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

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

EXPERT PANEL ON INTEGRATED GUIDELINES FOR CARDIOVASCULAR HEALTH AND RISK REDUCTION IN CHILDREN AND ADOLESCENTS

ABBREVIATIONS

CVD—cardiovascular disease
NHLBI—National Heart, Lung, and Blood Institute
RCT—randomized controlled trial
PDAY—Pathobiological Determinants of Atherosclerosis in Youth
BP—blood pressure
HDL—high-density lipoprotein
DM—diabetes mellitus
CIMT—carotid intima-media thickness
LDL—low-density lipoprotein
T1DM—type 1 diabetes mellitus
T2DM—type 2 diabetes mellitus
TC—total cholesterol
AAP—American Academy of Pediatrics
DGA—*Dietary Guidelines for Americans*
NCEP—National Cholesterol Education Program
DASH—Dietary Approaches to Stop Hypertension
CHILD—Cardiovascular Health Integrated Lifestyle Die
FLP—fasting lipid profile
CDC—Centers for Disease Control and Prevention
AMA—American Medical Association
MCHB—Maternal and Child Health Bureau
FDA—Food and Drug Administration
AHA—American Heart Association

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(Continued on last page)

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 toward clinical disease. In response, the former director of the National Heart, Lung, and Blood Institute (NHLBI), Dr Elizabeth Nabel, initiated development of cardiovascular health guidelines for pediatric care providers based on a formal evidence review of the science with an integrated format addressing all the major cardiovascular risk factors simultaneously. An expert panel was appointed to develop the guidelines in the fall of 2006.

The goal of the expert panel was to develop comprehensive evidence-based guidelines that address the known risk factors for CVD (Table 1-1) to assist all primary pediatric care providers in both the promotion of cardiovascular 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 cardiovascular risk reduction in children and adolescents addresses a disease process (atherosclerosis) in which the clinical end point of manifest CVD is remote. The recommendations, therefore, need to address 2 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 1 or, at most, a small number of finite questions that address 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 presenting of results. The results of the review lead to the conclusions, independent of interpretation.

By contrast, given the scope of the charge to the expert 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 time frame extended back to 1985, ~5 years before the review for the last NHLBI guideline addressing lipids in children published in 1992.[1] This evidence is largely available in the form of epidemiologic observational studies

TABLE 1-1 Evaluated Risk Factors

Family history
Age
Gender
Nutrition/diet
Physical inactivity
Tobacco exposure
BP
Lipid levels
Overweight/obesity
Diabetes mellitus
Predisposing conditions
Metabolic syndrome
Inflammatory markers
Perinatal factors

TABLE 1-2 Evidence Grading System: Quality Grades

Grade	Evidence
A	Well-designed RCTs or diagnostic studies performed on a population similar to the guideline's target population
B	RCTs 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(3):874–877.

(rather than RCTs) that, therefore, must 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. 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 that justifies 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 the 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 in which the evidence was inadequate. When this occurred, recommendations were made on the basis of a consensus of the expert panel. The schema used in grading the evidence appears in Tables 1-2 and 1-3; expert consensus opinions are identified as grade D.

The NHLBI expert panel integrated guidelines for cardiovascular health and risk reduction in children and adolescents contain recommendations based on the evidence review and are directed toward 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 according to risk factor, discussion of the expert panel's rationale for recommendations, and >1000 citations from the published literature and is available at 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's recommendations for patient care relative to cardiovascular health and risk-factor detection and management with only the references cited in the text provided. It begins with a state-of-the-science synopsis of the evidence, which indicates that atherosclerosis begins in childhood, and the extent of atherosclerosis is linked directly to the presence and intensity of known risk factors. This is followed by a cardiovascular health schedule (Section 3), which summarizes the expert panel's age-based recommendations according to risk factor in a 1-page periodic table. Risk factor specific sections follow, with the graded conclusions of the evidence review, normative tables, and age-specific recommendations. These recommendations 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 www.nhlbi.nih.gov/guidelines/cvd_ped/index.htm.

It is the hope of the NHLBI and the expert panel that these recommendations will be useful for all those who provide cardiovascular health care to children.

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 cardiovascular 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 lipids 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

TABLE 1-3 Evidence Grading System: 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 that 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) have found 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.

Adapted from American Academy of Pediatrics, Steering Committee on Quality Improvement and Management. *Pediatrics*. 2004;114(3):874–877.

