Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents

SUMMARY REPORT

U.S. Department of Health and Human Services
National Institutes of Health
National Heart, Lung, and Blood Institute

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Dr. Benuck, Dr. Christakis, Dr. Dennison, Dr. O'Donnell, Dr. Rocchini, and Dr. Washington have declared no relevant relationships.

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Contents

1. Introduction

Atherosclerotic cardiovascular disease (CVD) remains the leading cause of death in North Americans but manifest disease in childhood and adolescence is rare. By contrast, risk factors and risk behaviors that accelerate the development of atherosclerosis begin in childhood and there is increasing evidence that risk reduction delays progression towards clinical disease. In 2006, the Director of the National Heart, Lung, and Blood Institute (NHLBI), Dr. Elizabeth Nabel, appointed an Expert Panel to develop cardiovascular (CV) health guidelines for pediatric care providers based on a formal evidence review of the science, with an integrated format addressing all the major CV risk factors simultaneously.

The goal of the Expert Panel was the development of comprehensive evidence-based guidelines addressing the known risk factors for CVD (Table 1–1) to assist all primary pediatric care providers in both the promotion of CV health and the identification and management of specific risk factors from infancy into young adult life. An innovative approach was needed because a focus on CV risk reduction in children and adolescents addresses a disease process—atherosclerosis—in which the clinical endpoint of manifest CVD is remote. The recommendations therefore need to address two different goals: the prevention of risk factor development—primordial prevention—and the prevention of future CVD by effective management of identified risk factors—primary prevention.

The evidence review also required an innovative approach. Most systematic evidence reviews include one or, at most, a small number of finite questions addressing the impact of specific interventions on specific health outcomes, and a rigorous literature review often results in only a handful of in-scope articles for inclusion. Typically, evidence is limited to randomized controlled trials (RCTs), systematic reviews, and meta-analyses published over a defined time period. There is a defined format for abstracting studies, grading the evidence and presentation of results. The results of the review lead to the conclusions, independent of interpretation.

By contrast, given the scope of the charge to the Panel, this evidence review needed to address a broad array of questions concerning the development, progression, and management of multiple risk factors extending from birth through 21 years of age, including studies with follow-up into later adult life. The timeframe extended back to 1985, roughly 5 years before the review for the last NHLBI guideline addressing lipids in children published in 1992. Rather than RCTs, this evidence is largely available in the form of epidemiologic observational studies which must therefore be included in the review. In addition, the review required critical appraisal of the body of evidence that addresses the impact of managing risk factors in childhood on the development and progression of atherosclerosis. Finally, because of known gaps in the evidence base relating risk factors and risk reduction in childhood to clinical events in adult life, the review must include the available evidence justifying evaluation and treatment of risk factors in childhood. The process of identifying, assembling and organizing the evidence was extensive, the review process was complex and conclusions could only be developed by interpretation of the body of evidence. Even with inclusion of every relevant study from the evidence review, there were important areas where evidence was inadequate. Where this occurred, recommendations are a consensus of the Expert Panel. The schema used in grading the evidence appears in Table 1–2; expert consensus opinions are identified as Grade D.

The Expert Panel Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents contain recommendations based on the evidence review and are directed towards all primary pediatric care providers—

pediatricians, family practitioners, nurses and nurse practitioners, physician assistants, and registered dietitians. The Full Report contains complete background information on the state of the science, methodology of the evidence review and the guideline development process, summaries of the evidence reviews by risk factor, discussion of the Expert Panel's rationale for recommendations, and more than 1,000 citations from the published literature, and is available at: <*http://www.nhlbi.nih.gov/guidelines/cvd_ped/index.htm*> The complete evidence tables will be available as a direct link from that site. This Summary Report presents the Expert Panel recommendations for patient care relative to CV health and risk factor detection and management, without references. It begins with a state-of-the-science synopsis of the evidence that atherosclerosis begins in childhood and that the extent of atherosclerosis is linked directly to the presence and intensity of known risk factors.

This is followed by the "Cardiovascular Health Schedule" which summarizes the Expert Panel's age-based recommendations by risk factor in a one page periodic table. Risk factor specific sections follow, with the graded conclusions of the evidence review, normative tables, and age-specific recommendations. These are often accompanied by *Supportive Actions* which represent expert consensus suggestions from the panel provided to support implementation of the recommendations. The Summary Report will be released simultaneously with online availability of the Full Report with references for each section and the evidence tables at: <*http://www.nhlbi.nih.gov/guidelines/cvd_ped/index.htm*>

It is the hope of the Expert Panel that these recommendations will be useful for all those who provide cardiovascular health care to children.

Table 1–1. **EVALUATED RISK FACTORS**

Family history	Lipids
Age	Overweight/Obesity
Gender	Diabetes mellitus
Nutrition/Diet	Predisposing conditions
Physical inactivity	Metabolic syndrome
Tobacco exposure	Inflammatory markers
Blood pressure	Perinatal factors

Table 1–2. **EVIDENCE GRADING SYSTEM***

Quality Grades:

Grade	Evidence
A	Well-designed randomized controlled trials or diagnostic studies performed on a population similar to the guideline's target population
B	Randomized controlled trials or diagnostic studies with minor limitations; genetic natural history studies; overwhelmingly consistent evidence from observational studies
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, or reasoning from first principles (bench research or animal studies)

* Adapted from American Academy of Pediatrics, Steering Committee on Quality Improvement and Management. *Pediatrics* 2004;114:874-877.

Table 1–2. **EVIDENCE GRADING SYSTEM (continued)**

Strength of Recommendations:

Statement Type	Definition	Implication
Strong recommendation	The Expert Panel believes that the benefits of the recommended approach clearly exceed the harms and that the quality of the supporting evidence is excellent. (Grade A or B) In some clearly defined circumstances, strong recommendations may be made on the basis of lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits clearly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Recommendation	The Expert Panel feels that the benefits exceed the harms but the quality of the evidence is not as strong. (Grade B or C) In some clearly defined circumstances, recommendations may be made on the basis of lesser evidence when high-quality evidence is impossible to obtain and when the anticipated benefits clearly outweigh the harms.	Clinicians should generally follow a recommendation but remain alert to new information and sensitive to patient preferences.
Optional	Either the quality of the evidence that exists is suspect (Grade D) or well-performed studies (Grade A, B, or C) show little clear advantage to one approach versus another.	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set boundaries on alternatives; patient and family preference should have a substantial influencing role.
No recommendation	There is both a lack of pertinent evidence (Grade D) and an unclear balance between benefits and harms.	Clinicians should not be constrained in their decision-making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient and family preference should have a substantial influencing role.

2. State of the Science:
Cardiovascular Risk Factors and the Development of Atherosclerosis in Childhood

Atherosclerosis begins in youth and this process, from its earliest phases, is related to the presence and intensity of the known CV risk factors shown in Table 1–1. Clinical events such as myocardial infarction, stroke, peripheral arterial disease, and ruptured aortic aneurysm are the culmination of the lifelong vascular process of atherosclerosis. Pathologically, the process begins with the accumulation of abnormal lipid in the vascular intima, a reversible stage, progresses to an advanced stage in which a core of extracellular lipid is covered by a fibromuscular cap, and culminates in thrombosis, vascular rupture, or acute ischemic syndromes.

Evidence Linking Risk Factors in Childhood to Atherosclerosis at Autopsy

Atherosclerosis at a young age was first identified in Korean and Vietnam War casualties. Two major contemporary studies, the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study and the Bogalusa Heart Study, have subsequently evaluated the extent of atherosclerosis in children, adolescents and young adults who died accidentally. The Bogalusa study measured CV risk factors (lipids, blood pressure, body mass index, and tobacco use) as part of a comprehensive school-based epidemiologic study in a biracial community. These results were related to atherosclerosis measured at autopsy after accidental death. Strong correlations were shown between the presence and intensity of risk factors and the extent and severity of atherosclerosis. In the PDAY study, risk factors and surrogate measures of risk factors were measured post mortem in 15- to 34-year olds dying accidentally of external causes. Strong relationships were demonstrated between atherosclerotic severity and extent, and age, non-HDL cholesterol, HDL cholesterol, hypertension (determined by renal artery thickness), tobacco use (thiocyanate concentration), diabetes mellitus (DM) (glycohemoglobin), and (in men), obesity. There was a striking increase in both severity and extent as age and the number of risk factors increased. By contrast, absence of risk factors was shown to be associated with a virtual absence of advanced atherosclerotic lesions, even in the oldest subjects in the study.

Evidence Linking Risk Factors in Childhood to Atherosclerosis Assessed Non-Invasively

Over the last decade, measures of sub-clinical atherosclerosis have developed, including the demonstration of coronary calcium on electron beam computed tomography (EBCT) imaging, increased medial thickness in the carotid artery assessed with ultrasound (cIMT), endothelial dysfunction (reduced arterial dilation) with brachial ultrasound imaging, and increased left ventricular mass with cardiac ultrasound. These measures have been assessed in young individuals with severe abnormalities of individual risk factors.

- In adolescents with marked elevation of LDL cholesterol due to familial heterozygous hypercholesterolemia, abnormal levels of coronary calcium, increased cIMT, and impaired endothelial function have been demonstrated.
- Children with hypertension have been shown to have increased cIMT, increased left ventricular mass, and eccentric left ventricular geometry.
- Children with type 1 DM have significantly abnormal endothelial function and, in some studies, increased cIMT.
- Children and young adults with a family history of myocardial infarction have increased cIMT, higher prevalence of coronary calcium, and endothelial dysfunction.
- Endothelial dysfunction has been demonstrated by ultrasound and plethysmography in

association with cigarette smoking (passive and active) and obesity. In obese children, improvement in endothelial function occurs with regular exercise.

- Left ventricular hypertrophy at levels associated with excess mortality in adults has been demonstrated in children with severe obesity.

Four longitudinal studies have shown relationships of risk factors measured in youth—specifically LDL cholesterol, non-HDL cholesterol and serum apolipoproteins, obesity, hypertension, tobacco use, and diabetes—to measures of subclinical atherosclerosis in adulthood. In many of these studies, risk factors measured in childhood and adolescence were better predictors of the severity of adult atherosclerosis than were risk factors measured at the time of the subclinical atherosclerosis study.

Evidence Linking Risk Factors in Childhood to Clinical CVD

The most important evidence relating risk in youth to clinical CVD is the observed association of risk factors for atherosclerosis to clinically manifest CV conditions. Genetic disorders related to high cholesterol are the biologic model for risk factor impact on the atherosclerotic process. In homozygous hypercholesterolemia, where LDL cholesterol levels exceed 800 mg/dL beginning in infancy, coronary events begin in the first decade of life and lifespan is severely shortened. In heterozygous hypercholesterolemia in which LDL cholesterol levels are minimally 160 mg/dL and typically over 200 mg/dL and total cholesterol levels exceed 250 mg/dL beginning in infancy, 50 percent of men and 25 percent of women experience clinical coronary events by age 50. By contrast, genetic traits associated with low cholesterol are associated with longer life expectancy. In PDAY, every 30 mg/dL increase in non-HDL cholesterol was associated with a visible incremental increase in the extent and severity of atherosclerosis. In natural history studies of DM, early CVD mortality is so consistently observed that the presence of DM is considered evidence of vascular disease in adults. Consonant with this, in 15- to 19-year olds in PDAY, the presence of hyperglycemia was associated with the demonstration of advanced atherosclerotic lesions of the coronary arteries. In PDAY, there is also a very strong relationship between abdominal aortic atherosclerosis and tobacco use. Finally, in a 25 year follow-up, the presence of the metabolic syndrome risk factor cluster in childhood predicted clinical CVD in adult subjects at 30 to 48-years of age.

The Impact of Racial/Ethnic Background and Socioeconomic Status in Childhood on the Development of Atherosclerosis

CVD has been observed in diverse geographic areas and all racial and ethnic backgrounds. Cross-sectional research in children has shown differences by race and ethnicity, and by geography for prevalence of CV risk factors; these differences are often partially explained by differences in socioeconomic status. No group within the United States is without a significant prevalence of risk. Several longitudinal cohort studies referenced extensively in this report (Bogalusa Heart Study, PDAY, and CARDIA) are biracial and other studies have been conducted outside the United States. However, longitudinal data in Hispanic, Native American, and Asian children are lacking. Clinically important differences in prevalence of risk factors exist by race and gender, particularly with regard to tobacco use rates, obesity prevalence, hypertension, and dyslipidemia. Low socioeconomic status in and of itself confers substantial risk. However, evidence is not adequate for the recommendations provided in this report to be specific to racial or ethnic groups or socioeconomic status.

Evidence for Risk Factor Clustering in Childhood on the Development of Atherosclerosis

From a population standpoint, clustering of multiple risk factors is the most common association with premature atherosclerosis. The pathologic studies reviewed above show clearly that the presence of multiple risk factors is associated with striking evidence of an accelerated atherosclerotic process. Among the most prevalent multiple risk combinations are the use of tobacco with one other risk factor, and the development of obesity which is often associated with insulin resistance, elevated triglycerides, reduced HDL cholesterol and elevated blood pressure, a combination known as the metabolic syndrome in adults. There is ample evidence from both

cross-sectional and longitudinal studies that the increasing prevalence of obesity in childhood is associated with the same obesity-related risk factor clustering seen in adults and that this continues into adult life. This high risk combination is among the reasons that the current obesity epidemic with its relationship to future CVD and DM is considered one of the most important public health challenges in contemporary society. One other prevalent multiple risk combination is the association of low cardiorespiratory fitness, identified in 33.6% of adolescents in the NHANES surveys from 1999 to 2002, with overweight and obesity, elevated total cholesterol and systolic blood pressure, and reduced HDL-C.

Risk Factor Tracking From Childhood Into Adult Life

Tracking studies from childhood to adulthood exist for all the major risk factors:

- *Obesity* tracks more strongly than any other risk factor: among many reports demonstrating this, one of the most recent is a report from the Bogalusa study where more than 2,000 children were followed from initial evaluation at 5 to 14 years of age to adult follow-up at a mean age of 27 years. Based on BMI percentiles derived from the study population, 84% of those with a BMI in the 95th to 99th percentile as children were obese as adults and all of those with a BMI > 99th percentile were obese in adulthood. Increased correlation is seen with increasing age at which the elevated BMI occurs.
- *For cholesterol and blood pressure,* tracking correlation coefficients in the range of 0.4 have been reported consistently across many studies, correlating these measures in children 5 to 10 years of age with results 20 to 30 years later. These data suggest that having cholesterol or blood pressure levels in the upper portion of the pediatric distribution makes having these as adult risk factors likely but not certain. Those who develop obesity have been shown to be more likely to develop hypertension or dyslipidemia as adults.
- Tracking data on *physical fitness* are more limited. Physical activity levels do track but not as strongly as other risk factors.
- By its addictive nature, *tobacco use* persists into adulthood though approximately 50 percent of those who have ever smoked eventually quit.
- *Type 1 diabetes mellitus* is a lifelong condition.
- The insulin resistance of type 2 DM can be alleviated by exercise, weight loss, and bariatric surgery, but the long term outcome of type 2 DM diagnosed in childhood is not known.
- As above, risk factor clusters such as those seen with *obesity* and the *metabolic syndrome* have been shown to track from childhood into adulthood.

Cardiovascular Disease Prevention Beginning In Youth

The rationale for these guidelines comes from the evidence:

- Atherosclerosis, the pathologic basis for clinical CVD, originates in childhood
- Risk factors for the development of atherosclerosis can be identified in childhood
- Development and progression of atherosclerosis clearly relates to the number and intensity of CV risk factors, beginning in childhood
- Risk factors track from childhood into adult life
- Interventions exist for management of identified risk factors

The evidence for the first 4 bullets is reviewed in this section, while the evidence surrounding interventions for identified risk factors is addressed in the RF-specific sections of the guideline to follow.

It is important to distinguish between the goals of prevention at a young age and those at older ages where atherosclerosis is well established, morbidity may already exist, and the process is only minimally reversible. At a young age, there have historically been two goals of prevention: (1) prevent the development of risk factors (primordial prevention); and (2) recognize and manage those children and adolescents at increased risk due to the presence of identified risk factors (primary prevention). It is well established that a population that enters adulthood with lower risk will have less atherosclerosis and will collectively have lower CVD rates. This concept is supported by research that shows that: (1) societies with low levels of CV risk factors have low CVD rates and that changes in risk in those societies are associated with change in cardiovascular disease rates; (2) in adults, control of risk factors leads to

decline in CVD morbidity and mortality; and (3) those without childhood risk have minimal atherosclerosis at age 30- to 34-years, absence of subclinical atherosclerosis as young adults, extended life expectancy and a better quality of life, free from CVD.

The Pathway to Recommending Clinical Practice-Based Prevention

The most direct means of establishing evidence for active CVD prevention beginning at a young age would be to randomize young individuals with defined risks to treatment of CV risk factors or to no treatment and follow both groups over sufficient time to determine if CV events are prevented without undue increase in morbidity arising from treatment. This direct approach is intellectually attractive because atherosclerosis prevention would begin at the earliest stage of the disease process, thereby maximizing benefit. Unfortunately, this approach is as unachievable as it is attractive primarily because such studies would be extremely expensive and would be several decades in duration, a time period in which changes in environment and medical practice would diminish the relevance of the results.

The recognition that evidence from this direct pathway is unlikely to be achieved requires an alternate stepwise approach, where segments of an evidence chain are linked in a manner that serves as a sufficiently rigorous proxy for the causal inference of a clinical trial. The evidence reviewed in this section provides the critical rationale for CV prevention beginning in childhood: evidence that atherosclerosis begins in youth, evidence that the atherosclerotic process relates to risk factors which can be identified in childhood, and evidence that the presence of these risk factors in a given child predicts an adult with risk if no intervention occurs. The remaining evidence links pertain to the demonstration that interventions to lower risk will have a health benefit, and that the risk and cost of interventions to improve risk are outweighed by the reduction in CVD morbidity and mortality. These issues are captured in the evidence reviews of each risk factor. The recommendations reflect a complex decision process that integrates the strength of the evidence with knowledge of the natural history of atherosclerotic vascular disease, estimates of intervention risk, and the physician's responsibility to provide both health education and effective disease treatment. These recommendations for those caring for children will be most effective when complemented by a broader public health strategy.

The Childhood Medical Office Visit as the Setting for CV Health Management

One cornerstone of pediatric care is placing clinical recommendations in a developmental context. Pediatric recommendations must consider not only the relation of age to disease expression but the ability of the patient and family to understand and implement medical advice. For each risk factor, recommendations must be specific to age and developmental stage. The "Bright Futures" concept of the American Academy of Pediatrics (AAP) is used to provide a framework for these guidelines with CV risk reduction recommendations for each age group.

This document provides recommendations for preventing the development of risk factors and optimizing CV health beginning in infancy, based on the results of the evidence review. Pediatric care providers—pediatricians, family practitioners, nurses, nurse practitioners, physician assistants, registered dietitians—are ideally positioned to reinforce CV health behaviors as part of routine care. The guideline also offers specific guidance on primary prevention, with age-specific, evidence-based recommendations for individual risk factor detection. Management algorithms provide staged care recommendations for risk reduction within the pediatric care setting and identify risk factor levels requiring specialist referral. The guidelines also identify specific medical conditions such as diabetes and chronic kidney disease that are associated with increased risk for accelerated atherosclerosis. Recommendations for ongoing CV health management for children and adolescents with these diagnoses are provided.

A cornerstone of pediatric care is the provision of health education. In the U.S. health care system, physicians and nurses are perceived as credible messengers for health information. The childhood health maintenance visit provides an ideal context for effective delivery of the CV health message. Pediatric care providers provide an effective team, educated to initiate behavior change to diminish risk of CVD and promote lifelong CV health in their patients, from infancy into young adult life.

3. Integrated Cardiovascular Health Schedule

Table 3–1. INTEGRATED CARDIOVASCULAR HEALTH SCHEDULE

Risk Factor	AGE					
	Birth–12 m	**1–4 y**	**5–8 y**	**9–11 y**	**12–17 y**	**18–21 y**
FAMILY HISTORY (FHx) OF EARLY CVD		At age 3 y, evaluate FHx for early CVD: parents, grandparents, aunts/uncles, M ≤ 55 y, F ≤ 65 y. Review with parents, refer prn. (+) FHx identifies children for intensive CVD RF attention.	Update at each nonurgent health encounter.	Reevaluate FHx for early CVD in parents, grandparents, aunts/uncles, M ≤ 55 y, F ≤ 65 y.	Update at each nonurgent health encounter.	Repeat FHx evaluation with patient.
TOBACCO EXPOSURE	Advise smoke-free home; offer smoking cessation assistance or referral to parents.	Continue active antismoking advice with parents. Offer smoking cessation assistance and referral as needed.	Begin active antismoking advice with child.	Assess smoking status of child. Active antismoking counseling or referral as needed.	Continue active antismoking counseling with patient. Offer smoking cessation assistance or referral as needed.	Reinforce strong antismoking message. Offer smoking cessation assistance or referral as needed.
NUTRITION/ DIET	Support breastfeeding as optimal to age 12 m if possible. Add formula if breastfeeding decreases or stops before age 12 m.	Age 12-24 m, may change to cow's milk with % fat per family & pediatric care provider. After age 2 y, fat-free milk for all; juice ≤ 4 oz/d; transition to CHILD 1 by age 2 y.	Reinforce CHILD 1 messages.	Reinforce CHILD 1messages as needed.	Obtain diet information from child and use to reinforce healthy diet and limitations and provide counseling as needed.	Review healthy diet with patient.
GROWTH, OVERWEIGHT/ OBESITY	Review FHx for obesity → Discuss wt for ht tracking, growth chart, and healthy diet.	Chart ht/wt/BMI → classify wt by BMI from age 2 y; review with parent.	Chart ht/wt/BMI and review with parent. BMI > 85th%ile, crossing %iles→ intensify diet/activity focus x 6m. If no change → RD referral, manage per obesity algorithms. BMI ≥ 95th%ile, manage per obesity algorithms.	Chart ht/wt/BMI and review with parent and child. BMI > 85th%ile, crossing %iles→ intensify diet/activity focus x 6m. If no change → RD referral, manage per obesity algorithms. BMI ≥ 95th%ile, manage per obesity algorithms	Chart ht/wt/BMI and review with child and parent. BMI > 85th%ile, crossing %iles→ intensify diet/activity focus x 6m. If no change → RD referral, manage per obesity algorithms. BMI ≥ 95th%ile, manage per obesity algorithms.	Review ht/wt/BMI and norms for health with patient. BMI > 85th%ile, crossing %iles →intensify diet/activity focus x 6 m. If no change → RD referral, manage per obesity algorithms. BMI ≥ 95th%ile, manage per obesity algorithms.
LIPIDS	No routine lipid screening.	Obtain fasting lipid profile only if FHx (+), parent with dyslipidemia, any other RFs (+), or high-risk condition.	Obtain fasting lipid profile only if FHx (+), parent with dyslipidemia, any other RFs (+), or high-risk condition.	Obtain universal lipid screen with nonfasting non-HDL = TC – HDL, or fasting lipid profile → manage per lipid algorithms as needed.	Obtain fasting lipid profile if FHx newly (+), parent with dyslipidemia, any other RFs (+), or high-risk condition; manage per lipid algorithms as needed.	Measure nonfasting non-HDL-C or fasting lipid profile in all x 1 → Review with patient; manage with lipid algorithms per *ATP* as needed.
BLOOD PRESSURE	Measure BP in infants with renal/ urologic/cardiac diagnosis or Hx of neonatal ICU.	Measure annual BP in all from age 3 y; chart for age/gender/ht %ile and review with parent.	Check BP annually and chart for age/gender/ht → Review with parent; work up and/or manage per BP algorithm as needed.	Check BP annually and chart for age/gender/ht → Review with parent, work up and/or manage per BP algorithm as needed.	Check BP annually and chart for age/gender/ht → Review with adolescent and parent, work up and/or manage per BP algorithm as needed.	Measure BP → Review with patient. Evaluate and treat as per *JNC* guidelines.
PHYSICAL ACTIVITY	Encourage parents to model routine activity. No screen time before age 2 y.	Encourage active play; limit sedentary/ screen time to ≤ 2 h/d. No TV in bedroom.	Recommend MVPA ≥ 1h/d; limit screen/sedentary time to ≤ 2 h/d.	Obtain activity Hx from child → recommend MVPA ≥ 1 h/d; screen/sedentary time ≤ 2 h/d.	Use activity Hx with adolescent to reinforce MVPA ≥ 1 h/d, leisure screen time ≤ 2 h/d.	Discuss lifelong activity, sedentary time limits with patient.
DIABETES				Measure fasting glucose per ADA guidelines, refer to endocrinologist as needed.	Measure fasting glucose per ADA guidelines, refer to endocrinologist as needed.	Obtain fasting glucose if indicated, refer to endocrinologist as needed.

