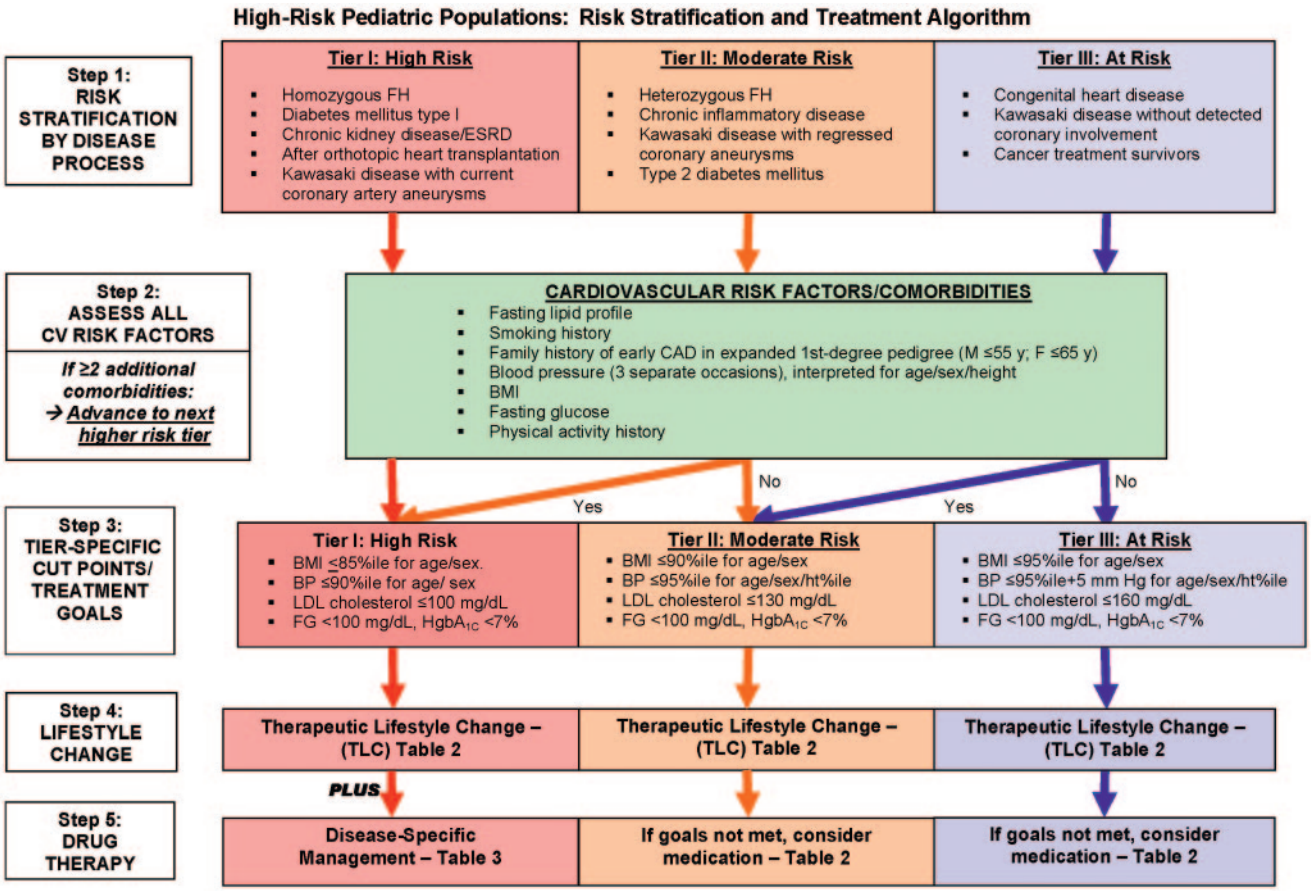

FIGURE 1

Directions: Step 1: risk stratification by disease process (Table 1). **Step 2:** assess all cardiovascular risk factors. If there are ≥2 comorbidities, assign patient to the next higher risk tier for subsequent management. **Step 3:** tier-specific intervention cut points/treatment goals defined. **Step 4:** initial therapy: for tier I, initial management is therapeutic lifestyle change (Table 2) plus disease-specific management (Table 3). For tiers II and III, initial management is therapeutic lifestyle change (Table 2). **Step 5:** for tiers II and III, if goals are not met after initial management, consider medication as outlined in Table 2. FH indicates familial hypercholesterolemia; ESRD, end-stage renal disease; CV, cardiovascular; CAD, coronary artery disease; %ile, percentile; BP, blood pressure; LDL, low-density lipoprotein; FG, fasting glucose; $HgbA_{1c,}$ hemoglobin A_{1C}; ht, height; pt, patient; TLC, therapeutic lifestyle change.