War casualties. Two major contemporary studies, the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study[2] and the Bogalusa Heart Study,[3] subsequently evaluated the extent of atherosclerosis in children, adolescents, and young adults who died accidentally. The Bogalusa study[3] measured cardiovascular risk factors (lipid levels, blood pressure [BP], BMI, 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,[2] risk factors and surrogate measures of risk factors were measured after death in 15- to 34-year olds who died accidentally of external causes. Strong relationships were found between atherosclerotic severity and extent, and age, non–high-density lipoprotein (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, the 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 Noninvasively

Over the last decade, measures of subclinical atherosclerosis have developed, including the demonstration of coronary calcium on electron beam computed tomography imaging, increased carotid intima-media thickness (CIMT) assessed with ultrasound, endothelial dysfunction (reduced arterial dilation) with brachial ultrasound imaging, and increased left ventricular mass with cardiac ultrasound. These measures have been assessed in young people with severe abnormalities of individual risk factors:

- In adolescents with a marked elevation of low-density lipoprotein (LDL) cholesterol level caused by familial heterozygous hypercholesterolemia, abnormal levels of coronary calcium, increased CIMT, and impaired endothelial function have been found.
- Children with hypertension have been shown to have increased CIMT, increased left ventricular mass, and eccentric left ventricular geometry.
- Children with type 1 DM (T1DM) 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 shown by ultrasound and plethysmography in association with ciga-

rette 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 found in children with severe obesity.

Four longitudinal studies have found relationships of risk factors measured in youth (specifically LDL cholesterol, non-HDL cholesterol and serum apolipoproteins, obesity, hypertension, tobacco use, and DM) with 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 cardiovascular conditions. Genetic disorders related to high cholesterol are the biological model for risk-factor impact on the atherosclerotic process. With homozygous hypercholesterolemia, in which LDL cholesterol levels exceed 800 mg/dL beginning in infancy, coronary events begin in the first decade of life and life span is severely shortened. With heterozygous hypercholesterolemia, in which LDL cholesterol levels are minimally 160 mg/dL and typically >200 mg/dL and total cholesterol (TC) levels exceed 250 mg/dL beginning in infancy, 50% of men and 25% of women experience clinical coronary events by the age of 50. By contrast, genetic traits associated with low cholesterol are associated with longer life expectancy. In the PDAY study,[2] every 30 mg/dL increase in non-HDL cholesterol level 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 evidence, in 15- to 19-year olds in the PDAY study, the presence of hyperglycemia was associated with the demonstration of advanced atherosclerotic lesions of the coronary arteries. In the PDAY study, there was also a 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.[4]

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 found differences according to race and ethnicity and according to geography for prevalence of cardiovascular 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,[3] the PDAY study,[2] and the Coronary Artery Risk Development in Young Adults [CARDIA] study[5]) have included racially diverse populations, and other studies have been conducted outside the United States. However, longitudinal data on Hispanic, Native American, and Asian children are lacking. Clinically important differences in prevalence of risk factors exist according to 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.

The Impact of 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 clearly showed 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 1 other risk factor and the development of obesity, which is often associated with insulin resistance, elevated triglyceride levels, reduced HDL cholesterol levels, and elevated BP, a combination known in adults as the metabolic syndrome. 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 it 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 National Health and Nutrition Examination Surveys [NHANES] from 1999 to 2002[6]) with overweight and obesity, elevated TC level and systolic BP, and a reduced HDL cholesterol level.

Risk-Factor Tracking From Childhood Into Adult Life

Tracking studies from childhood to adulthood have been performed for all the major risk factors.

- Obesity tracks more strongly than any other risk factor; among many reports from studies that have demonstrated this fact, one of the most recent is from the Bogalusa study,[7] in which >2000 children were followed from initial evaluation at 5 to 14 years of age to adult follow-up at a mean age of 27 years. On the basis of 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 at the >99th percentile were obese in adulthood. Increased correlation is seen with increasing age at which the elevated BMI occurs.
- For cholesterol and BP, tracking correlation coefficients in the range of 0.4 have been reported consistently from 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 BP levels in the upper portion of the pediatric distribution makes having them 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, although ~50% of those who have ever smoked eventually quit.
- T1DM is a lifelong condition.
- The insulin resistance of T2DM can be alleviated by exercise, weight loss, and bariatric surgery, but the long-term outcome of those with T2DM diagnosed in childhood is not known.
- As already discussed, risk-factor clusters such as those seen with obesity and the metabolic syndrome have been shown to track from childhood into adulthood.