Abbreviations: m = month(s); y = year(s); FHx = family history; M = male; F = female; RF = risk factor; % = percent; BMI = body mass index; %ile = percentile; ADA = American Diabetes Association; MVPA = moderate-to-vigorous physical activity; *ATP = Adult Treatment Panel III (Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults);* CHILD 1= **C**ardiovascular **H**ealth **I**ntegrated **L**ifestyle **D**iet; *JNC = The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure;* BP = blood pressure; h/d = hours per day

The Full and Summary Report of the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents may also be found on the NHLBI Web site at: http://www.nhlbi.nih.gov/

4. Family History of Early Atherosclerotic Cardiovascular Disease

A family history of CVD represents the net effect of shared genetic, biochemical, behavioral and environmental components. In adults, epidemiologic studies have demonstrated that a family history of premature coronary heart disease in a first degree relative—heart attack, treated angina, percutaneous coronary catheter interventional procedure, coronary artery bypass surgery, stroke or sudden cardiac death in a male parent or sibling before the age of 55 years or a female parent or sibling before the age of 65 years—is an important independent risk factor for future CVD. The process of atherosclerosis is complex and involves many genetic loci and multiple environmental and personal risk factors. Nonetheless, the presence of a positive parental history has been consistently shown to significantly increase baseline risk for CVD. The risk for CVD in offspring is strongly inversely related to the age of the parent at the time of the index event. The association of a positive family history with increased CV risk has been confirmed for men, women, and siblings and in different racial and ethnic groups. The evidence review identified all randomized controlled trials (RCTs), systematic reviews, meta-analyses, and observational studies that addressed family history of premature atherosclerotic disease and the development and progression of atherosclerosis from childhood into young adult life.

Conclusions and Grading of the Evidence Review for the Role of Family History in Cardiovascular Health

- Evidence from observational studies strongly supports inclusion of a positive family history of early coronary heart disease in identifying children at risk for accelerated atherosclerosis and for the presence of an abnormal risk profile. (Grade B)
- For adults, a positive family history is defined as a parent and/or sibling with a history of treated angina, myocardial infarction, percutaneous coronary catheter interventional procedure, coronary artery bypass grafting, stroke or sudden cardiac death before 55 years in men or 65 years in women. Because the parents and siblings of children and adolescents are usually young themselves, it was the panel consensus that when evaluating family history in a child, history should also be ascertained for the occurrence of cardiovascular disease in grandparents, aunts, and uncles although the evidence supporting this is insufficient to date. (Grade D)
- Identification of a positive family history for CV disease and/or CV risk factors should lead to evaluation of all family members, especially parents, for CV risk factors. (Grade B)
- Family history evolves as a child matures so regular updates are necessary as part of routine pediatric care. (Grade D)
- Education about the importance of accurate and complete family health information should be part of routine care for children and adolescents. As genetic sophistication increases, linking family history to specific genetic abnormalities will provide important new knowledge about the atherosclerotic process. (Grade D)

Table 4–1. EVIDENCE–BASED RECOMMENDATIONS FOR USE OF FAMILY HISTORY IN CARDIOVASCULAR HEALTH PROMOTION

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.
Supportive actions represent expert consensus suggestions from the Expert Panel provided to support implementation of the recommendations; they are not graded.

Birth–17 y	Take detailed family history (FHx) of CVD* at initial encounter and/or at 3y, 9-11y & 18y	Grade B *Recommend*
	If (+) FHx identified, evaluate patient for other CV risk factors, including dyslipidemia, hypertension, diabetes, obesity, history of smoking, and sedentary lifestyle	Grade B *Recommend*
	If (+) FHx and/or CV risk factors identified, evaluate family, especially parents, for CV risk factors	Grade B *Recommend*
	Update FHx at each non-urgent health encounter	Grade D *Recommend*
	Use FHx to stratify risk for CVD risk as risk profile evolves	Grade D *Recommend*
	Supportive actions: Educate parents about the importance of FHx in estimating future health risks for all family members	
	* Parent, grandparent, aunt, uncle, or sibling with heart attack, treated angina, CABG/stent/angioplasty, stroke, or sudden cardiac death at < 55 y in males, < 65 y in females	
18–21 y	Review FHx of heart disease with young adult patient	Grade B *Strongly recommend*
	Supportive actions: Educate patient about family/personal risk for early heart disease including need for evaluation for all CV risk factors	

5. Nutrition and Diet

The 2010 *Dietary Guidelines for Americans* (2010 *DGA*) include important recommendations for the population over the age of 2. The National Cholesterol Education Program Pediatric Panel Report in 1992 provided dietary recommendations for all children as part of a population-based approach to reducing cardiovascular risk. Evidence relative to diet and the development of atherosclerosis in childhood and adolescence was identified by the evidence review for this guideline, and collectively, this provides the rationale for new dietary prevention efforts initiated early in life.

These new pediatric CV guidelines not only build upon the recommendations for achieving nutrient adequacy in growing children as stated in the 2010 *DGA* but also add evidence regarding the efficacy of specific dietary changes to reduce CV risk from the current evidence review for the use of pediatric care providers in the care of their patients. Because the focus of these guidelines is on CV risk reduction, the evidence review specifically evaluated dietary fatty acid and energy components as major contributors to hypercholesterolemia and obesity, as well as dietary composition and micronutrients as they affect hypertension. New evidence from multiple dietary trials addressing CV risk reduction in children provides important information for these recommendations.

Conclusions and Grading of the Evidence Review for Diet and Nutrition in Cardiovascular Risk Reduction

The Expert Panel concluded that there is strong and consistent evidence that good nutrition beginning at birth has profound health benefits, with the potential to decrease future risk for CVD. The Expert Panel accepts the 2010 *DGA* as containing appropriate recommendations for diet and nutrition in children 2 years and older. The recommendations in these guidelines are intended for pediatric care providers to use with their patients to address CV risk reduction. The conclusions of the Expert Panel's review of the entire body of evidence in a specific nutrition area with grades are summarized below. Where evidence is inadequate yet nutrition guidance is needed, recommendations for pediatric care providers are based on a consensus of the Expert Panel. (Grade D) The age- and evidence-based recommendations of the Expert Panel follow.

In accordance with the Surgeon General's Office, WHO, the AAP, and the AAFP, exclusive breastfeeding is recommended for the first 6 months of life. Continued breastfeeding is recommended to at least age 12 months, with the addition of complementary foods. If breastfeeding *per se* is not possible, feeding human milk by bottle is second best, with formula feeding as the third choice.

- Long term follow-up studies demonstrate that subjects who were breastfed have sustained CV health benefits, including lower cholesterol levels, lower BMI, reduced prevalence of type 2 diabetes, and lower cIMT in adulthood. (Grade B)
- Ongoing nutrition counseling has been effective in assisting children and families to adopt and sustain recommended diets for both nutrient adequacy and reducing CV risk. (Grade A)
- Within appropriate age- and gender-based requirements for growth and nutrition, in normal children and in children with hypercholesterolemia, intake of total fat can be safely limited to 30% of total calories, saturated fat intake limited to 7-10% of calories, and dietary cholesterol limited to 300 mg/d. Under the guidance of qualified nutritionists, this dietary composition has been shown to result in

lower TC and LDL-C levels, less obesity, and less insulin resistance. (Grade A) Under similar conditions and with ongoing follow-up, these levels of fat intake may have similar effects starting in infancy. (Grade B) Fats are important to infant diets due to their role in brain and cognitive development. Fat intake in infants less than 12 months of age should not be restricted without medical indication.

- The remaining 20% of fat intake should be comprised of a combination of monounsaturated and polyunsaturated fats. (Grade D) Intake of *trans* fat should be limited as much as possible. (Grade D)
- For adults, the current NCEP guidelines recommend that adults consume 25-35% of calories from fat. The 2010 *DGA* supports the IOM recommendations for 30-40% of calories from fat for ages 1-3 years, 25-35% of calories from fat for ages 4-18 years, and 20-35% of calories from fat for adults. For growing children, milk provides essential nutrients, including protein, calcium, magnesium, and vitamin D, that are not readily available elsewhere in the diet. Consumption of fat-free milk in childhood after age 2 years and through adolescence optimizes these benefits, without compromising nutrient quality while avoiding excess saturated fat and calorie intake. (Grade A) Between ages 1 and 2 years as children transition from breastmilk or formula, milk reduced in fat (ranging from 2% milk to fat-free milk) can be used based on the child's growth, appetite, intake of other nutrient-dense foods, intake of other sources of fat, and risk for obesity and CVD. Milk with reduced fat should be used only in the context of an overall diet that supplies 30% of calories from fat. Dietary intervention should be tailored to each specific child's needs.
- Optimal intakes of total protein and total carbohydrate in children were not specifically addressed, but with a recommended total fat intake of 30% of energy, the Expert Panel recommends that the remaining 70% of calories include 15-20% from protein and 50-55% from carbohydrate sources. (no grade) These recommended ranges fall within the acceptable macronutrient distribution range specified by the 2010 *DGA*: 10-30% of calories from protein and 45-65% of calories from carbohydrate for children ages 4-18 years.
- Sodium intake was not addressed by the evidence review for this section on nutrition and diet. From the evidence review for Section 8. High Blood Pressure, lower sodium intake is associated with lower systolic and diastolic BPs in infants, children, and adolescents.
- Plant-based foods are important low calorie sources of nutrients including vitamins and fiber in the diets of children; increasing access to fruits and vegetables has been shown to increase their intake. (Grade A) However, increasing fruit and vegetable intake is an ongoing challenge.
- Reduced intake of sugar-sweetened beverages is associated with decreased obesity measures. (Grade B) Specific information about fruit juice intake is too limited for an evidence-based recommendation. Recommendations for intake of naturally sweetened fruit juice (without added sugar) in infants are a consensus of the Expert Panel (Grade D) and are in agreement with those of the AAP.
- Per the 2010 *DGA*, energy intake should not exceed energy needed for adequate growth and physical activity. Calorie intake needs to match growth demands and physical activity needs. (Grade A) Estimated calorie requirements by gender and age group at three levels of physical activity from the Dietary Guidelines are shown in Table 5–3. For children of normal weight whose activity is minimal, most calories are needed to meet nutritional requirements, leaving only about 5-15% of calorie intake from extra calories. These calories can be derived from fat or sugar added to nutrient-dense foods to allow their consumption as sweets, desserts, or snack foods. (Grade D)
- Dietary fiber intake is inversely associated with energy density and with increased levels of body fat and is positively associated with nutrient density (Grade B); a daily total dietary fiber intake from food sources of at least age plus 5 g for young children and up to 14 g/1,000 kcal for older children and adolescents is recommended. (Grade D)

- The Expert Panel supports the 2008 recommendation of the AAP for vitamin D supplementation with 400 IU/day for all infants and children. No other vitamin, mineral or dietary supplements are recommended. (Grade D) The new RDA for vitamin D for those 1-70 years old is 600 IU/day.
- Use of dietary patterns modeled on those shown to be beneficial in adults (e.g., DASH pattern) is a promising approach to improving nutrition and decreasing CV risk. (Grade B)
- All diet recommendations must be interpreted for each child and family to address individual diet patterns and patient sensitivities such as lactose intolerance and food allergies. (Grade D)

Graded, age-specific recommendations for pediatric care providers to use in optimizing CV health in their patients are summarized below in Table 5–1: Cardiovascular Health Integrated Lifestyle Diet (CHILD 1). CHILD 1 is the first stage in dietary change for children with identified dyslipidemia, overweight and obesity, risk factor clustering, and high-risk medical conditions that may ultimately require more intensive dietary change. CHILD 1 is also the recommended diet for children with a positive family history of early CV disease, dyslipidemia, obesity, primary hypertension, diabetes, or exposure to smoking in the home. Any dietary modification must provide nutrients and calories needed for optimal growth and development. Likewise, recommended intakes are adequately met by a DASH-style eating plan, which emphasizes fat-free/low-fat dairy and increased intake of fruits and vegetables. This has been modified for use in children ages 4 years and older based on daily energy needs by food group and is shown in Table 5–2 as one example of a heart healthy eating plan using the CHILD 1 recommendations.

Table 5– 1. EVIDENCE–BASED RECOMMENDATIONS FOR DIET AND NUTRITION: CARDIOVASCULAR HEALTH INTEGRATED LIFESTYLE DIET (CHILD 1)

CHILD 1 is the recommended first step diet for all children and adolescents at elevated cardiovascular risk.

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.
Supportive actions represent expert consensus suggestions from the Expert Panel provided to support implementation of the recommendations; they are not graded.

Birth–6 m	Infants should be exclusively breastfed (no supplemental formula or other foods) until age 6 m.*	Grade B *Strongly recommend*
	* Infants that cannot be fed directly at the breast should be fed expressed milk. Infants for whom expressed milk is not available should be fed iron-fortified infant formula.	
6–12 m	Continue breastfeeding* until at least age 12 m while gradually adding solids; transition to iron-fortified formula until 12 m if reducing breastfeeding.	Grade B *Strongly recommend*
	Fat intake in infants less than 12 months of age should not be restricted without medical indication.	Grade D *Recommend*
	Limit other drinks to 100% fruit juice ≤ 4 oz/d; No sweetened beverages; encourage water.	Grade D *Recommend*
	* Infants that cannot be fed directly at the breast should be fed expressed milk. Infants for whom expressed milk is not available should be fed iron-fortified infant formula.	
12–24 m	Transition to reduced-fat* (2% to fat-free) unflavored cow's milk** (see *Supportive Actions* bullet 1)	Grade B *Recommend*
	Limit/avoid sugar-sweetened beverage intake; encourage water	Grade B *Strongly recommend*
	Transition to table food with:	
	• Total fat 30% of daily kcal/EER***	Grade B *Recommend*
	• Saturated fat 8-10% of daily kcal/EER	Grade B *Recommend*
	• Avoid *trans* fat as much as possible	Grade D *Strongly recommend*
	• Monounsaturated and polyunsaturated fat up to 20% of daily kcal/EER	Grade D *Recommend*
	• Cholesterol < 300 mg/d	Grade B *Strongly recommend*
	Supportive actions:	
	• The fat content of cow's milk to introduce at age 12-24 m should be decided together by parents and health care providers based on the child's growth, appetite, intake of other nutrient dense foods, intake of other sources of fat, and potential risk for obesity and CVD	
	• 100% fruit juice (from a cup) no more than 4 oz/d	
	• Limit sodium intake	
	• Consider DASH-type diet rich in fruits, vegetables, whole grains, low-fat/fat-free milk and milk products; lower in sugar (Table 5–2)	
	* Toddlers 12-24 m of age with a family history of obesity, heart disease, or high cholesterol, should discuss transition to reduced-fat milk with pediatric care provider after 12 months of age.	
	** Continued breastfeeding is still appropriate and nutritionally superior to cow's milk. Milk reduced in fat should be used only in the context of an overall diet that supplies 30% of calories from fat.	
	*** EER = Estimated Energy Requirements/d for age/gender (Table 5–3)	

2–10 y

Primary beverage: Fat-free unflavored milk — Grade A, *Strongly recommend*

Limit/avoid sugar-sweetened beverages; encourage water. — Grade B, *Recommend*

Fat content:

- Total fat 25-30% of daily kcal/EER** — Grade A, *Strongly recommend*
- Saturated fat 8-10% of daily kcal/EER — Grade A, *Strongly recommend*
- Avoid *trans* fat as much as possible — Grade D, *Recommend*
- Monounsaturated and polyunsaturated fat up to 20% of daily kcal/EER — Grade D, *Recommend*
- Cholesterol < 300 mg/d — Grade A, *Strongly recommend*

Encourage high dietary fiber intake from foods* — Grade B, *Recommend*

Supportive actions:

- Teach portions based on EER for age/sex/activity (Table 5–3)
- Encourage moderately increased energy intake during periods of rapid growth and/or regular moderate-to-vigorous physical activity
- Encourage dietary fiber from foods: Age plus 5 g/d*
- Limit naturally sweetened juice (no added sugar) to 4 oz/d
- Limit sodium intake
- Support DASH-style eating plan as outlined below (Table 5–3)

* Naturally fiber-rich foods are recommended (fruits, vegetables, whole grains); fiber supplements are not advised
Limit refined carbohydrates (sugars, white rice, and white bread)

** EER = Estimated Energy Requirements/d for age/gender (Table 5–3)

11–21 y

Primary beverage: Fat-free unflavored milk — Grade A, *Strongly recommend*

Limit/avoid sugar-sweetened beverages; encourage water — Grade B, *Recommend*

Fat content:

- Total fat 25-30% of daily kcal/EER** — Grade A, *Strongly recommend*
- Saturated fat 8-10% of daily kcal/EER — Grade A, *Strongly recommend*
- Avoid *trans* fat as much as possible — Grade D, *Recommend*
- Monounsaturated and polyunsaturated fat up to 20% of daily kcal/EER — Grade D, *Recommend*
- Cholesterol < 300 mg/d — Grade A, *Strongly recommend*

Encourage high dietary fiber intake from foods* — Grade B, *Recommend*

Supportive actions:

- Teach portions based on EER for age/sex/activity (Table 5–3)
- Encourage moderately increased energy intake during periods of rapid growth and/or regular moderate-to-vigorous physical activity
- Advocate dietary fiber: Goal of 14 g/1,000 kcal *
- Limit naturally sweetened juice (no added sugar) to 4-6 oz/d
- Limit sodium intake
- Encourage healthy eating habits: Breakfast every day, eating meals as a family, limiting fast food meals
- Support DASH-style eating plan as outlined below (Table 5–2)

* Naturally fiber-rich foods are recommended (fruits, vegetables, whole grains); fiber supplements are not advised.
Limit refined carbohydrates (sugars, white rice, and white bread)

** EER = Estimated Energy Requirements/d for age/gender (Table 5–3)

Table 5–2. DASH EATING PLAN: SERVINGS PER DAY BY FOOD GROUP AND TOTAL ENERGY INTAKE

(Table 5–3 provides estimated energy requirements (EER) by age, gender, and activity level.)

Food Group	1,200 Calories	1,400 Calories	1,600 Calories	1,800 Calories	2,000 Calories	2,600 Calories	Serving Sizes	Examples and Notes	Significance of Each Food Group to the DASH Eating Plan
Grains*	4-5	5-6	6	6	6-8	10-11	1 slice bread 1 oz dry cereal** ½ cup cooked rice, pasta, or cereal**	Whole wheat bread and rolls, whole wheat pasta, English muffin, pita bread, bagel, cereals, grits, oatmeal, brown rice, unsalted pretzels and popcorn	Major sources of energy and fiber
Vegetables	3-4	3-4	3-4	4-5	4-5	5-6	1 cup raw leafy vegetable ½ cup cut-up raw or cooked vegetable ½ cup vegetable juice	Broccoli, carrots, collards, green beans, green peas, kale, lima beans, potatoes, spinach, squash, sweet potatoes, tomatoes	Rich sources of potassium, magnesium, and fiber
Fruits	3-4	4	4	4-5	4-5	5-6	1 medium fruit ¼ cup dried fruit ½ cup fresh, frozen, or canned fruit ½ cup fruit juice	Apples, apricots, bananas, dates, grapes, oranges, grapefruit, grapefruit juice, mangoes, melons, peaches, pineapples, raisins, strawberries, tangerines	Important sources of potassium, magnesium, and fiber
Fat-free or low-fat milk and milk products	2-3	2-3	2-3	2-3	2-3	3	1 cup milk or yogurt 1½ oz cheese	Fat-free milk or buttermilk, fat-free, low-fat, or reduced-fat cheese, fat-free/low-fat regular or frozen yogurt	Major sources of calcium and protein

Table 5–2. DASH EATING PLAN: SERVINGS PER DAY BY FOOD GROUP AND TOTAL ENERGY INTAKE (continued)

(Table 5–3 provides estimated energy requirements (EER) by age, gender, and activity level.)

Food Group	1,200 Calories	1,400 Calories	1,600 Calories	1,800 Calories	2,000 Calories	2,600 Calories	Serving Sizes	Examples and Notes	Significance of Each Food Group to the DASH Eating Plan
Lean meats, poultry, and fish	3 or less	3-4 or less	3-4 or less	6 or less	6 or less	6 or less	1 oz cooked meats, poultry, or fish 1 egg†	Select only lean; trim away visible fats; broil, roast, or poach; remove skin from poultry	Rich sources of protein and magnesium
Nuts, seeds, and legumes	3 per week	3 per week	3-4 per week	4 per week	4-5 per week	1	1/3 cup or 1½ oz nuts 2 Tbsp peanut butter 2 Tbsp or ½ oz seeds ½ cup cooked legumes (dry beans and peas)	Almonds, filberts, mixed nuts, peanuts, walnuts, sunflower seeds, peanut butter, kidney beans, lentils, split peas	Rich sources of energy, magnesium, protein, and fiber
Fats and oils‡	1	1	2	2-3	2-3	3	1 tsp soft margarine 1 tsp vegetable oil 1 Tbsp mayonnaise 2 Tbsp salad dressing	Soft margarine, vegetable oil (such as canola, corn, olive, or safflower), low-fat mayonnaise, light salad dressing	The DASH study had 27 percent of calories as fat, including fat in or added to foods
Sweets and added sugars	3 or less per week	3 or less per week	3 or less per week	5 or less per week	5 or less per week	≤ 2	1 Tbsp sugar 1 Tbsp jelly or jam ½ cup sorbet, gelatin 1 cup lemonade	Fruit-flavored gelatin, fruit punch, hard candy, jelly, maple syrup, sorbet and ices, sugar	Sweets should be low in fat

The Food and Drug Administration (FDA) and the Environmental Protection Agency are advising women of childbearing age who may become pregnant, pregnant women, nursing mothers, and young children to avoid some types of fish and shellfish and eat fish and shellfish that are low in mercury. For more information, call the FDA's food information line toll free at 1-888-SAFEFOOD or visit www.fda.gov/Food/FoodSafety/Product-specificinformation/Seafood/FoodbornePathogensContaminants/Methylmercury/ucm115644.htm.

* Whole grains are recommended for most grain servings as a good source of fiber and nutrients.