Tier I. Pathologic and/or clinical evidence for manifest coronary disease before 30 years of age;

Tier II. Pathophysiologic evidence for arterial dysfunction indicative of accelerated atherosclerosis before 30 years of age;

Tier III. Increased cardiovascular risk factors with epidemiologic evidence for coronary disease early in adult life but after 30 years of age.

Recommendations for cardiovascular risk management for each tier were tailored to the specific disease setting and adjusted for risk intensity. For children at the

TABLE 2 Tiers I, II, and III: Treatment Recommendations

Growth/diet

- Nutritionist evaluation, diet education for all: total fat <30% of calories, saturated fat <10% of calories, cholesterol <300 mg/d, avoid trans fats; adequate calories for growth.
- Calculate BMI percentile for sex/height.[a]
  - If initial BMI >95th percentile:
    - → Step 1:
      - Age-appropriate reduced-calorie training for child and family
      - Specific diet/weight F/U every 2 to 4 weeks for 6 months; repeat BMI calculation at 6 months
      - Activity counseling (see below)
  - If F/U BMI >85th percentile for tier I, >90th percentile for tier II, or >95th percentile for tier III:
    - → Step 2:
      - Weight-loss program referral plus exercise training program appropriate for cardiac status

Blood pressure (tiers I, II, and III)

- BP measurement/interpretation for age/sex/height
  - If SBP and/or DBP = 90th to 95th percentile or BP > 120/80 mm Hg (3 separate occasions within 1 month):
    - → Step 1: decreased calorie intake, increased activity for 6 months
  - If initial SBP and/or DBP > 95th percentile (confirmed within 1 week) or 6-month F/U SBP and/or DBP > 95th percentile:
    - → Step 2: initiate pharmacological therapy per Fourth Task Force recommendations

Lipids

- LDL-C (tiers II and III)
  - See Table 3 for recommendations for LDL-C for tier I.
  - If initial LDL-C ≥ 130 mg/dL (tier II) or > 160 mg/dL (tier III):
    - → Step 1: nutritionist training for diet with <30% of calories from fat, <7% of calories from saturated fat, cholesterol <200 mg/d, avoidance of trans fats for 6 months
  - If repeat LDL-C > 130 mg/dL in tier II or > 160 mg/dL in tier III and child >10 y old:
    - → Step 2: initiate statin therapy with LDL goal of 130 mg/dL
- Triglycerides
  - If initial TG = 150 to 400 mg/dL:
    - → Step 1:
      - Nutritionist training for low simple carbohydrate, low-fat diet
      - If elevated TGs are associated with excess weight, nutritionist referral for weight loss management: energy balance training plus activity recommendations (see below)
  - If TG > 700 to 1000 mg/dL, initial or F/U:
    - → Step 2:
      - Consider fibrate or niacin if >10 y old.[b]
      - Weight loss recommended when TG elevation is associated with overweight/obesity.

Glucose (tiers I, II, and III, except for patients with diabetes mellitus)

- If fasting glucose = 100 to 126 mg/dL:
  - → Step 1: reduced-calorie diet, increased activity aimed at 5% to 10% decrease in weight over 6 months
- If repeat fasting glucose = 100 to 126 mg/dL:
  - → Step 2: insulin-sensitizing medication per endocrinologist
- Casual glucose > 200 mg/dL or fasting glucose > 126 mg/dL = diabetes mellitus → endocrine referral for evaluation and management
- Maintain HbA_{1C} < 7%

Smoking (tiers I, II, and III)

- → Step 1: parental smoking history at every visit; child smoking history beginning at age 10. Active antismoking counseling for all; smoke-free home strongly recommended at each encounter.
- → Step 2: smoking cessation referral for any history of cigarette smoking.

Activity (tiers I, II and III)

- For children in all tiers, participation in activity is at the discretion of the physician(s) directing care. For specific cardiac diagnoses such as Kawasaki disease and congenital heart disease, activity guidelines are referenced.
  - → Step 1: specific activity history for each child, focusing on time spent in active play and screen time (television + computer + video games). Goal is ≥1 hour of active play per day; screen time limited to ≤2 hours/d.
- Encourage activity at every encounter.
  - → Step 2: after 6 months, if goals not met, consider referral for exercise testing, recommendations from exercise specialist.