** Serving sizes vary between 1/2 cup and 1-1/4 cups, depending on cereal type. Check product's Nutrition Facts label.

† Since eggs are high in cholesterol, limit egg yolk intake to no more than four per week; two egg whites have the same protein content as 1 oz meat.

‡ Fat content changes serving amount for fats and oils. For example, 1 Tbsp regular salad dressing = 1 serving; 1 Tbsp low-fat dressing = 1/2 serving; 1 Tbsp fat-free dressing = zero servings.

Abbreviations: oz = ounce; Tbsp = tablespoon; tsp = teaspoon.

Table 5–3. ESTIMATED CALORIE NEEDS PER DAY BY AGE, GENDER, AND PHYSICAL ACTIVITY LEVEL*

Estimated amounts of calories needed to maintain caloric balance for various gender and age groups at three different levels of physical activity. The estimates are rounded to the nearest 200 calories. An individual's calorie needs may be higher or lower than these average estimates.

Gender	Age (years)	Calorie Requirements (kcals) by Activity Level**		
		Sedentary	Moderately Active	Active
	2-3	1,000-1,200	1,000-1,400***	1,000-1,400***
Female****	4-8	1,200-1,400	1,400-1,600	1,400-1,800
	9-13	1,400-1,600	1,600-2,000	1,800-2,200
	14-18	1,800	2,000	2,400
	19-30	1,800-2,000	2,000-2,200	2,400
Male	4-8	1,200-1,400	1,400-1,600	1,600-2,000
	9-13	1,600-2,000	1,800-2,200	2,000-2,600
	14-18	2,000-2,400	2,400-2,800	2,800-3,200
	19-30	2,400-2,600	2,600-2,800	3,000

* Based on Estimated Energy Requirements (EER) equations, using reference heights (average) and reference weights (healthy) for each age/gender group. For children and adolescents, reference height and weight vary. For adults, the reference man is 5 feet 10 inches tall and weighs 154 pounds. The reference woman is 5 feet 4 inches tall and weighs 126 pounds. EER equations are from the Institute of Medicine. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids. Washington (DC): The National Academies Press; 2002.

** Sedentary means a lifestyle that includes only the light physical activity associated with typical day-to-day life. Moderately active means a lifestyle that includes physical activity equivalent to walking about 1.5 to 3 miles per day at 3 to 4 miles per hour, in addition to the light physical activity associated with typical day-to-day life. Active means a lifestyle that includes physical activity equivalent to walking more than 3 miles per day at 3 to 4 miles per hour, in addition to the light physical activity associated with typical day-to-day life.

*** The calorie ranges shown are to accommodate needs of different ages within the group. For children and adolescents, more calories are needed at older ages. For adults, fewer calories are needed at older ages.

**** Estimates for females do not include women who are pregnant or breastfeeding.

6. Physical Activity

Physical activity is any bodily movement produced by contraction of skeletal muscle that increases energy expenditure above a basal level. Physical activity can be focused on strengthening muscles, bones and joints but because these guidelines address CV health, the evidence review concentrated on aerobic activity and on the opposite of activity, sedentary behavior. There is strong evidence for beneficial effects of physical activity and disadvantageous effects of a sedentary lifestyle on the overall health of children and adolescents across a broad array of domains. Our review focused on the effects of activity on CV health because physical inactivity has been identified as an independent risk factor for coronary heart disease in adults. Over the last several decades, there has been a steady decrease in the amount of time that children spend being physically active and an accompanying increase in time spent in sedentary activities. The evidence review identified many studies in youth ranging in age from 4 to 21 years that strongly link increased time spent in sedentary activities with reduced overall activity levels and with disadvantageous lipid profiles, higher systolic blood pressure, higher levels of obesity and higher levels of all the obesity-related cardiovascular risk factors including hypertension, insulin resistance and type 2 diabetes.

Conclusions and Grading of the Evidence Review for Physical Activity

The Expert Panel felt that the evidence strongly supports the role of physical activity in optimizing cardiovascular health in children and adolescents.

- There is reasonably good evidence that physical activity patterns established in childhood are carried forward into adulthood. (Grade C)
- There is strong evidence that increases in moderate-to-vigorous physical activity are associated with lower systolic and diastolic blood pressure; decreased measures of body fat; decreased BMI; improved fitness measures; lower total cholesterol; lower LDL cholesterol; lower triglycerides; higher HDL cholesterol; and decreased insulin resistance in childhood and adolescence. (Grade A)
- There is limited but strong and consistent evidence that physical exercise interventions improve subclinical measures of atherosclerosis. (Grade B)
- Physical activity patterns, dietary choices, and smoking behaviors cluster together. (Grade C)
- There is no evidence of harm associated with increased physical activity or limitation of sedentary activity in normal children. (Grade A)
- There is strong evidence that physical activity should be promoted in schools. (Grade A)

There is less specific information on the type and amount of physical exercise required for optimum CV health. Reported activity interventions ranged from 20-60 minutes 2 to 5 times/week in children ages 3-17 years and included a wide variety of dynamic and isometric exercises. Extrapolating from these interventions that occurred in supervised settings to the real world of childhood and adolescence, the Expert Panel recommends at least 1 hour of moderate-to-vigorous activity every day

of the week for children over 5 years of age. In agreement with the "Physical Activity Guidelines Advisory Committee Report, 2008" from the U.S. Department of Health and Human Services, the Expert Panel recommends that activity be vigorous on 3 days/week (www.health.gov/paguidelines). In working with children and families, the Expert Panel suggested that moderate-to-vigorous activity could be compared to jogging or playing baseball and that vigorous physical activity could be compared with running, playing singles tennis or soccer. Similarly, reducing sedentary time is convincingly associated with a favorable CV profile, and the Expert Panel agreed with the recommendation from the AAP for limiting leisure screen time to less than 2 hrs/day.

Table 6–1. EVIDENCE–BASED ACTIVITY RECOMMENDATIONS FOR CARDIOVASCULAR HEALTH

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.
Supportive actions represent expert consensus suggestions from the Expert Panel provided to support implementation of the recommendations; they are not graded.

Birth–12 m	Parents should create an environment promoting and modeling physical activity and limiting sedentary time	Grade D *Recommend*
	Supportive actions: Discourage TV viewing altogether	
1–4 y	**Unlimited active playtime in safe, supportive environment**	Grade D *Recommend*
	Limit sedentary time, especially TV/video	Grade D *Recommend*
	Supportive Actions: For children < 2 years, discourage television viewing altogether	
	Limit total media time to no more than 1-2 hours of quality programming per day	
	No TV in child's bedroom	
	Encourage family activity at least once a week	
	Counsel routine activity for parents as role models for children	
5–10 y	**Moderate-to-vigorous physical activity* every day**	Grade A *Strongly recommend*
	Limit daily leisure screen time (TV/video/computer)	Grade B *Strongly recommend*
	Supportive Actions: Prescribe moderate-to-vigorous activity* 1 h/d with vigorous intensity physical activity** on 3 d/wk	
	Limit total media time to no more than 1-2 hours of quality programming per day	
	No TV in child's bedroom	
	Take activity and screen time history from child once a year	
	Match physical activity recommendations with energy intake (See Table 5–1 in Section 5. Nutrition and Diet for Estimated Energy Requirements) by gender and age group at three levels of physical activity	
	Recommend appropriate safety equipment relative to each sport	
	Support recommendations for daily physical education in schools	

Table 6–1. **EVIDENCE–BASED ACTIVITY RECOMMENDATIONS FOR CARDIOVASCULAR HEALTH (continued)**

11–17 y	**Moderate-to-vigorous physical activity* every day**	Grade A *Strongly recommend*
	Limit leisure time TV/video/computer use	Grade B *Strongly recommend*
	Supportive Actions: Encourage adolescents to aim for 1 h/d of moderate-to-vigorous daily activity*, with vigorous intense physical activity** on 3 d/wk	
	No TV in child's bedroom	
	Limit total media time to no more than 1-2 hours of quality programming per day	
	Match activity recommendations with energy intake	
	Take activity and screen time history from adolescent at health supervision visits	
	Encourage involvement in year-round, physical activities	
	Support continued family activity once a week and/or family support of adolescent's physical activity program	
	Endorse appropriate safety equipment relative to each sport	
18–21 y	**Moderate-to-vigorous physical activity* every day**	Grade A *Strongly recommend*
	Limit leisure time TV/video/computer use	Grade B *Strongly recommend*
	Supportive Actions: Support goal of 1 h/d of moderate-to-vigorous daily activity* with vigorous intense physical activity** on 3 d/wk	
	Recommend that combined leisure screen time not exceed 2 h/d	
	Activity and screen time history at health supervision visits	
	Encourage involvement in year-round, lifelong physical activities	

* Examples of moderate-to-vigorous physical activities are jogging or playing baseball.
** Examples of vigorous physical activities are running, playing singles tennis or soccer.

7. Tobacco Exposure

Tobacco dependence is responsible for approximately 4 million annual deaths worldwide, and in utero exposure to tobacco products, involuntary tobacco smoke exposure (secondhand smoke), and tobacco use directly impair health in fetuses, infants, children, and adolescents. Based on an analysis of published causes of death, tobacco use is the leading actual cause of death in the United States. The evidence that cigarette use is harmful and addictive is unequivocal. In childhood, nicotine is highly addicting with symptoms of tobacco dependence demonstrated after brief intermittent use. Cigarette use among high school students declined from 1997 to 2003. Rates were stable from 2003 to 2007 with more than 20% of high school students reporting daily smoking. From a public health standpoint, the need to reduce tobacco exposure is compelling, and a role for pediatric health care providers is essential.

A clinical practice guideline update from the U.S. Public Health Service published in May 2008 systematically reviewed almost 9,000 publications and concluded that smoking prevention and cessation interventions are effective in adults. These same methods should be safely applicable in childhood and adolescence since behavioral interventions to alter smoking behaviors have little if any morbidity, and since morbidity with pharmacologic treatment is limited. Physicians who care for children are well positioned to provide prevention and treatment interventions for their patients. Youth interventions must target parents as well as children since parental smoking is both a risk factor for child smoking and provides secondhand smoke exposure to fetuses and children. The evidence review assessed prevention and treatment interventions in each of these areas.

Conclusions and Grading of the Evidence on Preventing Tobacco Exposure

Among all the known risk factors for CV disease, the dichotomy between known benefits of risk elimination and the paucity of evidence for effective interventions to achieve risk reduction in pediatric care provider settings is greatest for tobacco exposure. The quality of the evidence regarding the harm of smoking and the benefits of avoiding passive smoke exposure, smoking prevention and smoking cessation is uniformly Grade A. The reason that evidence grades in the recommendations are less than Grade A reflects the lack of existing evidence on interventions impacting smoking behaviors in specific pediatric age groups as opposed to the collective evidence.

- Good quality interventions in pediatric care settings to decrease children's environmental smoke exposure have shown mixed results. (Grade B)
- Intervention studies to prevent smoking initiation have had moderate success, although long-term results are limited. (Grade B)
- Practice-based interventions to achieve smoking cessation in adolescents have had moderate success with limited long term follow-up. (Grade B)
- School-based smoking prevention programs have been moderately successful, with limited long term follow-up. (Grade B)

Although the evidence base for effective office-based approaches to tobacco interventions is moderate and mixed, the evidence that cigarette use is harmful and addictive is unequivocal. The need to reduce tobacco exposure is so compelling that a role for pediatric health care providers is essential. The lack of harm associated with such interventions and the importance of communicating the message of risk associated with

tobacco provides the rationale for "Strongly Recommend," despite the lack of conclusive evidence that office-based interventions reliably reduce tobacco initiation or smoking cessation. Physicians and nurses who care for children are well positioned to provide intervention to patients who smoke. The Expert Panel feels that such providers should routinely identify patients who smoke using the medical history. Patients should be explicitly informed about the addictive and adverse health effects of tobacco use. By using the 5 A's (ask, advise, assess, assist, arrange), providers can assess readiness to quit and assist in providing resources to support smoking cessation efforts. Information about telephone quit lines (e.g., 1-800-QUIT-NOW), community cessation programs, and pharmacotherapy should also be made available.

As described, practice-based interventions to decrease environmental smoke exposure have shown mixed results. Nonetheless, the Expert Panel believes that pediatric care providers should identify parents and other caregivers who smoke and explicitly recommend that children not be exposed to tobacco smoke in the home, in automobiles, and in any other space where exposure can occur. For the parent who smokes, information provided should include statements about health benefits to the individual, child and/or fetus as well as referral to smoking cessation care providers.

Table 7–1. EVIDENCE–BASED RECOMMENDATIONS TO PREVENT TOBACCO EXPOSURE

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.
Supportive actions represent expert consensus suggestions from the Expert Panel provided to support implementation of the recommendations; they are not graded.

Prenatal	Smoking history from mothers → Provide explicit smoking cessation message before and during pregnancy	Grade A *Strongly recommend*
	Supportive Actions: • Identify resources to support maternal smoking cessation efforts • Advocate for school and community-based smoke-free interventions • See Perinatal Factors section	
Birth–12 m, 1–4 y	Smoke-free home environment	Grade B *Strongly recommend*
	Reinforce this message at every encounter, including urgent visits for respiratory problems	Grade C *Recommend*
	Supportive Actions: • Provide information about health benefits of a smoke-free home to parents and children • Advocate for school and community-based smoke-free interventions	
5–10 y	Obtain smoke exposure history from child, including personal history of tobacco use.	Grade C *Recommend*
	Counsel patients strongly about not smoking, including providing explicit information about the addictive and adverse health effects of smoking	Grade C *Recommend*
11–17 y 18–21 y	Obtain personal smoking history at every non-urgent health encounter	Grade B *Strongly recommend*
	Explicitly recommend against smoking	Grade B *Strongly recommend*
	Provide specific smoking cessation guidance	Grade B *Strongly recommend*

	Supportive Actions:
	• Use 5A questions to assess readiness to quit
	• Establish your health care practice as a resource for smoking cessation
	  ▪ Provide quit line number
	  ▪ Identify community cessation resources
	  ▪ Provide information about pharmacotherapy for cessation
	• Advocate for school and community-based smoke-free interventions	

8. High Blood Pressure

In 2004, an NHLBI Task Force published *The Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents.* This report included a complete review of the current evidence on this subject and detailed recommendations for managing blood pressure throughout childhood. These recommendations were used as the basic recommendations for these guidelines, considered complete until 2003 when the review for the report ended. This evidence review for blood pressure for these guidelines was therefore limited to studies published between January 1, 2003, and June 30, 2007, with the addition of selected studies through June 30, 2008, identified by the Expert Panel that meet all the criteria for inclusion. Repeating the review performed by *The Fourth Report* Task Force was not felt to be necessary, given the short time since publication of that report, nor a judicious use of the resources available for development of these guidelines. Recommendations regarding blood pressure are all graded as expert opinion (Grade D) as they are based on the expert consensus conclusions of *The Fourth Report.*

Conclusions of the Evidence Review Update for High Blood Pressure (2003-2008)

- The evidence review for the defined time period resulted in no major changes in the approach to BP evaluation and management.
- In epidemiologic surveys of children and adolescents over the past 20 years, blood pressure levels are increasing, and the prevalence of hypertension and prehypertension are increasing, explained partially by the rise in obesity.
- Prehypertension progresses to hypertension at a rate of approximately 7 percent per year; hypertension persists in almost one-third of boys and one-fourth of girls on 2-year longitudinal follow-up.
- Breastfeeding and supplementation of formula with polyunsaturated fatty acids in infancy are both associated with lower blood pressure at follow-up.
- A DASH-style diet, which is rich in fruits, vegetables, low-fat or fat-free dairy products, whole grains, fish, poultry, beans, seeds and nuts, and lower in sweets and added sugars, fats, and red meats than the typical American diet, is associated with lower blood pressure. The CHILD 1 combined with the DASH eating plan described in the Diet and Nutrition section is an appropriate diet for children, which meets the DASH study and *Dietary Guidelines for Americans 2010* nutrient goals.
- Lower dietary sodium intake is associated with lower blood pressure levels in infants, children, and adolescents.
- Losartan, amlodipine, felodipine, fosinopril, lisinopril, metoprolol, and valsartan can be added to the list of medications that are tolerated over short periods, and can reduce blood pressure in children from ages 6-17 years but predominantly are effective in adolescents. For African American children, greater doses of fosinopril may be needed for effective blood pressure control. Medications are shown in Table 8–5.
- In one study in small-for-gestational-age babies, a nutrient-enriched diet that promoted rapid weight gain was associated with higher blood pressure on follow-up in late childhood. This potential risk should be considered when such diets are selected in the clinical setting.
- In one study, transcendental meditation effectively lowered blood pressure in non-hypertensive adolescents.

Recommendations

The Fourth Report of the National High Blood Pressure Education Program provided an algorithm and flow diagram to assist clinicians in identifying hypertension in children. For these guidelines, *The Fourth Report* recommendations are stratified here to provide an age-appropriate approach congruent with other risk factor recommendations in other sections and this is also reflected in a series of revised algorithms (Table 8–1, and Figures 8–1 and 8–2). Conditions under which children < 3 years old should have blood pressure measured are shown in Table 8–2. The blood pressure norms for age, sex, and height are shown in Tables 8–3 and 8–4 below and are taken directly from *The Fourth Report*. Age-specific percentiles of blood pressure measurements from birth to 12 months are provided in *The Report of the 2nd Task Force for Blood Pressure Control in Children, 1987.* For all age groups the assessment of left ventricular mass by echocardiography is recommended as the best method to assess hypertensive target organ disease; this should be done for patients with Stage 2 hypertension and those with persistent Stage 1 hypertension. Elevated LV mass may be useful in establishing the need for pharmacologic treatment of hypertension. In Table 8–5, the medications used to achieve blood pressure control in children and adolescents are shown. At present, there are no data to support the use of specific antihypertensive agents for specific age groups.

Table 8–1. AGE–SPECIFIC RECOMMENDATIONS FOR BLOOD PRESSURE (BP) MEASUREMENT AND DIAGNOSIS OF HYPERTENSION

BP recommendations are based on *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents (The Fourth Report)*, with the evidence review updated from 2003.

Recommendations are all graded as expert opinion (Grade D) as they are based on the expert consensus conclusions of *The Fourth Report.*

Birth–2 y

No routine BP measurement

Measure BP if history (+) for neonatal complications, congenital heart disease, urinary/renal abnormality, solid-organ transplant, malignancy, drug Rx, or condition known to raise BP or increase intracranial pressure (Table 8–2)

If BP ≥ 90th%ile by oscillometry, confirm by auscultation
→ If BP confirmed ≥ 90th%ile, initiate evaluation for etiology and treatment per algorithm (Figure 8–2)

3–11 y

Annual BP measurement in all, interpreted for age/sex/height per Tables 8–3 and 8–4

- BP < 90th%ile, repeat in 1 year
- BP ≥ 90th%ile:
  - Repeat BP X 2 by auscultation
  - Average replicate measurements → Re-evaluate BP category

→ If BP confirmed ≥ 90th%ile, < 95th%ile = **Prehypertension (HTN)**
- Recommend weight management if indicated
- Repeat BP in 6 months

→ If BP ≥ 95th%ile, < 99th%ile + 5 mmHg
- Repeat BP in 1-2 weeks, average all BP measurements
- Re-evaluate BP category
- BP confirmed ≥ 95th%ile, < 99th%ile + 5 mmHg = **Stage 1 HTN**
- Basic work-up per Figure 8–2

→ If BP ≥ 99th%ile + 5 mmHg
- Repeat BP by auscultation X 3 *at that visit,* average all BP measurements
- Re-evaluate BP category
- BP confirmed ≥ 99th%ile + 5 mmHg = **Stage 2 HTN**
- **Refer to pediatric HTN expert within 1 week OR**
- **Begin BP treatment and initiate basic work-up, per Figure 8–2**

Table 8–1. AGE–SPECIFIC RECOMMENDATIONS FOR BP MEASUREMENT AND DIAGNOSIS OF HYPERTENSION (continued)

12–17 y

Annual BP measurement in all, interpreted for age/sex/height per Tables 8–3 and 8–4 below

- BP < 90th%ile, counsel on CHILD 1, activity recommendations, and repeat BP in 1 year
- BP ≥ 90th%ile **or** ≥ 120/80:
  - Repeat BP X 2 by auscultation
  - Average replicate measurements → Re-evaluate BP category

→ If BP confirmed ≥ 90th%ile, < 95th%ile **or** ≥ 120/80 = **Pre-HTN**
- CHILD 1, activity recommendations, weight management if indicated
- Repeat BP in 6 months

→ If BP ≥ 95th%ile, < 99th%ile + 5 mmHg
- Repeat BP in 1-2 weeks, average all BP measurements
- Re-evaluate BP category
- BP confirmed ≥ 95th%ile, < 99th%ile + 5 mmHg = **Stage 1 HTN**
- Basic work-up per Figure 8–2

→ If BP ≥ 99th%ile + 5 mmHg
- Repeat BP by auscultation X 3 *at that visit,* average all BP measurements
- Re-evaluate BP category
- BP confirmed ≥ 99th%ile + 5 mmHg = **Stage 2 HTN**
- **Refer to pediatric HTN expert within 1 week OR**
- **Begin BP treatment and initiate work-up, per Figure 8–2**

18–21 y

Measure BP at all health care visits

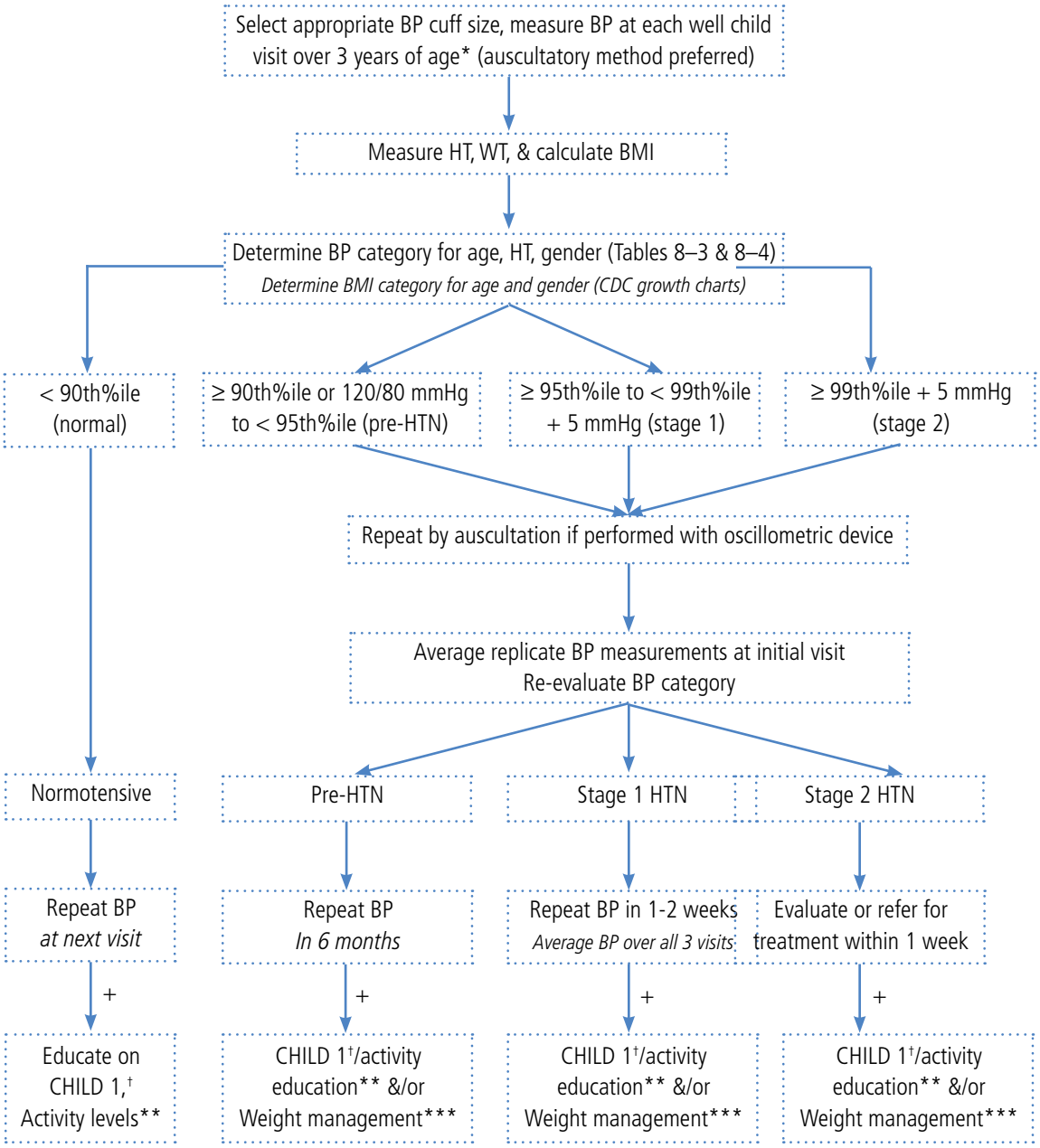
BP ≥ 120/80 to 139/89 = Pre-HTN
BP ≥ 140/90 to 159/99 = Stage 1 HTN
BP ≥ 160/100 = Stage 2 HTN

Evaluation/Treatment per *JNC* recommendations

Table 8–2. CONDITIONS UNDER WHICH CHILDREN < 3 YEARS OLD SHOULD HAVE BP MEASURED

- History of prematurity, very low birth weight, or other neonatal complication requiring intensive care
- Congenital heart disease (repaired or unrepaired)
- Recurrent urinary tract infections, hematuria, or proteinuria
- Known renal disease or urologic malformations
- Family history of congenital renal disease
- Solid-organ transplant
- Malignancy or bone marrow transplant
- Treatment with drugs known to raise BP
- Other systemic illnesses associated with hypertension (neurofibromatosis, tuberous sclerosis, etc.)
- Evidence of increased intracranial pressure

Figure 8–1. **BP MEASUREMENT AND CATEGORIZATION**



LEGEND:

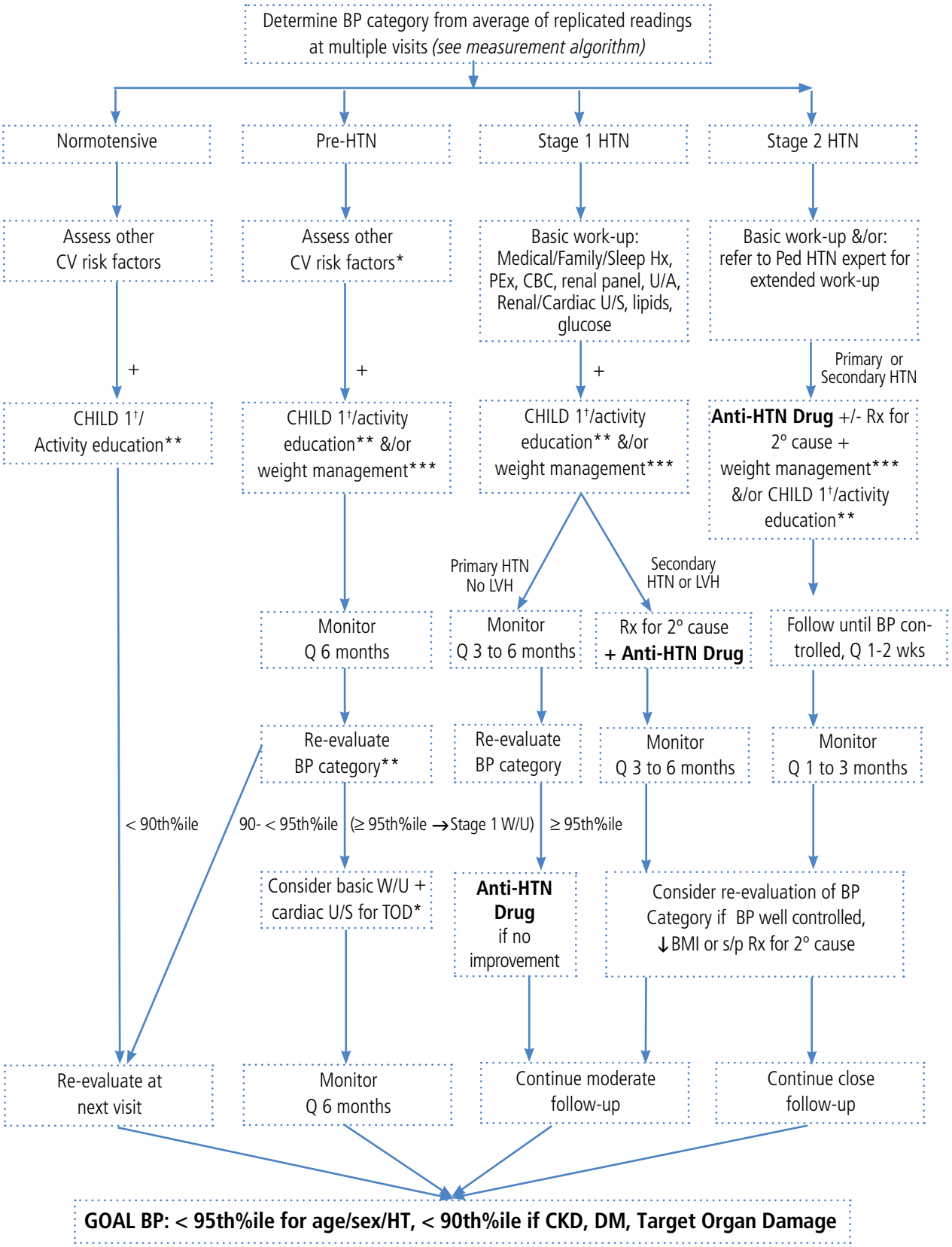
* See Table 8-1

† CHILD 1 = Cardiovascular Health Integrated Lifestyle Diet - Section 5. Nutrition and Diet

** Section 6. Physical Activity

*** Section 10. Overweight and Obesity

Figure 8–2. **BP MANAGEMENT BY CATEGORY**



LEGEND:

* Work-up for target organ damage (TOD)/LVH if obese or (+) for other CV risk factors.

† CHILD 1=Cardiovascular Health Integrated Lifestyle Diet; See Section 5. Nutrition and Diet.

** Activity Education. See Section 6. Physical Activity.

*** Weight management. See Section 10. Overweight and Obesity.

Table 8–3. BP NORMS FOR BOYS BY AGE AND HEIGHT PERCENTILE

Age, year	BP %ile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90

Table 8–3. BP NORMS FOR BOYS BY AGE AND HEIGHT PERCENTILE (continued)

Age, year	BP %ile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	**50th**	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	**50th**	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	**50th**	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	**50th**	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	**50th**	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	**50th**	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	**50th**	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

SD = standard deviation

The 90th%ile is 1.28 SD, the 95th%ile is 1.645 SD, and the 99th%ile is 2.326 SD over the mean.

Table 8–4. BP NORMS FOR GIRLS BY AGE AND HEIGHT PERCENTILE

Age year	BP %ile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88

Table 8–4. BP Norms For Girls By Age And Height Percentile (continued)

Age, year	BP %ile	SBP, mm Hg							DBP, mm Hg						
		Percentile of Height							Percentile of Height						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	**50th**	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	**50th**	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	**50th**	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	**50th**	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	**50th**	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	**50th**	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	**50th**	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

SD = standard deviation

The 90th%ile is 1.28 SD, the 95th%ile is 1.645 SD, and the 99th%ile is 2.326 SD over the mean.

Table 8–5. ANTI–HYPERTENSIVE MEDICATIONS WITH PEDIATRIC EXPERIENCE

Class	Drug	Initial Dose*	Maximal Dose	Dosing Interval	Evidence†	FDA‡	Comments§
Angiotensin-converting enzyme (ACE) inhibitor	**Benazepril**	0.2 mg/kg/day up to 10 mg/day	0.6 mg/kg/day up to 40 mg/day	qd	RCT	Yes	1. All ACE inhibitors are contraindicated in pregnancy; females of childbearing age should use reliable contraception. 2. Check serum potassium and creatinine periodically to monitor for hyperkalemia and azotemia. 3. Cough and angioedema are reportedly less common with newer members of this class than with captopril. 4. Benezapril and lisinopril labels contain information on the preparation of a suspension; captopril may also be compounded into a suspension. 5. FDA approval for ACE inhibitors with pediatric labeling is limited to children ≥ 6 years of age and to children with creatinine clearance ≥ 30 mL/min/1.73m^2. 6. Initial dose of fosinopril of 0.1 mg/kg/day may be effective, although African American patients may require a higher dose.
	Captopril	0.3-0.5 mg/kg/dose (> 12 months)	6 mg/kg/day	tid	RCT, CS	No	
	Fosinopril**	Children > 50 kg: 5-10 mg/day	40 mg/day	qd	RCT	Yes	
	Lisinopril**	0.07 mg/kg/day up to 5 mg/day	0.6 mg/kg/day up to 40 mg/day	qd	RCT	Yes	
	Quinapril	5-10 mg/day	80 mg/day	qd	RCT, EO	No	
Angiotensin-receptor blocker (ARB)	**Irbesartan**	6-12 years: 75-150 mg/day; ≥13 years: 150-300 mg/day	300 mg/day	qd	CS	Yes	1. All ARBs are contraindicated in pregnancy; females of childbearing age should use reliable contraception. 2. Check serum potassium and creatinine periodically to monitor for hyperkalemia and azotemia. 3. Losartan label contains information on the preparation of a suspension. 4. FDA approval for ARBs is limited to children ≥ 6 years of age and to children with creatinine clearance ≥ 30 mL/min/1.73m^2 .
	Losartan**	0.7 mg/kg/day up to 50 mg/day	1.4 mg/kg/day up to 100mg/day	qd–bid	RCT	Yes	
	Valsartan**	5 -10 mg/day 0.4 mg/kg/day	40-80 mg/day 3.4 mg/kg/day	qd	RCT	No	
Alpha- and beta-antagonist	**Labetalol**	1–3 mg/kg/day	10–12 mg/kg/day up to 1,200 mg/day	bid	CS, EO	No	1. Asthma and overt heart failure are relative contraindications. 2. Heart rate is dose limiting. 3. May impair athletic performance in athletes. 4. Should not be used in insulin-dependent diabetics.

Table 8–5. **ANTI–HYPERTENSIVE MEDICATIONS WITH PEDIATRIC EXPERIENCE (continued)**

Class	Drug	Initial Dose*	Maximal Dose	Dosing Interval	Evidence†	FDA ‡	Comments§
Beta-antagonist	**Atenolol**	0.5-1 mg/kg/day	2 mg/kg/day up to 100 mg/day	qd–bid	CS	No	1. Noncardioselective agents (propranolol) are contraindicated in asthma and heart failure. 2. Heart rate is dose limiting. 3. May impair athletic performance in athletes. 4. Should not be used in insulin-dependent diabetics. 5. A sustained-release, once-daily formulation of propranolol is available.
	Bisoprolol/ HCTZ	2.5-6.25 mg/day	10/6.25 mg/day	qd	RCT	No	
	Metoprolol**	Children > 6 years: 1 mg/kg/day (12.5-50 mg/day)	2 mg/kg/day up to 200 mg/day	bid	CS	Yes***	
	Propranolol	1-2 mg/kg/day	4 mg/kg/day up to 640 mg/day	bid–tid	RCT, EO	Yes	
Calcium channel blocker	**Amlodipine****	Children 6-17 years: 2.5 mg/day	5 mg/day	qd	RCT	Yes	1. Amlodipine and isradipine can be compounded into stable extemporaneous suspensions. 2. Felodipine and extended-release nifedipine tablets must be swallowed whole. 3. Isradipine is available in both immediate-release and sustained-release formulations; sustained release form is dosed qd or bid. 4. May cause tachycardia. 5. Doses up to 10 mg of amlodipine have been evaluated in children. 6. Contraindicated for children <1 year of age.
	Felodipine	2.5 mg/day	10 mg/day	qd	RCT, EO	No	
	Isradipine	0.15-0.2 mg/kg/day	0.8 mg/kg/day up to 20 mg/day	tid–qid	CS, EO	No	
	Extended-release nifedipine	0.25–0.5 mg/kg/day	3 mg/kg/day up to 120 mg/day	qd–bid	CS, EO	No	
Central alpha-agonist	**Clonidine**	Children ≥ 12 years: 0.2 mg/day	2.4 mg/day	bid	EO	Yes	1. May cause dry mouth and/or sedation. 2. Transdermal preparation is available. 3. Sudden cessation of therapy can lead to severe rebound hypertension.
Diuretic	**HCTZ**	1 mg/kg/day	3 mg/kg/day up to 50 mg/day	qd	EO	Yes	1. All patients treated with diuretics should have electrolytes monitored shortly after initiating therapy and periodically thereafter. 2. Useful as add-on therapy in patients being treated with drugs from other drug classes. 3. Potassium-sparing diuretics (spironolactione, triamterene, amiloride) may cause severe hyperkalemia, especially if given with ACE inhibitor or ARB.
	Chlorthalidone	0.3 mg/kg/day	2 mg/kg/day up to 50 mg/day	qd	EO	No	
	Furosemide	0.5–2.0 mg/kg/dose	6 mg/kg/day	qd–bid	EO	No	

Table 8–5. **ANTI–HYPERTENSIVE MEDICATIONS WITH PEDIATRIC EXPERIENCE (continued)**

Class	Drug	Initial Dose*	Maximal Dose	Dosing Interval	Evidence†	FDA ‡	Comments§
Diuretic	**Spironolactone**	1 mg/kg/day	3.3 mg/kg/day up to 100 mg/day	qd–bid	EO	No	4. Furosemide is labeled only for treatment of edema but may be useful as add-on therapy in children with resistant hypertension, particularly in children with renal disease. 5. Chlorthalidone may precipitate azotemia in patients with renal diseases and should be used with caution in those with severe renal impairment.
	Triamterene	1–2 mg/kg/day	3–4 mg/kg/day up to 300 mg/day	bid	EO	No	
	Amiloride	0.4-0.625 mg/kg/day	20 mg/day	qd	EO	No	
Peripheral alpha-antagonist	**Doxazosin**	1 mg/day	4 mg/day	qd	EO	No	1. May cause first-dose hypotension.
	Prazosin	0.05-0.1 mg/kg/day	0.5 mg/kg/day	tid	EO	No	
	Terazosin	1 mg/day	20 mg/day	qd	EO	No	
Vasodilator	**Hydralazine**	0.75 mg/kg/day	7.5 mg/kg/day up to 200 mg/day	qid	EO	Yes	1. Tachycardia and fluid retention are common side effects. 2. Hydralazine can cause a lupus-like syndrome in slow acetylators. 3. Prolonged use of minoxidil can cause hypertrichosis. 4. Minoxidil is usually reserved for patients with hypertension resistant to multiple drugs.
	Minoxidil	Children < 12 years: 0.2 mg/kg/day; children > 12 years: 5 mg/day	Children < 12 years; 50 mg/day; children ≥ 12 years: 100 mg/day	qd-tid	CS, EO	Yes	

RCT = randomized controlled trial

CS = case series

EO = expert opinion

* The maximal recommended adult dose should not be exceeded in routine clinical practice.

† Level of evidence on which recommendations are based.

‡ U.S. Food and Drug Administration (FDA)-approved pediatric labeling information is available for treatment of hypertension. Recommended doses for agents with FDA-approved pediatric labels contained in this table are the doses contained in the approved labels. Even when pediatric labeling information is not available, the FDA-approved label should be consulted for additional safety information.

§ Comments apply to all members of each drug class except where otherwise stated.

** Indicates drug added since *The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents* (2004).

*** Study did not reach primary end point (dose response for reduction in systolic blood pressure). Some prespecified secondary end points demonstrated effectiveness.

9. Lipids and Lipoproteins

Since the last NCEP Expert Panel report for lipid management in children and adolescents were published in 1992, both the knowledge base surrounding dyslipidemia in childhood and the clinical picture have changed. A series of critical observational studies have demonstrated a clear correlation between lipoprotein disorders and the onset and severity of atherosclerosis in children, adolescents and young adults. A major increase in the prevalence of obesity has led to a much larger population of children with dyslipidemia. At the time of the original guidelines, the focus was almost exclusively on identification of children with elevated low density lipoprotein cholesterol (LDL-C). Since then, the predominant dyslipidemic pattern in childhood is a combined pattern associated with obesity, with moderate to severe elevation in triglycerides (TG), normal to mild elevation in LDL-C and reduced high density lipoprotein cholesterol (HDL-C). Both dyslipidemic patterns have been shown to be associated with initiation and progression of atherosclerotic lesions in children and adolescents as demonstrated by pathology and imaging studies. Identification of children with dyslipidemias, which place them at increased risk for accelerated early atherosclerosis, must include a comprehensive assessment of serum lipids and lipoproteins.

The evidence review for lipids and lipoproteins addressed the association between dyslipidemia and atherosclerosis in childhood, lipid assessment in childhood and adolescence with tables of normative results provided, the dyslipidemias, dietary treatment of dyslipidemia and medication therapy.

Table 9–1. **ACCEPTABLE, BORDERLINE–HIGH AND HIGH PLASMA LIPID, LIPOPROTEIN AND APOLIPOPROTEIN CONCENTRATIONS (mg/dL) FOR CHILDREN AND ADOLESCENTS***

Note: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.

Category	Acceptable	Borderline	High+
TC	< 170	170-199	≥ 200
LDL-C	< 110	110-129	≥ 130
Non-HDL-C	< 120	120-144	≥ 145
ApoB	< 90	90-109	≥ 110
TG			
0-9 years	< 75	75-99	≥ 100
10-19 years	< 90	90-129	≥ 130

Category	Acceptable	Borderline	Low+
HDL-C	> 45	40-45	< 40
ApoA-1	> 120	115-120	< 115

* Values for plasma lipid and lipoprotein levels are from the National Cholesterol Education Program (NCEP) Expert Panel on Cholesterol Levels in Children. Non-HDL-C values from the Bogalusa Heart Study are equivalent to the NCEP Pediatric Panel cutpoints for LDL-C. Values for plasma ApoB and ApoA-1 are from the National Health and Nutrition Examination Survey III.

\+ The cutpoints for high and borderline high represent approximately the 95th and 75th%iles, respectively. Low cutpoints for HDL-C and ApoA-1 represent approximately the 10th%ile.

Table 9–2. RECOMMENDED CUTPOINTS FOR LIPID AND LIPOPROTEIN LEVELS (MG/DL) IN YOUNG ADULTS*

Category	Acceptable	Borderline High	High
TC	< 190	190-224	≥ 225
LDL-C	< 120	120-159	≥ 160
Non-HDL-C	< 150	150-189	≥ 190
TG	< 115	115-149	≥ 150

Category	Acceptable	Borderline Low	Low
HDL-C	> 45	40-44	< 40

* Values provided are from the Lipid Research Clinics Prevalence Study. The cutpoints for TC, LDL-C and non-HDL-C represent the 95th%ile for 20-24 year old subjects and are not identical with the cutpoints used in the most recent NHLBI *ATP III*, which are derived from combined data on adults of all ages. The age-specific cutpoints given here are provided for pediatric care providers to use in managing this young adult age group. For TC, LDL-C and non-HDL-C, borderline high values are between the 75th and 94th%ile, while acceptable are < 75th%ile. The high TG cutpoint represents approximately the 90th%ile with borderline high between the 75th and 89th%ile and acceptable < 75th%ile. The low HDL-C cutpoint represents roughly the 25th%ile, with borderline low between the 26th and 50th%ile and acceptable > the 50th%ile.

Table 9–3. CAUSES OF SECONDARY DYSLIPIDEMIA

Exogenous
Alcohol
Drug therapy:
- Corticosteroids
- Isoretinoin
- Beta-blockers
- Some oral contraceptives
- Select chemotherapeutic agents
- Select anti-retroviral agents

Endocrine/Metabolic
Hypothyroidism/hypopituitarism
Diabetes mellitus, type 1 and type 2
Pregnancy
Polycystic ovary syndrome
Lipodystrophy
Acute intermittent porphyria

Renal
Chronic renal disease
Hemolytic uremic syndrome
Nephrotic syndrome

Infectious
Acute viral/bacterial infection*
Human immunodeficiency virus infection (HIV)
Hepatitis

Hepatic
Obstructive liver disease/cholestatic conditions
Biliary cirrhosis
Alagille syndrome

Inflammatory Disease
Systemic lupus erythematosis
Juvenile rheumatoid arthritis

Storage Disease
Glycogen storage disease
Gaucher's disease
Cystine storage disease
Juvenile Tay-Sachs disease
Niemann-Pick disease

Other
Kawasaki disease
Anorexia nervosa
Post solid organ transplantation
Childhood cancer survivor
Progeria
Idiopathic hypercalcemia
Klinefelter syndrome
Werner's syndrome

* Delay measurement until ≥ 3 weeks postinfection.

Table 9–4. **SUMMARY OF MAJOR LIPID DISORDERS IN CHILDREN AND ADOLESCENTS**

Primary Lipid Disorders	Lipid/Lipoprotein Abnormality
Familial hypercholesterolemia	Homozygous: ↑↑LDL-C Heterozygous: ↑LDL-C*
Familial defective apolipoprotein B	↑LDL-C
Familial combined hyperlipidemia*	Type IIa: ↑LDL-C Type IV: ↑VLDL-C, ↑TG Type IIb: ↑LDL-C, ↑VLDL-C, ↑TG Types IIb and IV often with ↓HDL-C
Polygenic hypercholesterolemia	↑LDL-C
Familial hypertriglyceridemia (200-1,000 mg/dL)	↑VLDL-C, ↑TG
Severe hypertriglyceridemia (≥ 1,000 mg/dL)	↑Chylomicrons, ↑VLDL-C, ↑↑TG
Familial hypoalphalipoproteinemia	↓HDL-C
Dysbetalipoproteinemia (TC:250-500 mg/dL; TG: 250-600 mg/dL)	↑IDL-C, ↑chylomicron remnants

* These are the two lipid and lipoprotein disorders seen most frequently in childhood and adolescence; the latter most often manifests with obesity.
HDL-C = high-density lipoprotein cholesterol; IDL-C = intermediate-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; TC = total cholesterol; TG = triglyceride; VLDL-C = very-low-density lipoprotein cholesterol.