Specific treatment goals for each risk factor and each tier are given in the algorithm (Fig 1). F/U indicates follow-up; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; HbA_{1C}, hemoglobin A_{1C}.

[a] Normal BMI values for age and sex are available at www.cdc.gov/growthcharts.

[b] Elevation of triglycerides to ≥1000 mg/dL is associated with significant risk for acute pancreatitis. A fasting TG of 700 mg/dL is likely to rise to >1000 mg/dL postprandially. Treatment recommendation is congruent with guidelines for management of dyslipidemia in diabetic children.

TABLE 3 **Tier I Conditions: Specific Treatment Recommendations**

- Rigorous age-appropriate education in diet, activity, and smoking cessation for all
- Specific therapy as needed to achieve BP, LDL-C, glucose, and HbA_{1C} goals as indicated for each tier, as outlined in algorithm; timing individualized for each patient and diagnosis. Step 1 and step 2 therapy for all outlined in Table 2.

Homozygous FH
- LDL management: scheduled apheresis every 1 to 2 weeks beginning at diagnosis to maximally lower LDL-C, plus statin and cholesterol absorption inhibitor
- Rx per cardiologist/lipid specialist. (Specific therapeutic goals for LDL-C are not meaningful with this diagnosis.)
- Assess BMI, BP, and FG: step 1 management for 6 months
- If tier I goals not achieved, proceed to step 2.

Diabetes mellitus, type 1
- Intensive glucose management per endocrinologist, with frequent glucose monitoring/insulin titration to maintain PG < 200 mg/dL, HbA_{1C} < 7%
- Assess BMI, fasting lipids: step 1 management of weight, lipids for 6 months
- If goals not achieved, proceed to step 2; statin Rx if >10 y old to achieve tier I treatment goals
- Initial BP > 90th percentile: step 1 management plus no added salt, increased activity for 6 months
- BP consistently >95th percentile for age/sex/height: initiate ACE inhibitor therapy with BP goal <90th percentile or <130/80 mm Hg, whichever is lower.

CKD/end-stage renal disease
- Optimization of renal failure management with dialysis/transplantation per nephrology
- Assess BMI, BP, lipids, FG: step 1 management for 6 months
- If goals not achieved, proceed to step 2; statin Rx if >10 y old to achieve tier I treatment goals

After heart transplantation
- Optimization of antirejection therapy, treatment for CMV, routine evaluation by angiography/perfusion imaging per transplant physician
- Assess BMI, BP, lipids, FG: initiate step 2 therapy, including statins, immediately in all patients >1 y old to achieve tier I treatment goals

Kawasaki disease with coronary aneurysms
- Antithrombotic therapy, activity restriction, ongoing myocardial perfusion evaluation per cardiologist
- Assess BMI, BP, lipids, FG: step 1 management for 6 months
- If goals not achieved, proceed to step 2; statin Rx if >10 y old to achieve tier I treatment goals

BP indicates blood pressure; LDL-C, low-density lipoprotein cholesterol; HbA_{1C}, hemoglobin A_{1C}; FH, familial hypercholesterolemia; Rx, prescription/treatment; FG, fasting glucose; PG, plasma glucose; ACE, angiotensin-converting enzyme; CKD, chronic kidney disease; CMV, cytomegalovirus.

highest risk (tier I), the intervention strategy regards the diagnosis as a "coronary heart disease equivalent" with recommendations for risk reduction similar to secondary prevention guidelines for adults with established coronary disease. For tier II, complete risk factor assessment is recommended with specific defined therapeutic goals. For children with diagnoses in tier III, the focus is on complete risk factor assessment with therapeutic goals as defined for children in general.

Recommendations for evaluation and treatment are summarized in a treatment algorithm (Fig 1) and in 2 supporting tables (Tables 2 and 3). For review of the evidence for early coronary disease and the response to intervention as well as supporting references, readers are referred to the complete scientific statement.

Further research is needed to explore the pathophysiology of atherosclerosis unique to each of these diagnoses and to critically evaluate therapeutic interventions. Because the time course to clinical disease is short, disease settings like these offer a unique opportunity in pediatric cardiovascular research to perform prospective randomized trials of the efficacy and safety of interventions.

The recommendations presented here are directed toward the primary care providers and pediatric subspecialists who care for these patients in childhood as well as to the internists, family practitioners, and adult subspecialists who will assume their care when they reach adult life. As new information develops, the guidelines will need to be modified to improve guidance on cardiovascular risk reduction in such high-risk pediatric settings. Finally, decisions on the management of individual patients must be tailored to their unique circumstances.

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