Conclusions and Grading of the Evidence Review for Lipid Assessment in Childhood and Adolescence

- Combined evidence from autopsy studies, vascular studies and cohort studies strongly indicates that abnormal lipid levels in childhood are associated with increased evidence of atherosclerosis. (Grade B)
- The evidence review supports the concept that early identification and control of dyslipidemia throughout youth and into adulthood will substantially reduce clinical CVD risk beginning in young adult life. Preliminary evidence in children with heterozygous FH with markedly elevated LDL-C indicates that earlier treatment is associated with reduced subclinical evidence of atherosclerosis. (Grade B)
- Multiple prospective screening cohort studies have demonstrated the normal lipid and lipoprotein distributions in childhood, adolescence, and young adult life (Tables 9–1 and 9–2). (Grade B) Cohort studies have also demonstrated significant tracking of elevated lipid levels from childhood into adulthood, with lipid and lipoprotein results in childhood predictive of future adult lipoprotein profiles; the strongest statistical correlation occurs between results in late childhood and in the third and fourth decades of life. (Grade B)
- TC and LDL-C levels fall as much as 10-20% or more during puberty. (Grade B) Based on this normal pattern of change in lipid and lipoprotein levels with growth and maturation, age 10 years (range age 9-11 years) is a stable time for lipid assessment in children. (Grade D) For most children, this age range will precede onset of puberty.
- Significant evidence exists that using family history of premature CVD or of cholesterol disorders as the primary factor in determining lipid screening for children misses approximately 30-60% of children with dyslipidemias, and accurate and reliable measures of family history are not available. (Grade B) In the absence of a clinical or historic marker, identification of children with lipid disorders that predispose them to accelerated atherosclerosis requires universal lipid assessment. (Grade B)
- Non-HDL-C has now been identified as a significant predictor of the presence of atherosclerosis, as powerful as any other lipoprotein cholesterol measure in children and adolescents. For both children and adults, non-HDL-C appears to be more predictive of persistent dyslipidemia and therefore atherosclerosis and future events than TC,

LDL-C or HDL-C alone. A major advantage of non-HDL-C is that it can be accurately calculated in a non-fasting state and is therefore very practical to obtain in clinical practice. The Expert Panel felt that non-HDL-C should be added as a screening tool for identification of a dyslipidemic state in childhood. (Grade B)

- In terms of other lipid measurements: (1) most but not all studies indicate that measurement of apoB and apoA-1 for universal screening provides no additional advantage over measuring non-HDL-C, LDL-C, and HDL-C; (2) measurement of Lp(a) is useful in the assessment of children with both hemorrhagic and ischemic stroke; (3) in offspring of a parent with premature CVD and no other identifiable risk factors, elevations of apoB, apoA-1, and Lp(a) have been noted; and (4) measurement of lipoprotein subclasses and their sizes by advanced lipoprotein testing has not been shown to have sufficient clinical utility in children at this time. (Grade B)
- Obesity is commonly associated with a combined dyslipidemia pattern with mild elevation in TC and LDL-C, moderate to severe elevation in TG and low HDL-C. This is the most common dyslipidemic pattern seen in childhood, and lipid assessment of overweight and obese children identifies an important proportion with significant lipid abnormalities. (Grade B)
- Dyslipidemias can be acquired genetically but also secondary to specific conditions such as diabetes, nephrotic syndrome, chronic renal disease, postorthotopic heart transplant, history of Kawasaki disease with persistent coronary involvement, chronic inflammatory disease, hypothyroidism, and other causes as outlined in Table 9–3. There is impressive evidence for accelerated atherosclerosis both clinically and as assessed with noninvasive methods in some of these conditions, which accordingly have been designated as special risk diagnoses for accelerated atherosclerosis (Table 9–7); management of these is described in Section 11. Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis. Lipid evaluation of these patients contributes to risk assessment and identifies an important proportion with dyslipidemia. (Grade B)
- The complete phenotypic expression of some inherited disorders like FCHL may be delayed until adulthood. Evaluation in children and adolescents from high risk families with FCHL should therefore begin in childhood and continue through adulthood (per NCEP adult treatment guidelines) and will lead to early detection of those with abnormalities. (Grade B)

Age-specific recommendations for lipid assessment are outlined in Table 9–5. Specific management for children with identified dyslipidemia is outlined in the algorithms in Figures 9–1 and 9–2. Definitions of the risk factors and special risk conditions for use with the recommendations and in the algorithms appear in Tables 9–6 and 9–7. The first step proposed for management of children with identified lipid abnormalities is a focused intervention on diet and physical activity.

Table 9–5. EVIDENCE–BASED RECOMMENDATIONS FOR LIPID ASSESSMENT

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.

Note: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.

Birth–2 y	No lipid screening	Grade C *Recommend*
2–8 y	No routine lipid screening	Grade B *Recommend*
	Measure fasting lipid profile (FLP) × 2*, average results** if:	
	• Parent, grandparent, aunt/uncle, or sibling with myocardial infarction (MI), angina, stroke, coronary artery bypass graft (CABG)/stent/angioplasty at < 55 years in males, < 65 years in females	Grade B *Strongly recommend*
	• Parent with TC ≥ 240 mg/dL or known dyslipidemia	Grade B *Strongly recommend*
	• Child has diabetes, hypertension, BMI ≥ 95th%ile or smokes cigarettes	Grade B *Strongly recommend*
	• Child has a moderate- or high-risk medical condition (Table 9–7)	Grade B *Strongly recommend*
	* Interval between FLP measurements: after 2 weeks but within 3 months. ** Use Table 9–1 for interpretation of results; use lipid algorithms in Figures 9–1 and 9–2 for management of results.	
9–11 y	**Universal Screening** • Non-FLP: Calculate non-HDL-C: Non-HDL-C = TC – HDL-C*	Grade B *Strongly recommend*
	Non-HDL ≥ 145 mg/dL, HDL < 40 mg/dL → FLP × 2, Lipid algorithms below** OR • FLP: LDL-C ≥ 130 mg/dL, non-HDL-C ≥ 145 mg/dL HDL-C < 40 mg/dL, TG ≥ 100 mg/dL if < 10 years; ≥ 130 mg/dL if ≥ 10 years → Repeat FLP after 2 weeks but within 3 months → lipid algorithms below**	
	* Disregard TG and LDL-C in nonfasting sample. ** Use Table 9–1 for interpretation of results; use lipid algorithms in Figures 9–1 and 9–2 for management of results.	

Table 9–5. EVIDENCE–BASED RECOMMENDATIONS FOR LIPID ASSESSMENT (CONTINUED)

12–16 y	No routine screening*	Grade B *Recommend*
	Measure FLP × 2**, average results, if new knowledge of:	
	• Parent, grandparent, aunt/uncle or sibling with MI, angina, stroke, CABG/stent/ angioplasty, sudden death at < 55 years in males, < 65 years in females	Grade B *Strongly recommend*
	• Parent with TC ≥ 240 mg/dL or known dyslipidemia	Grade B *Strongly recommend*
	• Patient has diabetes, hypertension, BMI ≥ 85th%ile or smokes cigarettes	Grade B *Strongly recommend*
	• Patient has a moderate- or high-risk medical condition (Table 9–7)	Grade B *Strongly recommend*

* Lipid screening is not recommended for those ages 12-16 years because of significantly decreased sensitivity and specificity for predicting adult LDL-C levels and significantly increased false-negative results in this age group. Selective screening is recommended for those with the clinical indications outlined.

** Interval between FLP measurements: after 2 weeks but within 3 months.

17–21 y	**Universal screening once in this time period:**	Grade B *Recommend*
	Non-FLP: Calculate non-HDL-C: Non-HDL-C = TC – HDL-C*	
	17–19 y: Non-HDL-C ≥ 145 mg/dL, HDL-C < 40 mg/dL → FLP × 2,*** lipid algorithm below (Figure 9–1) OR FLP: LDL-C ≥ 130 mg/dL, non-HDL-C ≥ 145 mg/dL HDL-C < 40 mg/dL, TG ≥ 130 mg/dL → Repeat FLP after 2 weeks but within 3 months → lipid algorithms in Figures 9–1 and 9–2	
	20–21 y: Non-HDL-C ≥ 190 mg/dL, HDL-C < 40 mg/dL** → FLP × 2,*** average results → *Adult Treatment Panel III (ATP III)* management algorithm OR FLP: LDL-C ≥ 160 mg/dL, non-HDL-C ≥ 190 mg/dL HDL-C < 40 mg/dL, TG ≥ 150 mg/dL → Repeat FLP after 2 weeks but within 3 months, average results → *ATP III* management algorithm	

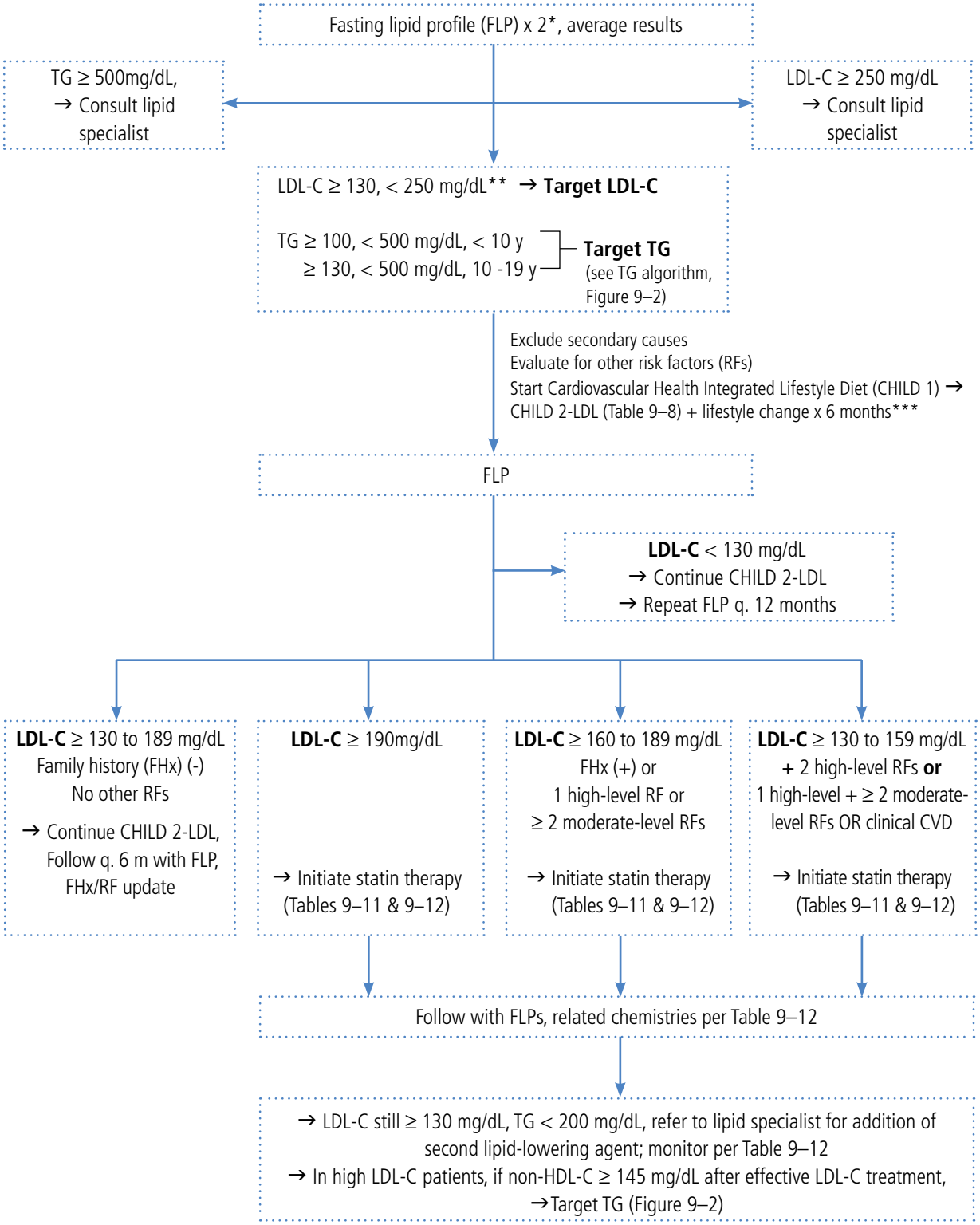
* Use Table 9–1 for interpretation of results of 7– to 19–year olds and lipid algorithms in Figures 9–1 and 9–2 for management. Use Table 9–2 for interpretation of results of 20– to 21–year olds and *ATP III* algorithms for management.

** Disregard TG and LDL-C in nonfasting sample.

*** Interval between FLP measurements: after 2 weeks but within 3 months.

Figure 9–1. DYSLIPIDEMIA ALGORITHM: TARGET LDL–C (LOW-DENSITY LIPOPROTEIN CHOLESTEROL)

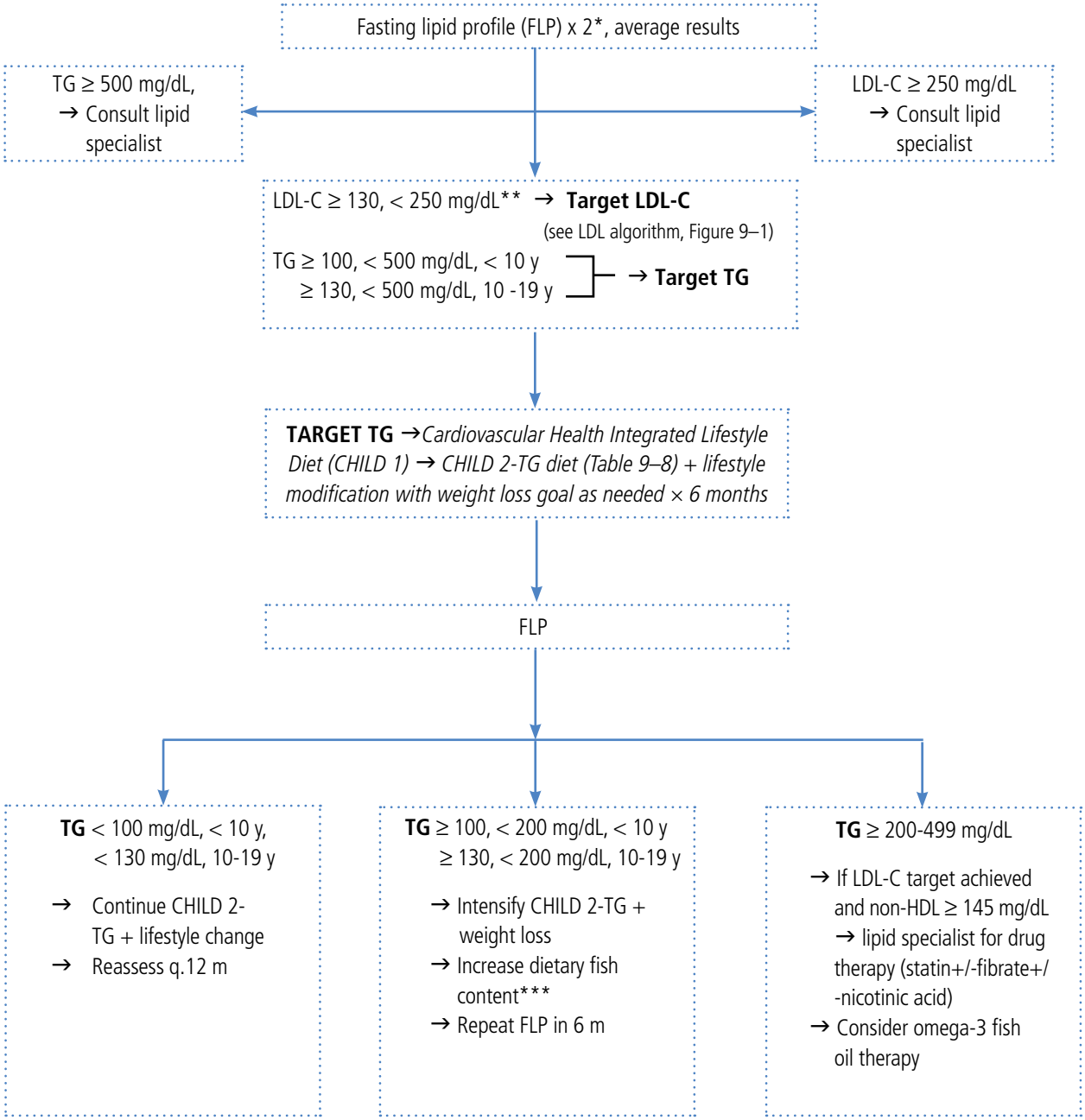
Note: Values given are in mg/dL. To convert to SI units, divide results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.



* Obtain FLPs at least 2 weeks but no more than 3 months apart.
** Per Table 9-5, use of drug therapy is limited to children ≥ 10 y with defined risk profiles.
*** In a child with LDL-C > 190 mg/dL and other RFs, trial of CHILD 2-LDL may be abbreviated.

Figure 9–2. **DYSLIPIDEMIA ALGORITHM: TARGET TG (TRIGLYCERIDES)**

Note: Values given are in mg/dL. To convert to SI units, divide results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.



* Obtain FLPs at least 2 weeks but no more than 3 months apart.

** Per Table 9-5, use of drug therapy is limited to children ≥ 10 y with defined risk profiles.

*** The Food and Drug Administration (FDA) and the Environmental Protection Agency are advising women of childbearing age who may become pregnant, pregnant women, nursing mothers, and young children to avoid some types of fish and shellfish and eat fish and shellfish that are lower in mercury. For more information, call the FDA's food information line toll free at 1-888-SAFEFOOD or visit www.fda.gov/Food/FoodSafety/Product-specificinformation/Seafood/FoodbornePathogensContaminants/Methylmercury/ucm115644.htm.

Table 9–6. RISK FACTOR (RF) DEFINITIONS FOR DYSLIPIDEMIA ALGORITHMS

(+) Family history: myocardial infarction, angina, coronary artery bypass graft/stent/angioplasty, sudden cardiac death in parent, grandparent, aunt, or uncle, male < 55 y, female < 65 y

High Level Risk Factors:

- Hypertension requiring drug therapy (BP ≥ 99th%ile + 5 mmHg)
- Current cigarette smoker
- BMI ≥ 97th%ile
- Presence of high risk conditions (Table 9–7)

  (Diabetes mellitus [DM] is also a high level risk factor but it is classified here as a high risk condition to correspond with *Adult Treatment Panel III* recommendations for adults that DM is considered a CVD equivalent.)

Moderate-Level RFs:

- Hypertension not requiring drug therapy
- BMI ≥ 95th%ile, < 97th%ile
- HDL-C < 40 mg/dL
- Presence of moderate risk conditions (Table 9–7)

Table 9–7. SPECIAL RISK CONDITIONS

High Risk

- Diabetes mellitus, type 1 and type 2
- Chronic kidney disease/end-stage renal disease/ postrenal transplant
- Postorthotopic heart transplant
- Kawasaki disease with current aneurysms

Moderate Risk

- Kawasaki disease with regressed coronary aneurysms
- Chronic inflammatory disease (systemic lupus erythematosus, juvenile rheumatoid arthritis)
- Human immunodeficiency virus infection (HIV)
- Nephrotic syndrome

Conclusions and Grading of the Evidence Review for Dietary Management of Dyslipidemia

- A diet with total fat at 25-30% of calories, saturated fat less than 10% of calories, and cholesterol intake less than 300 mg/d, as recommended by the original NCEP Pediatric Panel, has been shown to safely and effectively reduce the levels of TC and LDL-C in healthy children. (Grade A) There is some evidence this is also the case when the diet begins in infancy and is sustained throughout childhood into adolescence. (Grade B) The Cardiovascular Health Integrated Lifestyle Diet (CHILD 1) described in Section 5. Nutrition and Diet of these Guidelines, has this composition.
- In children with identified hypercholesterolemia and elevated LDL-C, a more stringent diet with saturated fat ≤ 7% of calories and dietary cholesterol limited to 200 mg/d has been shown to be safe and modestly effective in lowering the LDL-C level. (Grade A) (CHILD 2-LDL, Table 9–8)
- Use of dietary adjuncts such as plant sterol or stanol esters up to 20 g/d can safely enhance LDL-C lowering effects short term in children with FH. (Grade A) However, long-term studies on the safety and effectiveness of plant sterol and stanol esters have not been completed. Their use is therefore usually reserved for children with primary elevations of LDL-C who do not achieve LDL-C goals with dietary treatment alone. Such an approach may lower LDL-C sufficiently to avoid the necessity of drug treatment. Food products containing plant stanol esters, such as some margarine, are marketed directly to the general public. In two short-term trials, they have been shown to be safe with minimal LDL-lowering effects in healthy children. (Grade B)
- Evidence for use of other dietary supplements is insufficient for any recommendation. (No grade)
- In children with elevated TG, reduction of simple carbohydrate intake and weight loss are associated with decreased TG levels. (Grade B) Reduction of simple carbohydrate intake needs to be associated with increased intake of complex carbohydrates and reduced saturated fat intake. When TG elevation is associated with obesity, decreased calorie intake and increased activity levels are of paramount importance. The CHILD 2-TG diet in Table 9–8 is recommended as the primary diet therapy in this setting.
- A behavioral approach that engages the child and family delivered by a registered dietitian has been shown to be the most consistently effective approach for achieving dietary change. (Grade B)

The approach to management of dyslipidemias is staged, as in the original NCEP Pediatric Panel recommendations. For all children with identified dyslipidemia in whom the response to a low-fat/low saturated fat/low cholesterol diet has not been evaluated, the CHILD 1 described in Section 5. Nutrition and Diet is recommended as the first step, with implementation guided by a registered dietitian. For obese children with identified dyslipidemia, age- and BMI-specific additional recommendations addressing calorie restriction and increased activity appear in Section 10. Overweight and Obesity. If, after a 3-month trial of CHILD 1/lifestyle management, fasting lipid profile findings exceed the therapeutic goals in Tables 9–1 and 9–2, lipid parameter-specific diet changes outlined in Table 9–8 are recommended. Dyslipidemia management is also outlined in the algorithms in Figures 9–1 and 9–2.

Table 9–8. EVIDENCE–BASED RECOMMENDATIONS FOR DIETARY MANAGEMENT OF ELEVATED LDL–C, NON–HDL–C, AND TG

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.
Supportive actions represent expert consensus suggestions from the Expert Panel provided to support implementation of the recommendations; they are not graded.

Note: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.

Elevated LDL-C: CHILD 2–LDL

2–21 y	Refer to a registered dietitian for family medical nutrition therapy:	Grade B *Strongly recommend*
	• 25-30% of calories from fat, ≤ 7% from saturated fat, ~10% from monounsaturated fat; < 200 mg/d of cholesterol; avoid *trans* fat as much as possible.	Grade A *Recommend*

Supportive Actions:

- Plant sterol esters and/or plant stanol esters* up to 2 g/d as replacement for usual fat sources can be used after age 2 years in children with familial hypercholesterolemia.
- Plant stanol esters as part of a regular diet are marketed directly to the public. Short-term studies show no harmful effects in healthy children.
- The water-soluble fiber psyllium can be added to a low-fat, low saturated fat diet as cereal enriched with psyllium at a dose of 6 g/d for children 2-12 years, and 12 g/d for those ≥ 12 years.
- As in all children, 1 hour/day (h/d) of moderate-to-vigorous physical activity and < 2 h/d of sedentary screen time are recommended.

* Can be found added to some foods, such as some margarines.

Elevated TG or non-HDL-C: CHILD 2–TG

2–21 y	Refer to a registered dietitian for family medical nutrition therapy:*	Grade B *Strongly recommend*
	• 25-30% of calories from fat, ≤ 7% from saturated fat, ~10% from monounsaturated fat; < 200 mg/d of cholesterol; avoid *trans* fat as much as possible	Grade A *Recommend*

	• Decrease sugar intake:
	  ▪ Replace simple with complex carbohydrates
	  ▪ No sugar-sweetened beverages
		Grade B
		Recommend

	• Increase dietary fish to increase omega-3 fatty acids**	Grade D *Recommend*

* If child is obese, nutrition therapy should include calorie restriction, and increased activity (beyond that recommended for all children) should be prescribed. See Section 10. Overweight and Obesity for additional age-specific recommendations.

** The Food and Drug Administration (FDA) and the Environmental Protection Agency are advising women of childbearing age who may become pregnant, pregnant women, nursing mothers, and young children to avoid some types of fish and shellfish and eat fish and shellfish that are low in mercury. For more information, call the FDA's food information line toll free at 1–888–SAFEFOOD or visit www.fda.gov/Food/FoodSafety/Product-specificinformation/Seafood/FoodbornePathogensContaminants/Methylmercury/ucm115644.htm

Conclusions and Grading of the Evidence Review for Use of Medication to Treat Dyslipidemia

When medication is recommended, this should always be in the context of the complete CV risk profile of the patient and in consultation with the patient and the family.

Note: Values given are in mg/dL; to convert to SI units, divide the results for TC, LDL-C, HDL-C and non-HDL-C by 38.6; for TG, divide by 88.6.

- Decisions regarding the need for medication therapy should be based on the average of results from at least two fasting lipid profiles obtained at least 2 weeks but no more than 3 months apart. (Grade C) (Figure 9–1)
- The cutpoints used to define the level at which drug therapy should be considered from the 1992 *NCEP Pediatric Guidelines* have been used as the basis for multiple drug safety and efficacy trials in dyslipidemic children: (Grade B)
  - LDL-C ≥ 190 mg/dL after a 6-month trial of lifestyle management (CHILD 1 → CHILD 2-LDL) for children ≥ 10 years.
  - LDL-C 160–189 mg/dL after a 6-month trial of lifestyle/diet management (CHILD 1 → CHILD 2-LDL) in a child ≥ 10 years with a positive family history of premature CVD/events in first-degree relatives (Table 9–6) or at least one high-level risk factor or risk condition or at least 2 moderate-level risk factors or risk conditions (Tables 9–6, 9–7, and 9–12) (Figure 9–1).
  - LDL-C 130–190 mg/dL in a child ≥ 10 years with a negative family history of premature CVD in first-degree relatives and no high-level or moderate-level risk factor or risk condition: Management should continue to focus on lifestyle changes (CHILD 1→ CHILD 2-LDL) based on lipid profile findings (Figure 9–1) plus weight management if BMI ≥ 85th percentile.
  - **The goal of LDL-lowering therapy in childhood and adolescence is LDL-C below the 95th percentile (≤ 130 mg/dL).**
- Children with homozygous FH and extremely elevated LDL-C levels (> 500 mg/dL) have undergone effective LDL-lowering therapy with biweekly LDL apheresis under the care of lipid specialists in academic medical centers. (Grade C)
- Multiple cohort studies series have shown that the benefits of LDL-lowering therapy in children at high risk for accelerated atherosclerosis (such as those with chronic kidney disease, T1DM or T2DM, Kawasaki disease with coronary aneurysms, or postcardiac transplantation) should be considered for initiation of medication therapy. (Grade C) (see Section 11. Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis)
- The bile acid sequestrants are medications that bind bile salts within the intestinal lumen and prevent their enterohepatic reuptake in the terminal ileum, resulting in a depletion of bile salts in the liver and a signal for increased production. Since bile salts are synthesized from intracellular cholesterol in the liver, the intracellular pool of cholesterol becomes depleted, signaling increased production of LDL receptors and increased clearance of circulating LDL-C to replenish the intracellular cholesterol pool for increased production of bile salts. Studies of bile acid sequestrants in children and adolescents ages 6-18 years with LDL-C levels from 131 to 190 mg/dL show TC reduction of 7-17 percent and reduction of LDL-C of 10-20 percent, sometimes with a modest elevation in TG levels. The bile acid sequestrants commonly have gastrointestinal side effects, and these significantly affect compliance. However, they are safe and moderately effective. (Grade A)
- Statin medications inhibit hydroxymethylglutaryl coenzyme A reductase, which is a rate-limiting enzyme in the endogenous cholesterol synthesis pathway. This results in a decrease in the intracellular pool of cholesterol, which signals upregulation of LDL receptors and increased clearance of circulating LDL-C. As a group, statins have been shown to reduce LDL-C in children and adolescents with marked LDL-C elevation or FH (defined as elevated LDL-C in the child in conjunction with a family history of elevated LDL-C and/or atherosclerosis or CAD) when used from 8 weeks to 2 years for children ages 8-18 years. The lower LDL-C level for eligibility into the statin trials was ≥ 190 mg/dL

or ≥ 160 mg/dL with 2 or more additional risk factors, after a trial period on diet. Trial subjects were monitored carefully throughout treatment; adverse impacts on growth, development, or sexual maturation were not seen, and adverse event profiles and efficacy were similar to those in studies of adults. (Grade A)

- Adverse effects from statins are rare at standard doses but include myopathy and hepatic enzyme elevation. In the meta-analysis of statin use in children, evidence of hepatic enzyme elevation and muscle toxicity did not differ between the statin and placebo groups. Routine monitoring of hepatic enzymes and clinical assessment for muscle toxicity are strongly recommended for children and adolescents on statin therapy (Table 9–12). The risk of adverse events increases with use of higher doses and interacting drugs, the latter occurring primarily with drugs that are metabolized by the cytochrome P–450 system, which is the primary mode of metabolism for the majority of statins. Drugs that potentially interact with statins include fibrates, azol antifungals, macrolide antibiotics, antiarrhythmics, and protease inhibitors. (Grade A)
- Bile acid-binding sequestrants may be used in combination with a statin for patients who fail to meet LDL-C target levels with either medication alone. One pediatric study assessed this combination and showed no increase in adverse effects. The efficacy of the two agents together appears to be additive. (Grade B)
- There is limited published experience in children with use of niacin and fibrates, which have been useful in treating adult patients with combined dyslipidemias. Efficacy and safety data are limited, and no data are available regarding newer formulations. In adults, cholesterol absorption inhibitors have been advocated as an adjunct to statin therapy for patients who do not reach LDL-C therapeutic targets. Since their action is independent of and complementary to that of statins, the LDL-C-lowering effect is additive. No pediatric studies of monotherapy with cholesterol absorption inhibitors had been published during the time period for this evidence review. Use of niacin, fibrates, and cholesterol absorption inhibitors should be instituted only in consultation with a lipid specialist. (Grade C)
- Medication therapy is rarely needed for children with elevated TG who respond well to weight loss and lifestyle changes. (Grade B) (Figure 9-2) (Table 9–8) When TG levels exceed 500 mg/dL, patients are at risk for pancreatitis and require care in consultation with a lipid specialist. (Grade B) In adults, use of omega-3 fish oil has been shown to lower TG by 30-40 percent and to raise HDL by 6-17 percent. Experience with fish oil in children is limited to small case series with no safety concerns identified; there have been no RCTs of fish oil in children. (Grade D)

Age-Based Recommendations for Medication Therapy of Children With Dyslipidemia

Children Younger Than Age 10 Years

- Children < age 10 years should not be treated with a medication unless they have a severe primary hyperlipidemia or a high-risk condition that is associated with serious medical morbidity (homozygous hypercholesterolemia/LDL-C ≥ 400 mg/dL; primary hypertriglyceridemia with TG ≥ 500 mg/dL; evident CVD in the first two decades of life; post-cardiac transplantation.) (Grade C)

Children Ages 10–21 Years (See Algorithms, Figures 9–1 and 9–2)

- Decisions regarding the need for medication therapy should be based on the average of results from at least two FLPs obtained at least 2 weeks apart but no more than 3 months apart. (Grade C) (Figure 9–1)
- Children with average LDL-C ≥ 250 mg/dL or average TG ≥ 500 mg/dL should be referred directly to a lipid specialist. (Grade B)
- Children with lipid abnormalities should have a detailed family history taken and be assessed for causes of hyperlipidemia, additional risk factors, and risk conditions. (Grade C) (Tables 9–3, 9–6, and 9–7)
- Children with lipid abnormalities (other than LDL-C ≥ 250 mg/dL or TG > 500 mg/dL) should be initially managed for 3-6 months with diet changes (CHILD 1→CHILD 2-LDL or CHILD 2-TG, Table 9–8) based on specific lipid profile findings (Figures 9–1 and 9–2); if BMI is

≥ 85th percentile, add increased physical activity, reduced screen time, and calorie restriction. Assessment for associated secondary causes (Table 9–3), additional risk factors, or high-risk conditions (Tables 9–6 and 9–7) is recommended. Children at high risk who are unlikely to achieve lipid targets with this strategy alone (severe primary dyslipidemia, cardiac transplantation) should concomitantly be considered for initiation of medication therapy. (Grade C) (Section 11. Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis)

LDL-C: Treatment for children with severe elevation of LDL-C is based on assessment of lipid levels and associated risk factors or risk conditions (Tables 9–6 and 9–7; Figures 9–1 and 9–2)

- Children with average LDL-C ≥ 250 mg/dL should be referred directly to a lipid specialist. (Grade B)
- If LDL-C remains ≥ 190 mg/dL after a 6-month trial of lifestyle/diet management (CHILD 1→CHILD 2-LDL) for children ages 10 years and older, statin therapy should be considered. (Grade A) (Figure 9–1) (Table 9–12)
- If LDL-C remains ≥ 130 mg/dL to < 190 mg/dL in a child age 10 years or older with a negative family history of premature CVD in first-degree relatives and no high-level or moderate-level risk factor or risk condition (Tables 9–6 and 9–7), management should continue to focus on diet changes (CHILD 2-LDL) based on lipid profile findings (Figure 9–1) plus weight management if BMI ≥ 85th percentile. Pharmacologic therapy is not generally indicated, but treatment with bile acid sequestrants might be considered, the latter in consultation with a lipid specialist. (Grade B)
- If LDL-C remains ≥ 160 to 189 mg/dL after a trial of lifestyle/diet management (CHILD 1→CHILD 2- LDL) in a child age 10 years or older with a positive family history of premature CVD/events in first-degree relatives (Table 9–6) or at least one high-level risk factor or risk condition or at least two moderate-level risk factors or risk conditions (Tables 9–6 and 9–7), then statin therapy should be considered. (Grade B) (Figure 9–1) (Table 9–12)
- If LDL-C remains ≥ 130 to 159 mg/dL after a trial of lifestyle/diet management (CHILD 1→CHILD 2- LDL) in a child age 10 years or older with at least two high-level risk factors or risk conditions or at least one high-level risk factor or risk condition together with at least two moderate-level risk factors or risk conditions (Tables 9–6 and 9–7), then statin therapy should be considered. (Grade C) (Figure 9–1) (Table 9–12)
- For children ages 8 and 9 years with LDL-C persistently ≥ 190 mg/dL after a trial of lifestyle/diet management (CHILD 1→CHILD 2-LDL), together with multiple first-degree family members with premature CVD/events, or the presence of at least one high-level risk factor or risk condition or the presence of at least two moderate-level risk factors or risk conditions (Figure 9–1) (Tables 9–6 and 9–7), statin therapy might be considered. (Grade B) (Table 9–12)
- Statin use should begin with the lowest available dose given once daily. If LDL-C target levels are not achieved with at least 3 months of compliant use, then the dose may be increased by one increment (usually 10 mg). If LDL-C target levels are still not achieved with at least 3 months of compliant use, then the dose may be further increased by one increment. The risk and effectiveness of dose escalation has been explored in several of the statin clinical trials in children with no additional safety issues identified. (Grade B) Alternatively, a second agent such as a bile acid sequestrant or cholesterol absorption inhibitor may be added under the direction of a lipid specialist. (Grade B) (Table 9–12)
- Children taking a statin should have routine clinical monitoring for symptoms of muscle toxicity and assessment of hepatic transaminases and creatine kinase. (Grade A) (Table 9–12)
- Pediatric care providers should be on the alert for, and children and their families should be counseled about, potential medication interactions. (Grade D) (Table 9-12)
- Females taking a statin should be counseled about risks associated with pregnancy and appropriate contraception strategies if indicated. Use of oral contraceptives in combination with statins is not contraindicated. (Grade D) (Table 9–12)

TG, non-HDL-C: Children with elevated TG or elevated non-HDL-C after control of LDL-C are managed based on lipid levels (Figure 9–2)

- Children with average fasting levels of TG ≥ 500 mg/dL or any single measurement ≥ 1,000 mg/dL related to a primary hypertriglyceridemia should be treated in conjunction with a lipid specialist; the CHILD 2-TG diet (Table 9–8) should be started and use of fish oil, fibrate, or niacin to prevent pancreatitis should be considered. (Grade D) (Figure 9–2) (Tables 9–10 and 9–11)
- Children with fasting levels of TG ≥ 200 to 499 mg/dL after a trial of lifestyle/diet management with CHILD 1→CHILD 2-TG (Table 9–8) should have non-HDL recalculated and be managed to a goal of < 145 mg/dL. (Grade D)
- Children with fasting levels of TG ≥ 200 to 499 mg/dL, non-HDL > 145 mg/dL, after a trial of lifestyle/diet management with CHILD 1→CHILD 2-TG (Table 9–8) and increased fish intake, may be considered for fish oil supplementation. (Grade D) (Table 9–10)
- Children ≥ 10 years with non-HDL-C levels ≥ 145 mg/dL after the LDL-C goal is achieved may be considered for further intensification of statin therapy or additional therapy with a fibrate or niacin, in conjunction with referral to a lipid specialist. (Grade D) (Figure 9–1) (Tables 9–10 and 9–11)
- Children with severe or complex mixed dyslipidemias, particularly where multiple medications are being considered, should be referred for consultation with a lipid specialist. (Grade D) (Figures 9–1 and 9–2)

The age-specific recommendations for pharmacologic management of dyslipidemia are summarized in Table 9–9.

Table 9–9. EVIDENCE–BASED RECOMMENDATIONS FOR PHARMACOLOGIC TREATMENT OF DYSLIPIDEMIA

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.

When medication is recommended, this should always be in the context of the complete cardiovascular risk profile of the patient and in consultation with the patient and the family.

Note: Values given are in mg/dL. To convert to SI units, divide the results for total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C by 38.6; for triglycerides (TG), divide by 88.6.

Birth–10 y	Pharmacologic treatment is limited to children with severe primary hyperlipidemia (homozygous familial hypercholesterolemia, primary hypertriglyceridemia with TG ≥ 500 mg/dL) or a high-risk condition (Tables 9–6 and 9–7) or evident cardiovascular disease; all under the care of a lipid specialist.	Grade C *Recommend*
11– 21 y	Detailed family history (FHx) and risk factor (RF) assessment required before initiation of drug therapy.* High- to moderate-level RFs and risk conditions (RCs) in Tables 9–6 and 9–7.	Grade C *Strongly recommend*
	LDL-C: If average LDL-C ≥ 250 mg/dL*, consult lipid specialist.	Grade B *Strongly recommend*
	If average LDL-C ≥ 130–250 mg/dL, or non-HDL ≥ 145 mg/dL: • Refer to dietitian for medical nutrition therapy with Cardiovascular Health Integrated Lifestyle Diet (CHILD 1) → CHILD 2-LDL (Table 9–8) × 6 months → repeat fasting lipid panel (FLP)	Grade A *Strongly recommend*
	Repeat FLP: • → LDL-C < 130 mg/dL, continue CHILD 2- LDL, reevaluate in 12 months	Grade A *Strongly recommend*
	• → LDL-C ≥ 190** mg/dL, consider initiation of statin therapy per Tables 9–11 and 9–12	Grade A *Strongly recommend*
	• → LDL-C ≥ 130–189 mg/dL, FHx (-), no other RF or RC, continue CHILD 2-LDL, reevaluate q. 6 months	Grade B *Recommend*
	• → LDL-C = 160–189 mg/dL + FHx positive OR ≥ 1 high-level RF/RC OR ≥ 2 moderate-level RFs/RCs, consider statin therapy per Tables 9–11 and 9–12	Grade B *Recommend*
	• → LDL-C ≥ 130–159 mg/dL + ≥ 2 high-level RFs/RCs OR 1 high-level + 2 moderate-level RFs/RCs, consider statin therapy per Tables 9–11 and 9–12	Grade B *Recommend*
	Children on statin therapy should be counseled and carefully monitored per Table 9–12.	Grade A *Strongly recommend*

* Consideration of drug therapy based on the average of ≥ 2 fasting lipid profiles (FLPs), obtained at least 2 weeks but no more than 3 months apart.

** If average LDL-C ≥ 190 mg/dL after CHILD 2-LDL & child is 8-9 y with (+) FHx OR ≥ 1 high level RF/RC OR ≥ 2 moderate-level RFs/RCs, statin therapy can be considered.

Table 9–9. **EVIDENCE–BASED RECOMMENDATIONS FOR PHARMACOLOGIC TREATMENT OF DYSLIPIDEMIA (continued)**

11–21 y	Detailed FHx and RF/RC assessment required before initiation of drug therapy.* High- and moderate-level RFs/RCs in Tables 9–6 and 9–7**	Grade C *Strongly recommend*
	TG: If average TG ≥ 500 mg/dL, consult lipid specialist	Grade B *Recommend*
	If average TG ≥ 100 mg/dL in a child < 10 years, ≥ 130 mg/dL in a child age 10-19 years, < 500 mg/dL: • Refer to dietitian for medical nutrition therapy with CHILD 1 → CHILD 2-TG (Table 9–8) × 6 months	Grade B *Strongly recommend*
	Repeat fasting lipid profile: • → TG < 100 (130) mg/dL, continue CHILD 2-TG, monitor q. 6–12 months	Grade B *Strongly recommend*
	• → TG > 100 (130) mg/dL, reconsult dietitian for intensified CHILD 2-TG diet counseling	Grade C *Recommend*
	• → TG ≥ 200–499 mg/dL, non-HDL ≥ 145 mg/dL, consider fish oil +/- consult lipid specialist	Grade D *Recommend*
	Non-HDL-C: Children ≥ 10 years with non-HDL-C ≥ 145 mg/dL after LDL-C goal achieved may be considered for additional treatment with statins, fibrates, or niacin in conjunction with a lipid specialist.	Grade D *Optional*

* Consideration of drug therapy based on the average of ≥ 2 fasting lipid profiles obtained at least 2 weeks but no more than 3 months apart.

** If child is obese, nutrition therapy should include calorie restriction and increased activity beyond that recommended for all children. See Section 10. Overweight and Obesity for additional age-specific recommendations.

Table 9–10. MEDICATIONS FOR MANAGING HYPERLIPIDEMIA

Type of Medication	Mechanism of Action	Major Effects	Examples	Adverse Reactions	FDA Approval in Youths as of This Writing
HMG CoA reductase inhibitors (statins)	Inhibit cholesterol synthesis in hepatic cells, decreases cholesterol pool, resulting in up-regulation of LDL receptors.	Mainly lowers LDL-C; some decrease in TG and modest increase in HDL-C	Atorvastatin Fluvastatin Lovastatin Pravastatin Rosuvastatin Simvastatin	Raised hepatic enzymes, raised creatine kinase, myopathy possibly progressing to rhabdomyolysis	All statins listed approved as an adjunct to diet to lower LDL-C in adolescent boys and postmenarchal girls ages 10-18 years (8+ years for pravastatin) with heFH and LDL-C ≥ 190 mg/dL, or ≥ 160 mg/dL with FHx of premature CVD and 2+ CVD risk factors in the pediatric patient
Bile acid sequestrants	Bind intestinal bile acids interrupting enterohepatic recirculation, more cholesterol converted into bile acids, decreases hepatic cholesterol pool and up-regulates LDL receptors.	Lowers LDL-C, small increase in HDL, raises TG	Cholestyramine, Colestipol Colesevelam	Limited to gastrointestinal tract: gas, bloating, constipation, cramps	No pediatric indication listed for cholestyramine or colestipol; colesevelam indicated as monotherapy or with statin for LDL-C reduction in boys and postmenarchal girls ages 10-17 years with FH after diet trial if LDL-C ≥ 190 mg/dL or if LDL-C ≥ 160 mg/dL with FHx premature CVD or 2+ more CVD risk factors in the pediatric patient
Cholesterol absorption inhibitors	Inhibit intestinal absorption of cholesterol and plant sterols, decreases hepatic cholesterol pool, and up-regulates LDL receptors.	Mainly lowers LDL-C; small decrease in TG and small increase in HDL-C	Ezetimibe	Myopathy, gastrointestinal upset, headache	No
Fibric acid derivatives	Agonist for PPAR alpha nuclear receptors that up-regulate LPL and apoC-III, both increasing degradation of VLDL-C & TG. Hepatic synthesis of VLDL-C may also be decreased.	Mainly lowers TG and raises HDL-C, with little effect on LDL-C	Fenofibrate Gemfibrozil	Dyspepsia, constipation, myositis, anemia	No
Nicotinic acid (extended release)	Inhibit release of FFA from adipose tissue; decreases VLDL-C and LDL-C production and HDL-C degradation.	Lowers TG and LDL-C and raises HDL-C; can decrease Lp (a)	Niacin, extended release	Flushing, hepatic toxicity, can increase fasting blood glucose, uric acid; hyperacidity	Use not recommended in children < age 2 years
Omega-3 fish oil	Decreases hepatic FA & TG synthesis while enhancing FA degradation/oxidation, with subsequent reduced VLDL-C release.	Lowers TG, raises HDL-C, increases LDL-C and LDL-C particle size	Omega-3 acid ethyl esters	Occasional gastrointestinal side effects but no adverse effect on glucose levels, or muscle or liver enzymes, or bleeding	Only one FDA-approved fish oil preparation for adults, but many generic fish oil capsules commercially available

Table 9–11. CLINICAL TRIALS OF LIPID–LOWERING MEDICATION THERAPY IN CHILDREN AND ADOLESCENTS

BILE ACID BINDING RESINS

Study	Medication	Subjects/ Gender/ Condition	Daily Dose	Effect on Lipid Profile			
				TC	LDL-C	HDL-C	TG
Tonstad et al. RCT 1 year	Cholestyramine	72/both/FH (LDL ≥ 190 mg/dL without FHx premature CVD or LDL ≥ 160 with FHx after 1-year diet; ages 6-11 years)	8 g	-12%	-17%	+8%	NA
McCrindle et al. RCT cross-over 2 x 8 weeks	Cholestyramine	40/both/FH (1 parent with FH; LDL-C ≥ 131 mg/dL; on diet; ages 10-18 years)	8 g	-7 to -11%	-10 to -15%	+2 to +4%	+6 to +9%
Tonstad et al. RCT 8 weeks; open label 44–52 weeks	Colestipol	66/both/FH (TC ≥ 239 mg/dL and TG ≤ 115 mg/dL; ages 10-16 years)	2–12 g	-17%	-20%	-7%	-13%
McCrindle et al. RCT cross-over 2 x 18 weeks	Colestipol	36/both/FH/FCHL (LDL ≥ 160 mg/dL after 6 months diet counseling; ages 8-18 years)	10 g	- 7%	-10%	+2%	+12%
Stein et al.	Colesevelam	191/both/FH (LDL ≥ 190 mg/dL or LDL ≥ plus 2 additional RFs after 6 months diet counseling; ages 10-17 years)	1.875 g 3.75 g	-3% -7%	-6% -13%	+5% +8%	+6% +5%

HMG COA REDUCTASE INHIBITORS (STATINS)

Study	Medication	Subjects/ Gender/ Condition	Daily Dose	Effect on Lipid Profile			
				TC	LDL-C	HDL-C	TG
McCrindle et al. RCT; open-label 26 weeks	Atorvastatin	187/both/FH/Severe hyperlipidemia (LDL-C ≥ 190 mg/dL or ≥ 160 mg/dL with FHx; and TG < 400 mg/dL; ages 10-17 years)	10–20 mg	-30%	-40%	+6%	-13%
Van der Graaf et al. open label 2 years	Fluvastatin	85/both/FH (LDL-C ≥ 190 mg/dL or LDL-C ≥ 160 mg/dL and 1+ risk factor or LDL receptor mutation; ages 10-16 years)	80 mg	-27%	-34%	+5%	-5%
Lambert et al. RCT 8 weeks	Lovastatin	69/males/FH (LDL-C > 95th%ile, FHx atherosclerosis and hyperlipidemia; on diet; mean age 13 years)	10 mg 20 mg 30 mg 40 mg	-17% -19% -21% -29%	-21% -24% -27% -36%	+9% +2% +11% +3%	-18% +9% +3% -9%
Stein et al. RCT 48 weeks	Lovastatin	132/males/FH (LDL 189–503 mg/dL + FHx of high LDL; or 220–503 mg/dL + FHx CAD death; AHA diet 4+ months; ages 10-17 years)	10 mg 20 mg 40 mg	-13% -19% -21%	-17% -24% -27%	+4% +4% +5%	+4% +8% +6%
Clauss et al. RCT 24 weeks	Lovastatin	54/females/FH (FHx FH; LDL 160–400 mg/dL and TG < 350 mg/dL; 4-week diet placebo run-in and 20-week tx; ages 10-17 years, postmenarchal)	40 mg	-22%	-27%	+3%	-23%
Knipscheer et al. RCT 12 weeks	Pravastatin	72/both/FH (FHx hypercholesterol or premature atherosclerosis; LDL > 95th%ile; diet × 8 weeks; ages 8-16 years)	5 mg 10 mg 20 mg	-18% -17% -25%	-23% -24% -33%	+4% +6% +11%	+2% +7% +3%

Table 9–11. CLINICAL TRIALS OF LIPID–LOWERING MEDICATION THERAPY IN CHILDREN AND ADOLESCENTS (continued)

HMG COA REDUCTASE INHIBITORS (STATINS) (continued)

Study	Medication	Subjects/ Gender/ Condition	Daily Dose	Effect on Lipid Profile			
				TC	LDL-C	HDL-C	TG
Wiegman et al. RCT 2 years	Pravastatin	214/both/FH (LDL-C ≥ 155 mg/dL and TG ≤ 350 mg/dL; diet × 3 months; ages 8-18 years)	20–40 mg	-19%	-24%	+6%	-17%
Rodenburg et al. open-label 2-year RCT; 4.5 year open-label follow-up	Pravastatin	186/both/FH (LDL-C ≥ 154 mg/dL and TG < 154 mg/dL; 3 months on diet; ages 8-18 years)	20 mg (ages < 14 years) or 40 mg (ages > 14 years)	-23%	-29%	+3%	-2%
de Jongh et al. RCT 48 weeks	Simvastatin	173/both/FH (LDL-C: 158–397 mg/dL; ages 10-17 years)	10–40 mg	-31%	-41%	+3%	-9%
de Jongh et al. RCT 28 weeks	Simvastatin	50/both/FH (LDL-C above 95th%ile, FHx hyperlipidemia, or LDL receptor mutation; ages 9-18 years)	40 mg	-30%	-40%	+5%	-17%
Avis et al. RCT 12 weeks; then, 40 week open-label follow-up	Rosuvastatin	177/both/FH (LDL-C ≥ 190 mg/dL or LDL-C > 160 mg/dL plus (+)FHx of early CVD or ≥ 2 other RFs for CVD	5 mg 10 mg 20 mg	-30% -34% -39%	-38% -45% -50%	+4% +10% +9%	-13% -15% -16%

OTHER AGENTS

Study	Medication	Subjects/ Gender/ Condition	Daily Dose	Effect on Lipid Profile			
				TC	LDL-C	HDL-C	TG
Wheeler et al. RCT 26 weeks	Bezafibrate	14/both/FH (TC > 269 mg/dL, nl TG + FHx of FH or premature CAD; ages 4-15 years)	10–20 mg	-22%	NC	+15%	-23%
Colletti et al. open-label 1-19 months	Niacin	21/both/FH (mean LDL = 243 ± 45 mg/dL on low-fat diet; mean TG = 87 ± 39 mg/dL; ages 4-14 years)	500–2,200 mg	-13%	-17%	+4%	+13%
McCrindle et al. RCT cross-over 2 × 18 weeks	Pravastatin and Colestipol	36/both/FH/FCHL (LDL > 160 mg/dL + FHx of FH or premature CAD; TG > 177 mg/dL in 10/36; ages 10-18 years)	Pravastatin, 10 mg (with Colestipol, 5g)	-13%	-17%	+4%	+8%
Van der Graaf et al. RCT 6 and 27 weeks; open-label to 53 weeks	Simvastatin and Ezetimibe	248/both/FH (LDL > 159 mg/dL + genotype-confirmed FH or + parental genotype-confirmed FH or + parental LDL > 210 mg/dL or + tendinous xanthomas or LDL > 189 mg/dL + FHx of hypercholesterolemia; ages 10-17 years)	Simvastatin 10–40 mg with Ezetimibe 10 mg	- 38%	- 49%	+7%	-17%
Addendum: *Goldberg et al.* Omega-3 fatty acid review in adults; *no RCTs in children*	*Omega-3 fish oils** (1 gram/ capsule)*		*1–4 g/d*	NC	*+17–31%*	*+6–17%*	*-30–40%*

ABBREVIATIONS: AHA = American Heart Association; CAD = coronary artery disease; d = day; FHx = family history; g = grams; mg = milligrams; NA = not available; NC = not calculated; TC = total cholesterol; FH = heterozygous familial hypercholesterolemia; FCHL = familial combined hyperlipidemia; RCT = randomized controlled trial; tx = treatment

** There is only one FDA-approved fish oil preparation, but there are many generic forms of fish oil capsules that are commercially available. The University of Wisconsin maintains a preventive cardiology patient education Web site http://www.heartdecision.org. The "fish oil" section includes information about the content of various preparations. The Web site is updated every 6 months: https://www.heartdecision.org/chdrisk/v_hd/patient_edu_docs/Fish_Oil_11-2007.pdf

Table 9–12. RECOMMENDATIONS FOR USE OF HMG–COA REDUCTASE INHIBITORS (STATINS) IN CHILDREN AND ADOLESCENTS

PATIENT SELECTION

1. Use algorithm (Figure 9–1) and risk factor categories (Tables 9–6 and 9–7) to select statin therapy for patients.
2. Include preferences of patient and family in decision making.
3. In general, do not start treatment with statins before age 10 years (patients with high-risk family history, high-risk conditions, or multiple risk factors [Tables 9–6 and 9–7] might be considered for medication initiation at age 10 years or younger.)
4. Precaution/contraindication with potentially interactive medications (cyclosporine, niacin, fibric acid derivatives, erythromycin, azole antifungals, nefazodone, many HIV protease inhibitors). **Check for potential interaction with all current medications at baseline.**
5. Conduct baseline hepatic panel and creatine kinase (CK) before initiating treatment.

INITIATION AND TITRATION

1. Choice of particular statin is a matter of preference. Clinicians are encouraged to develop familiarity and experience with one of the statins, including dosage regimen and potential drug-drug interactions.
2. Start with the lowest dose once daily, usually at bedtime. Atorvastatin and rosuvastatin can be taken in the morning or evening because of their long half-lives.
3. Measure baseline CK, alanine aminotransferase (ALT), and aspartate aminotransferase (AST).
4. Instruct the patient to report all potential adverse effects, especially muscle cramps, weakness, asthenia, and more diffuse symptoms suggestive of myopathy.
5. Advise female patients about concerns with pregnancy and the need for appropriate contraception.
6. Advise about potential future medication interactions, especially cyclosporine, niacin, fibric acid derivatives, erythromycin, azole antifungals, nefazodone, and HIV protease inhibitors. **Check for potential interaction whenever any new medication is initiated.**
7. Whenever potential myopathy symptoms present, stop medication and assess CK; determine relation to recent physical activity. The threshold for worrisome level of CK is 10 times above the upper limit of reported normal, considering the impact of physical activity. Monitor the patient for resolution of myopathy symptoms and any associated increase in CK. Consideration can be given to restarting the medication once symptoms and laboratory abnormalities have resolved.
8. After 4 weeks, measure fasting lipid profile (FLP), ALT, and AST and compare with laboratory-specific reported normal values.
   - The threshold for worrisome levels of ALT or AST is ≥ 3 times the upper limit of reported normal.
   - Target levels for LDL-C: Minimal < 130 mg/dL; Ideal < 110 mg/dL.
9. If target LDL-C levels are achieved and there are no potential myopathy symptoms or laboratory abnormalities, continue therapy and recheck FLP, ALT, and AST in 8 weeks and then 3 months.
10. If laboratory abnormalities are noted or symptoms are reported, temporarily withhold the medication and repeat the blood work in 2 weeks. When abnormalities resolve, the medication may be restarted with close monitoring.
11. If target LDL-C levels are not achieved, increase the dose by one increment (usually 10 mg) and repeat the blood work in 4 weeks. If target LDL-C levels are still not achieved, dose may be further increased by one increment or another agent (bile acid sequestrant or cholesterol absorption inhibitor) may be added under the direction of a lipid specialist.

MAINTENANCE MONITORING

1. Monitor growth (height, weight, and BMI relative to normal growth charts), sexual maturation, and development.
2. Whenever potential myopathy symptoms present, stop medication and assess CK.
3. Monitor fasting lipoprotein profile, ALT, and AST every 3-4 months in the first year, every 6 months in the second year and beyond, and whenever clinically indicated.
4. Monitor and encourage compliance with lipid-lowering dietary and medication therapy. Serially assess and counsel for other risk factors, such as weight gain, smoking, and inactivity.
5. Counsel adolescent females about statin contraindications in pregnancy and the need for abstinence or use of appropriate contraceptive measures. Use of oral contraceptives is not contraindicated if medically appropriate. Seek referral to an adolescent medicine or gynecologic specialist as appropriate.

10. Overweight and Obesity

Dramatic increases in childhood overweight and obesity in the United States since 1980 are an important public health focus. Despite efforts over the last decade to prevent and control obesity, recent reports from NHANES show sustained high prevalence with 17% of children and adolescents with a BMI above the 95th percentile for age and gender. The presence of obesity in childhood and adolescence is associated with increased evidence of atherosclerosis at autopsy and of subclinical measures of atherosclerosis on vascular imaging. Because of its strong association with many of the other established risk factors for CV disease, obesity is even more powerfully correlated with atherosclerosis; this association has been shown for blood pressure, dyslipidemia and insulin resistance in each of the major pediatric epidemiologic studies. Of all the risk factors, obesity tracks most strongly from childhood into adult life. Improvement in weight status and decrease in body fatness have been shown to be associated with improvement in all the obesity-related risk factors and in sub-clinical vascular changes. Higher BMI during childhood is directly associated with increased coronary heart disease in adult life. Extrapolation from current data suggests that adolescent obesity will likely increase adult CHD by 5 to 16% over the next 25 years with more than 100,000 excess cases of CHD attributable to increased obesity in childhood. The evidence review included RCTs, systematic reviews, meta-analyses and observational studies assessing the prevention and treatment of overweight and obesity in childhood and adolescence.

Identification of Overweight and Obese Children and Adolescents

To identify overweight and obesity in children living in the U.S., BMI percentile distributions relative to gender and age on the Centers for Disease Control and Prevention (CDC) 2000 growth charts are now the preferred reference. The CDC growth charts were not developed as a health-related standard. Instead, the growth charts present percentiles of the BMI distribution derived from measurements taken during several NHANES surveys as points of reference. Although the charts were published in 2000, they include selected data from the 1963 through 1980 surveys and thus are not representative of the U.S. population in 2000. These BMI percentile growth charts provide the best reference data available for describing normal growth in U.S. children. They are, however, a screening tool and not an instrument for the diagnosis of overweight and obesity.

An expert committee jointly convened by the American Medical Association (AMA), the CDC, and the Maternal and Child Health Bureau (MCHB) of the Health Resources and Services Administration, U.S. Department of Health and Human Services (HHS), recently recommended that BMI be used to assess weight for height relationships in children. This conclusion was reached because BMI can be easily calculated from height and weight, correlates strongly with direct measures of body fat (especially at higher BMI values), associates only weakly with height, and identifies individuals with the highest body fat correctly with acceptable accuracy, particularly above the 85th BMI percentile. Pediatric care providers need a feasible standard for identifying overweight and obesity in their patients, since parents recognize a child's overweight status in less than half of cases. The AMA/CDC/MCHB Expert Committee defined a BMI $\geq$ 95th percentile as obese and a BMI between the 85th and 94th percentiles as overweight; children in the latter BMI category have a great deal of variation with respect to prediction of future risk. The Expert Panel for these guidelines concluded that BMI is a sufficient measure for screening children and adolescents

to identify those who need evaluation for CV risk factors associated with body adiposity. The Expert Panel also concluded that the scientific evidence linking elevated BMI to CV risk factors and morbidity is strong and well supported.

The Expert Panel therefore recommends that children and adolescents ages 2-18 years with a BMI ≥ 95th percentile be described as "obese" and identified as needing assessment for CV risk factors. For children with a BMI that falls between the 85th and 95th percentiles, the term "overweight" should be used, and the position of the child's BMI on the growth chart should be used to express concern regarding weight-for-height disproportion. It is very important to follow the pattern of growth over time, using these cutpoints to identify children who require more frequent follow-up and further assessment rather than to assign a diagnosis. Some may feel that "obese" is an unacceptable term for children and parents, so as with all health conditions, the practitioner is encouraged to use descriptive terminology that is appropriate for each child and family, with a thorough explanation and discussion. Each patient and family should be considered on an individual basis in deciding how best to convey the seriousness of this issue and to develop management plans.

Conclusions of the Evidence Review on Prevention of Overweight and Obesity with Diet or Combined Diet and Physical Activity Interventions

The Expert Panel concluded that there is good evidence that the dietary behavior of children can safely be improved with interventions resulting in lower saturated fat intake, reduced intake of sweetened beverages and increased fruit and vegetable consumption. In a small number of studies, these changes are associated with lower BMI. No evidence that diets of this kind are harmful was identified. Most studies also had specific interventions aimed at changing physical activity behaviors, so it is difficult to separate benefits related to diet change alone. Although calorie balance is generally seen as a key issue for weight control, intervention studies addressing both diet and physical activity had mixed results, perhaps because most offered relatively weak interventions at the community level rather than targeting individual, at-risk youths.

The guideline recommendations for diet and nutrition for children at elevated cardiovascular risk (CHILD 1, Table 5–1, Section 5. Nutrition and Diet) specifically address optimizing the diet in each of these areas as well as increasing intake of whole grains and matching energy intake to growth and expenditure. For normal children, implementation of the CHILD 1 dietary recommendations with monitoring of BMI and dietary intake over time should be all that is needed from a nutritional standpoint to prevent obesity. No additional recommendations are indicated based on this evidence review.

Conclusions of the Evidence Review on Prevention of Overweight and Obesity with Physical Activity

A moderate number of RCTs have evaluated the effect of interventions that addressed only physical activity and/or sedentary behavior on prevention of overweight and obesity. In a small number of these, the intervention was effective. Notably, these successful interventions often addressed reduction in sedentary behavior rather than attempts to increase physical activity. In the majority of studies, there was no significant difference in body size measures. Sample sizes were often small and follow-up was often short, frequently less than six months. It is suggested that gender-specific programs may be more successful in changing activity behavior. Overall, the Expert Panel concluded that based on the evidence review, increasing activity in isolation is of little benefit in preventing obesity. By contrast, the review suggests that reducing sedentary behavior may be beneficial in preventing the development of obesity. The activity recommendations in the guideline specifically address limiting sedentary behavior and increasing physical activity in all children. Guidance on amounts and intensity of physical activity and limitations on sedentary screen time are provided in the recommendations in Section 6. Physical Activity. No additional specific recommendations addressing physical activity in preventing obesity are indicated, based on this evidence review.

Summary of the Evidence Review of Children at Increased Risk for Overweight and Obesity

Certain populations of children who are of normal weight are at risk for developing overweight and obesity as they grow older. Observational studies have identified risk factors that put these children at greater risk; however, research is lacking regarding an appropriate intervention. Despite that fact, epidemiologic associations suggest primary care providers should be alert to increasing BMI trends and excessive weight gain beyond what is anticipated for height increase when dealing with these children, and consider intervention before the child becomes overweight.

Observational studies have identified sample populations that are at special risk for obesity as follows:

1. Children with BMI between the 85th and 95th percentiles.
2. Children in whom there is a positive family history of obesity in one or both parents.
3. Early onset of increasing weight beyond that appropriate for increase in height. This can be identified early, beginning in the first year of life.
4. Excessive increase in weight during adolescence, particularly in African American girls.
5. Children who have been previously very active and become inactive, or adolescents who are inactive in general. (An example would be a child who has previously participated in organized sports and has stopped, particularly in adolescence.)

No RCTs that address these populations were identified. Despite this, the Expert Panel believes that lifestyle recommendations with a goal of prevention of excessive weight gain are needed for normal-weight children with characteristics consistent with special risk for development of overweight and obesity. The diet and activity recommendations proposed for children at elevated cardiovascular risk (Section 5. Nutrition and Diet; Section 6. Physical Activity) should be vigorously reinforced in these children. In any child, the development of a BMI between the 85th and 95th percentile should be taken as a sign that increased attention to diet and activity as well as BMI-specific follow-up is indicated.

Conclusions and Grading of the Evidence Review on Treatment of Obesity

- There is good evidence for the effectiveness of combined weight loss programs that included behavior change counseling, negative energy balance through diet, and increased physical activity in addressing obesity in children older than age 6 years with a BMI ≥ 95th percentile and no comorbidities. (Grade A) However, such programs have primarily been shown to be effective in a comprehensive weight loss program or research settings, with only a small number shown to be effective in primary care settings.
- No data were identified on weight loss programs for children younger than age 6 years.
- No single negative energy diet plan was identified from the evidence review. Dietary plans should be determined for each child, based on baseline body size, energy requirements for growth, and physical activity level. (Grade D)
- Increasing dietary fiber from corn bran, wheat flour, wheat bran, oat flakes, corn germ meal, or glucomannan does not significantly improve weight loss. (Grade A)
- Various diets have been inadequately studied as to their effects on obesity in children and adolescents including low glycemic load diets, low carbohydrate diets, fiber supplements, and protein-sparing modified fasts.
- For children ages 6-12 years:
  - Family-based programs in research settings that addressed both diet and activity have been shown to be effective at initiating and sustaining weight loss over a follow-up of 10 years. (Grade A)
  - The greatest weight loss is achieved when parents are the focus of the intervention. (Grade A)
- For adolescents:
  - Comprehensive programs in research settings were effective at achieving weight loss in the short term. (Grade A)
  - The greatest weight change was achieved when the adolescent was the primary focus of the intervention. (Grade B)

- Behavior change programs that involved peers achieved more sustained weight loss. (Grade B)

- In overweight and obese youth, the combination of diet and a specific physical activity intervention that reduced sedentary activity and/or increased physical activity was universally more effective at achieving decreases in weight and BMI as well as decreases in body fat compared with an isolated diet intervention:
  - In both children and adolescents, exercise training improved weight loss and body composition (decreasing fat mass and reducing visceral fat), decreased IR, reduced BP, normalized dyslipidemia, and normalized subclinical measures of atherosclerosis. (Grade A)
  - In children ages 7-12 years, reduction in sedentary activity, independent of increasing physical activity, produced weight loss. (Grade B) In this age group, reductions in sedentary activity were effectively accomplished by rewarding children for time spent being physically active with TV viewing time. (Grade B)
  - Girls did not respond as well as boys to combined treatments that both reduced sedentary behaviors and increased physical activity. (Grade B)

- For adolescents with or without significant comorbidities with a BMI > 95th percentile and for adolescents with a BMI > 35 kg/m^2 who have failed a comprehensive lifestyle weight loss program, addition of medication *under the care of a physician experienced in managing weight loss with medication,* can be safe and effective in achieving weight loss with follow-up of 4 to 12 months. However, long-term safety and efficacy data are not available:
  - In adolescents with severe obesity and insulin resistance, the addition of metformin to a comprehensive lifestyle weight loss program improved fasting insulin and significantly reduced weight and BMI. (Grade B) [Metformin is currently approved by the U.S. Food and Drug Administration (FDA) for pediatric patients age 10 years and older with T2DM but is not approved for weight loss for either children or adults.
  - For obese adolescents older than age 12 years, the addition of orlistat to a comprehensive lifestyle weight loss program improved weight loss and BMI (Grade A); however, use of this medication had a high rate of GI side effects. [Orlistat (under that trade name xenical) is approved by the FDA for weight loss in pediatric patients age 12 years and older in conjunction with a reduced calorie diet. In August 2009 the FDA released an early communication about an ongoing safety review regarding reports of liver-related adverse events in some patients taking orlistat. In May 2010, the orlistat labeling was updated to incorporate safety information pertaining to the occurrence of rare post-marketing cases of severe liver injury, including hepatic failure resulting in liver transplant or death.]

- Dropout rates are substantial for all weight treatment programs.

- No studies defining an appropriate rate for weight loss in any age group were identified by the Guidelines evidence review. The 2010 *DGA* recommends slowing weight gain while allowing normal growth and development. For those with BMI ≥ *95th percentile without comorbidities,* both the AMA/CDC/MCHB Expert Committee and the American Academy of Pediatrics (AAP) recommend weight maintenance resulting in decreasing BMI as age increases. With BMI ≥ *95th percentile with comorbidities,* the AMA/CDC/MCHB Expert Committee and the AAP recommend gradual weight loss not exceeding 1 pound per month in children ages 2-11 years or 2 pounds per week in adolescents. (no grade)

- For adolescents with BMI far above 35 kg/m^2 and associated comorbidities, bariatric surgery on a research protocol in conjunction with a comprehensive lifestyle weight loss program improved weight loss, BMI, and other outcomes such as IR, glucose tolerance, and CV measures in small case series. (Grade D)

Table 10–1. EVIDENCE–BASED RECOMMENDATIONS FOR MANAGEMENT OF OVERWEIGHT AND OBESITY

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.

Birth–24 m	No weight-for-height specific recommendations. CHILD 1 is recommended for pediatric care providers to use with their child and adolescent patients to reduce CV risk	
2–5 y	Identify children at high risk for obesity because of parental obesity and excessive BMI increase → Focused CHILD 1 and physical activity education	Grade B *Recommend*
	BMI%ile stable → reinforce current program, follow-up in 6 months *Increasing BMI %ile → registered dietitian (RD) counseling for energy-balanced diet, intensify physical activity change; 6 month follow-up*	
	BMI 85th - 95th%ile: Excess weight gain prevention with parents as focus for energy-balanced diet; reinforce physical activity recommendations X 6 months	Grade D *Recommend*
	Improvement in BMI%ile → continue current program *Increasing BMI%ile → RD counseling for energy-balanced diet, intensify physical activity recommendations; 6 month follow-up*	
	BMI ≥ 95th%ile: Specific assessment for comorbidities*	Grade B *Strongly recommend*
	Family-based weight gain prevention with parents as focus; RD counseling and follow-up for energy-balanced diet; moderate-to-vigorous physical activity (MVPA) prescription; limit sedentary screen time; 3 month follow-up	Grade B *Recommend*

* Comorbidities: Hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM)

Table 10–1. **EVIDENCE–BASED RECOMMENDATIONS FOR MANAGEMENT OF OVERWEIGHT AND OBESITY (continued)**

6–11 y	Identify children at increased risk for obesity because of parental obesity, change in physical activity +/– excessive gain in BMI for focused CHILD 1/physical activity education. *BMI%ile stable → reinforce current program, 6 month follow-up* *Increasing BMI%ile → RD counseling for energy-balanced CHILD 1, intensified physical activity, 3 month follow-up*	Grade B *Recommend*
	BMI 85th - 95th%ile: Excessive weight gain prevention with parents as focus for energy-balanced diet; reinforce physical activity recommendations, 6 month follow-up *Stable/improving BMI%ile → reinforce current program, 6 month follow-up* *Increasing BMI%ile → RD counseling for energy-balanced CHILD 1, intensified physical activity recommendations, 3 month follow-up*	Grade D *Recommend*
	BMI ≥ 95th%ile: Specific assessment for comorbidities.*	Grade B *Strongly recommend*
	BMI ≥ 95th%ile with no comorbidities: Office-based weight loss plan: Family-centered program with parents as focus for behavior modification, (-) energy-balanced diet counseling by RD, Rx for increased MVPA, decreased sedentary time x 6 months *Improvement in BMI%ile/comorbidities → continue current plan* *No improvement in BMI%ile → referral to comprehensive multidisciplinary lifestyle weight loss program*	Grade A *Strongly recommend*
	BMI ≥ 95th%ile with comorbidities, BMI > 97th%ile, or progressive rise in BMI despite therapy: Refer to comprehensive multidisciplinary weight loss program for intensive management x 6 months *Improvement in BMI%ile → continue present program* *No improvement in BMI%ile → consider referral to another comprehensive multidisciplinary weight loss program*	Grade A *Strongly recommend*

* Comorbidities: Hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM).

Table 10–1. **EVIDENCE–BASED RECOMMENDATIONS FOR MANAGEMENT OF OVERWEIGHT AND OBESITY (continued)**

12–21 y	Identify adolescents at increased risk for obesity because of parental obesity, change in physical activity +/– excess gain in BMI for focused diet/physical activity (PA) education X 6 months	Grade B *Recommend*
	BMI/BMI%ile stable → reinforce current program, 6 month follow-up *Increasing BMI/BMI%ile → RD counseling for energy-balanced CHILD 1, intensified physical activity x 3 months*	
	BMI 85th - 95th%ile: Excess weight gain prevention with adolescent as change agent for energy-balanced CHILD 1, reinforced physical activity recommendations x 6 months	Grade B *Recommend*
	Improvement in BMI%ile → continue current program *Increasing BMI%ile → RD counseling for energy-balanced weight control diet, intensified physical activity, 3 month follow-up*	
	BMI ≥ 95th%ile: Specific assessment for comorbidities:*	Grade B *Strongly recommend*
	BMI ≥ 95th%ile with no comorbidities: Office-based weight loss plan: Family-centered with adolescent as change agent for behavior modification counseling, RD counseling for (-) energy-balanced diet, Rx for increased MVPA, decreased sedentary time x 6 months	Grade B *Strongly recommend*
	Improvement in BMI/BMI%ile → continue current program *No improvement in BMI/BMI%ile → referral to comprehensive multidisciplinary weight loss program with peers* *No improvement in BMI/BMI%ile → consider initiation of medication (orlistat) under care of experienced MD x 6-12 months*	
	BMI ≥ 95th%ile with comorbidities or BMI > 35 kg/m^2: Refer to comprehensive lifestyle weight loss program for intensive management x 6-12 months	Grade A *Strongly recommend*
	Improvement in BMI/BMI%ile → continue present program *No improvement in BMI/BMI%ile → consider initiation of orlistat under care of experienced clinician x 6-12 months*	
	BMI far above 35 kg/m^2 and comorbidities unresponsive to lifestyle therapy for > 1 y, consider bariatric surgery/ referral to center with experience/expertise in procedures	

* Comorbidities: Hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM).

11. Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis

Diabetes mellitus is an established risk factor for early CVD. Metabolically, diabetes is characterized by hyperglycemia due to defects in insulin secretion (type 1 diabetes [T1DM]) and insulin function and/or secretion (type 2 diabetes [T2DM]). Both T1DM and T2DM are associated with vascular disease. Autopsy and noninvasive imaging studies suggest that the extent of vascular involvement reflects the duration of the disease and the severity of the chronic metabolic derangement. The epidemiologies of the two types differ significantly. T1DM presents at a younger age, with 25% of patients diagnosed between ages 5 and 10 years and another 40% between ages 10 and 15 years. If not treated adequately, the degree of hyperglycemia is severe, and patients are highly symptomatic. By contrast, in T2DM, the majority of patients present in adult life, but a small and growing number present in adolescence, and most are relatively asymptomatic, with only mild to moderate hyperglycemia in combination with obesity. Regardless of these differences, children with diabetes, type 1 or type 2, are at significantly increased risk for accelerated atherosclerosis and early cardiovascular disease.

In certain other pediatric disease states, the process of atherosclerosis is dramatically accelerated with clinical coronary events occurring in childhood and very early adult life. These conditions were the subject of a recent guideline from the American Heart Association (AHA). The Expert Panel elected to use the AHA guideline as the template for developing recommendations for children with conditions like diabetes that predispose them to very accelerated atherosclerosis since the evidence review identified only a very small number of studies addressing these conditions in a randomized trial format.

Conclusions of the Evidence Review for Diabetes Mellitus and Other Predisposing Conditions

Children with diabetes mellitus, type 1 or type 2, represent the prototype of the child at special risk for accelerated atherosclerosis and early clinical CVD. To maximize identification of T2DM in childhood and adolescence, the screening algorithm from the American Diabetes Association (ADA) is recommended for screening in all children (Table 11–1).

Limited high quality papers were found addressing CV risk reduction in children with conditions predisposing them to accelerated atherosclerosis, so the Expert Panel elected to modify the recommendations of an expert pediatric panel convened by the American Heart Association (AHA) that published their recommendations for risk factor management in 2006; these recommendations are endorsed by the American Academy of Pediatrics and are included in the guideline database for these guidelines.

The AHA statement recommends specific risk identification and management stratified by risk based on defined other conditions that parallel the recommendations for adults with diabetes or other CVD equivalents. For the high risk category (Table 11–2), the disease process has been associated with clinical coronary disease before 30 years of age. For the moderate risk category, the disease process has been shown to be associated with pathologic, physiologic or subclinical evidence of accelerated atherosclerosis.

The Expert Panel believes that these recommendations should be used for management of children and adolescents with diabetes and other predisposing conditions as outlined in the algorithm in Figure 11–1 and in Tables 11–2 and 11–3. With the growing evidence of vascular disease in children with T2DM, the Expert Panel

felt it was prudent to include both T1DM and T2DM in the High Risk category. With increasing evidence of vascular dysfunction in children with human immunodeficiency virus infection (HIV) and nephrotic syndrome, these two conditions are added to the selected disease settings in the moderate risk category. Patients in the high risk category require intensive management with more aggressive goals for therapy than those in the moderate risk category as outlined in the algorithm.

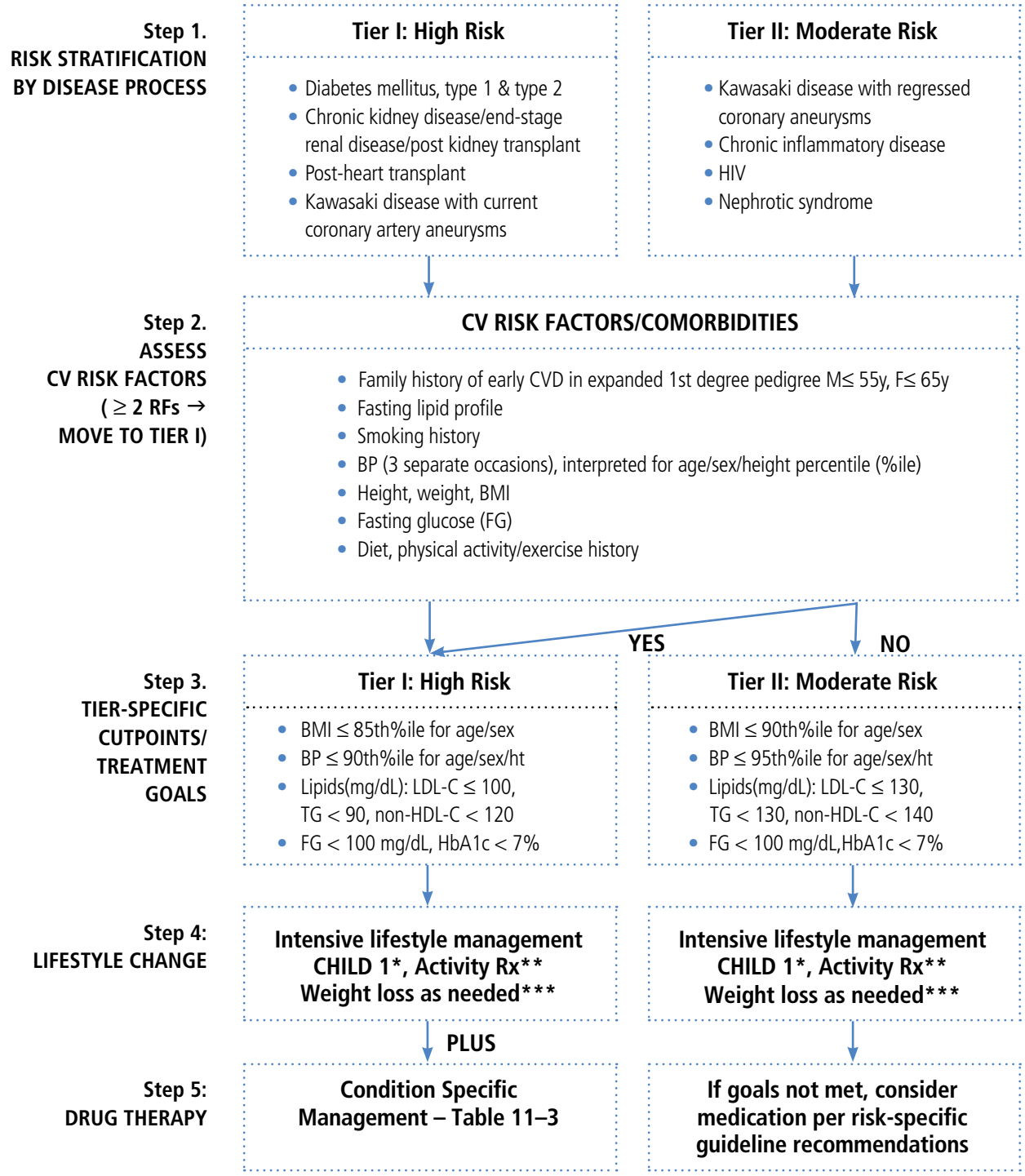
Table 11–1. AMERICAN DIABETES ASSOCIATION (ADA) SCREENING RECOMMENDATIONS FOR TYPE 2 DIABETES MELLITUS IN CHILDHOOD

Criteria:	Screening procedure:
• Overweight, defined by: – BMI ≥ 85th%ile for age and gender, OR – Weight for height ≥ 85th%ile, OR – Weight > 120% of ideal for height ***Plus*** any two of the following risk factors: • Family history of T2DM in first- or second-degree relative • Race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander) • Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, or polycystic ovary syndrome)	*Age of initiation:* ≥ 10 years, or at onset of puberty, if puberty occurs at a younger age *Frequency:* Every 2 years *Test:* Fasting plasma glucose

Table 11–2. SPECIAL RISK PEDIATRIC CONDITIONS: STRATIFICATION BY RISK CATEGORY

High risk:	Moderate risk:
Manifest coronary artery disease ≤ age 30 years: *Clinical evidence* • T1DM or T2DM • Chronic kidney disease/end-stage renal disease/postrenal transplant • Post orthotopic heart transplantation • Kawasaki disease with current coronary aneurysms	*Accelerated atherosclerosis: Pathophysiologic evidence* • Kawasaki disease with regressed coronary aneurysms • Chronic inflammatory disease (systemic lupus erythematosus, juvenile rheumatoid arthritis) • HIV • Nephrotic syndrome

Figure 11–1. RISK STRATIFICATION AND MANAGEMENT FOR CHILDREN WITH CONDITIONS PREDISPOSING TO ACCELERATED ATHEROSCLEROSIS AND EARLY CVD



Directions:
Step 1: Risk stratification by disease process (Table 11–2).
Step 2: Assess all cardiovascular risk factors. If there are ≥ 2 comorbidities, move Tier II patient to Tier I for subsequent management.
Step 3: Tier-specific treatment goals/cutpoints defined.
Step 4: Initial therapy: For Tier I, initial management is therapeutic lifestyle change PLUS disease-specific management (Table 11–3). For Tier II, initial management is therapeutic lifestyle change.
Step 5: For Tier II, if goals are not met, consider medication per risk factor specific recommendations in these guidelines.

* CHILD 1 – Cardiovascular Health Integrated Lifestyle Diet, per Section 5. Nutrition and Diet.
** Activity Rx – Activity recommendations per Section 6. Physical Activity.
*** Weight loss recommendations per Section 10. Overweight and Obesity.

Table 11–3. CONDITION–SPECIFIC TREATMENT RECOMMENDATIONS FOR HIGH RISK CONDITIONS

- Rigorous age-appropriate education in diet, activity, smoking cessation for all
- Specific therapy as needed to achieve blood pressure (BP), LDL-C, glucose, and HbA1c goals indicated for each tier, as outlined in algorithm; timing individualized for each patient and diagnosis

Diabetes mellitus, regardless of type:

- For T1DM, intensive glucose management per endocrinologist with frequent glucose monitoring/insulin titration to maintain optimal plasma glucose and HbA1c for age.
- For T2DM, intensive weight management and glucose control, in consultation with an endocrinologist as needed to maintain optimal plasma glucose and HbA1c for age.
- Assess body mass index (BMI), fasting lipids: Step 4 lifestyle management of weight, lipids for 6 months.
- If LDL goals not achieved, consider statin therapy if age ≥ 10 years to achieve Tier I treatment goals for LDL-C.
- Initial BP ≥ 90th%ile: Step 4 lifestyle management plus no added salt, increased activity for 6 months.
- If BP consistently ≥ 95th%ile for age/sex/height: initiate angiotensin-converting enzyme inhibitor therapy with BP goal < 90th%ile for sex/height, or < 120/80, whichever is lower.

Chronic kidney disease/end-stage renal disease/postrenal transplant:

- Optimization of renal failure management with dialysis/transplantation per nephrology.
- Assess BMI, BP, lipids, fasting glucose (FG): Step 4 lifestyle management for 6 months.
- If LDL goals not achieved, consider statin therapy if age ≥ 10 years to achieve Tier I treatment goals for LDL-C.
- If BP consistently ≥ 95th%ile for age/gender/height, initiate angiotensin-converting enzyme inhibitor therapy with BP goal < 90th%ile for gender/height, or < 120/80, whichever is lower.

After heart transplantation:

- Optimization of antirejection therapy, treatment for cytomegalovirus infection, routine evaluation by angiography/perfusion imaging per transplant physician.
- Assess BMI, BP, lipids, FG: Initiate Step 5 therapy, including statins, immediately in all patients age ≥ 1 year to achieve Tier I treatment goals.

Kawasaki disease with current coronary aneurysms:

- Antithrombotic therapy, activity restriction, ongoing myocardial perfusion evaluation per cardiologist.
- Assess BMI, BP, lipids, FG: Step 4 lifestyle management for 6 months.
- If goals not achieved, consider pharmacologic therapy for LDL-C and BP if age ≥ 10 years to achieve Tier I treatment goals.

12. Risk Factor Clustering and the Metabolic Syndrome

Traditional CV risk factors such as obesity, hypertension and dyslipidemia demonstrate clustering in youth. Risk behaviors like smoking, suboptimal diet and sedentary behavior also demonstrate clustering as do advantageous diet and exercise habits. Becoming obese increases the prevalence of the risk factor cluster in adults called the metabolic syndrome. The metabolic syndrome is defined as 3 or more of the following risk factors: elevated waist circumference, triglyceride levels, BP, and/or fasting glucose, and reduced HDL-cholesterol. In the United States, the metabolic syndrome is said to affect between 34% and 39% of adults including 7% of men and 6% of women in the 20- to 30-year old age group. The Expert Panel reviewed all the RCTs, SRs, meta-analyses and observational studies that addressed the childhood association between the risk factor cluster known as the metabolic syndrome and the development of atherosclerosis, and the identification and management of the cluster in children and adolescents.

There is a lack of consensus on how to define metabolic syndrome in youth, which has led to widely varying estimates of its frequency. A recent analysis of National Health and Nutrition Examination Survey data from 1999 to 2002 yielded prevalence estimates for all teens from 2.0% to 9.4% and for obese teens from 12.4 to 44.2%. Regardless of the definition used, the prevalence of the metabolic syndrome risk factor cluster is higher in older (12- to 14 year old) children compared with younger (8- to 11 year old) children. The specific etiology for metabolic syndrome is unknown; however, it is most likely caused by the expression of various genotypes modified by environmental interactions and mediated through abdominal obesity and insulin resistance. Longitudinal studies of cohorts where the metabolic syndrome cluster was present in childhood identify an increased incidence of both T2DM and clinical CV events over a follow-up of 25 years. A strong association between obesity with or without elevated insulin levels and/or hypertension in early childhood and subsequent development of the metabolic syndrome constellation in adulthood has been consistently demonstrated. Treatment of CV risk factor clustering in youth has not been thoroughly evaluated but maintenance of low levels of CV risk factors starting in childhood is associated with a lower prevalence of cardiovascular disease and with increased longevity in adult life.

Recommendations for Management of Risk Factor Clustering and the Metabolic Syndrome

The metabolic syndrome concept is important as it identifies a common multiple CV risk phenotype in pediatrics. However, the absence of a defined etiology, the lack of consensus on definition and the paucity of high level evidence addressing management in childhood led the Expert Panel to conclude that the metabolic syndrome should not be considered as a separate risk factor in childhood and adolescence. Prevention of obesity is the most important strategy to lower the prevalence of metabolic syndrome in adults and this appears strongly applicable in childhood per Section 10. Overweight and Obesity. Given the strong relationship of obesity and physical inactivity to the metabolic syndrome and insulin resistance, the Expert Panel makes the following recommendations. Due to the paucity of evidence available, the recommendations are a consensus of the Expert Panel. (Grade D)

- Presence of any combination of multiple risk factors should prompt intensification of therapy with an emphasis on lifestyle modification to address individual metabolic syndrome risk factor levels.
- Presence of obesity should prompt specific evaluation for all other CV risk factors including

family history of premature CVD, hypertension, dyslipidemia, diabetes and tobacco exposure.

- Coexistence of obesity with any other major CV risk factor should be recognized by clinicians as a setting where:
  1. Intensive weight reduction should be undertaken per the recommendations in Section 10. Overweight and Obesity, along with management of identified risk factors including initiation of pharmacologic therapy, per the risk factor-specific sections in these Guidelines (Section 8. High Blood Pressure; Section 9. Lipids and Lipoproteins; Section 11. Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis; Section 7. Tobacco Exposure).
  2. Prompt evaluation for diabetes mellitus, liver function abnormalities, left ventricular hypertrophy and sleep apnea should be undertaken.

These recommendations are supported by knowledge that CV morbidity has a continuous relationship across the risk distribution spectrum and that the youth with multiple borderline risk factors may, in fact, have risk equivalent to an individual with extreme abnormality of a single major risk factor. A presentation like this should lead to intense nutrition and exercise management with close follow-up, and if lifestyle intervention is unsuccessful, consideration should be given to endocrine referral. Table 12–1 provides definitions of component risk factor levels for evaluating children with multiple cardiovascular risk factors.

Table 12–1. **METABOLIC SYNDROME COMPONENT LEVELS FOR EVALUATION OF CHILDREN WITH MULTIPLE CARDIOVASCULAR RISK FACTORS**

Risk Factor			Cutpoint	Reference
Obesity	BMI		≥ 85 to < 95th%ile	CDC growth charts
	Waist circumference		≥ 90 to < 95th%ile	NHANES
Blood Pressure			≥ 90 to < 95th%ile	*The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents*
Dyslipidemia	HDL-C		≥ 40 to ≤ 45 mg/dL	See Lipid section of this report for normative values
	TG	Birth – 9 years	≥ 75 to < 100 mg/dL	
		≥ 10 years	≥ 90 to < 130 mg/dL	
	Non-HDL-C		≥ 120 to < 144 mg/dL	
Glycemia	Fasting glucose		≥ 100 to < 126 mg/dL	ADA screening recommendations
	Fasting insulin		Elevated fasting insulin level, above normal for gender, race and pubertal status is considered evidence of insulin resistance	

13. Perinatal Factors

Increasing evidence links prenatal exposures to adverse health outcomes. Perinatal risk reduction is an area where pediatric care providers can potentially be effective since they are often the only physicians that a mother sees between pregnancies. The Expert Panel identified three potential areas for consideration: maternal obesity, choice of neonatal feeding method, and maternal smoking cessation. Maternal obesity is associated with gestational diabetes, higher birth weight, childhood obesity measured by increased body mass index, and increased risk of the metabolic syndrome and T2DM in offspring. However, the Expert Panel could not identify any pre-pregnancy or postpartum studies addressing maternal obesity in a pediatric care setting, and more general approaches to preventing or treating obesity in women of reproductive age are beyond the scope of this report. A detailed discussion of childhood obesity itself is the subject of Section 10. Overweight and Obesity. With regard to choice of neonatal feeding method, the CV advantages of breastfeeding as the primary source of nutrition for infants are emphasized in the Section 5. Nutrition and Diet. The evidence review for this section therefore focused on maternal smoking cessation.

Conclusions and Grading of the Evidence Review on Maternal Smoking Cessation

- The Expert Panel finds that strong evidence supports a benefit for interventions directed at maternal smoking cessation during pregnancy. (Grade A) Weaker evidence suggests that these interventions do not prevent relapse postpartum. Trials of cessation in the postpartum period, which would be the most applicable to pediatric providers, are limited in number and suggest that for maternal smoking cessation to be sustained, specific continued support in the pediatric care setting is required.
- No smoking cessation interventions reported any adverse effects related to the interventions. (No grade)
- The Expert Panel believes that pediatric care providers can play a role in helping mothers to remain smoke-free or to quit smoking in the interpregnancy interval. For most women, this interval will extend to early first trimester of any subsequent pregnancy. The pediatric well-child schedule calls for about 10 visits in the first two years of life, and mothers attend most visits so the pediatric care provider usually sees women in this period more than any other health care professional. Pediatric care providers often have a sustained relationship with mother and baby, and many already advocate for parental smoking cessation in their efforts to promote a smoke-free environment for children. Pediatric providers and/or their staff need to be trained to either deliver or refer to a long-term maternal smoking cessation program. (No grade)

Table 13–1. EVIDENCE–BASED RECOMMENDATIONS FOR MATERNAL SMOKING CESSATION

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.
Supportive actions represent expert consensus suggestions from the Expert Panel provided to support implementation of the recommendations; they are not graded.

Smoking cessation guidance during pregnancy is strongly advised. Grade A
Strongly recommend

Supportive Action:

Pediatric care providers should be provided with appropriate training and materials to deliver, or refer to, a smoking cessation program in the postpartum period for all smoking women of childbearing age.

This intervention should be directly linked to ongoing smoke-free home recommendations directed at all young mothers and fathers as described in Section 7. Tobacco Exposure.

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