CVD Prevention Beginning in Youth

The rationale for these guidelines comes from the following 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 cardiovascular risk factors, which begin in childhood.
- Risk factors track from childhood into adult life.
- Interventions exist for the management of identified risk factors.

The evidence for the first 4 bullet points is reviewed in this section, and the evidence surrounding interventions for identified risk factors is addressed in the risk-factor–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 in which atherosclerosis is well established, morbidity may already exist, and the process is only minimally reversible. At a young age, there have historically been 2 goals of prevention: (1) prevent the development of risk factors (primordial prevention); and (2) recognize and manage those children and adolescents who are at increased risk as a result of 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 has found that (1) societies with low levels of cardiovascular risk factors have low CVD rates and that changes in risk in those societies are associated with a change in CVD rates, (2) in adults, control of risk factors leads to a decline in morbidity and mortality from CVD, and (3) those without childhood risk have minimal atherosclerosis at 30 to 34 years of age, 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 randomly assign young people with defined risks to treatment of cardiovascular risk factors or to no treatment and follow both groups over sufficient time to determine if cardiovascular 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 and thereby maximize the benefit. However, 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 alternative stepwise approach in which 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 cardiovascular prevention beginning in childhood: atherosclerosis begins in youth; the atherosclerotic process relates to risk factors that can be identified in childhood; and 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 Cardiovascular Health Management

One cornerstone of pediatric care is placing clinical recommendations in a developmental context. Those who make 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[8] (AAP) is used to provide a framework for these guidelines with cardiovascular risk-reduction recommendations for each age group.

This document provides recommendations for preventing the development of risk factors and optimizing cardiovascular health, beginning in infancy, that are 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 cardiovascular 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 that require specialist referral. The guidelines also identify specific medical conditions such as DM and chronic kidney disease that are associated with increased risk for accelerated atherosclerosis. Recommendations for ongoing cardiovascular health management for children and adolescents with these diagnoses are provided.

A cornerstone of pediatric care is the provision of health education. In the US 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 cardiovascular health message. Pediatric care providers provide an effective team educated to initiate behavior change to diminish risk of CVD and promote lifelong cardiovascular health in their patients from infancy into young adult life.

4. FAMILY HISTORY OF EARLY ATHEROSCLEROTIC CVD

A family history of CVD represents the net effect of shared genetic, biochemical, behavioral, and environmental components. In adults, epidemiologic studies have found 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 found 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 cardiovascular risk has been confirmed for men, women, and siblings and in different racial and ethnic groups. The evidence review identified all 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 interven-

tional 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 of a child, history should also be ascertained for the occurrence of CVD in grandparents, aunts, and uncles, although the evidence supporting this recommendation is insufficient to date (grade D).

- Identification of a positive family history for cardiovascular disease and/or cardiovascular risk factors should lead to evaluation of all family members, especially parents, for cardiovascular risk factors (grade B).
- Family history evolves as a child matures, so regular updates are a necessary 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).

Recommendations for the use of family history in cardiovascular health promotion are listed in Table 4-1.

5. NUTRITION AND DIET

The 2010 *Dietary Guidelines for Americans* (DGA)[8] include important recommendations for the population aged 2 years and older. In 1992, the National Cholesterol Education Program (NCEP) Pediatric Panel report[1] 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, provides the rationale for new dietary prevention efforts initiated early in life.

This new pediatric cardiovascular guideline not only builds on the recommendations for achieving nutrient adequacy in growing children as stated in the 2010 DGA but also adds evidence regarding the efficacy of specific dietary changes in reducing cardiovascular risk from the current evidence review for use by pediatric care providers in the care of their patients. Because the focus of these guidelines is on cardiovascular 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 that addressed cardiovascular risk reduction in children has provided 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 and the potential to decrease future risk for CVD. The expert panel accepts the 2010 DGA[8] as containing appropriate recommendations for diet and nutrition in children aged 2 years and older. The recommendations in these guidelines are intended for pediatric care providers to use with their patients to address cardiovascular 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. Where the 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, the World Health Organization, the AAP, and the American Academy of Family Physicians, exclusive breastfeeding is recommended for the first 6 months of life. Continued breastfeeding is recommended to at least 12 months of age with the addition of complementary foods. If breastfeeding per se is not possible, feeding human milk by bottle is second best, and formula-feeding is the third choice.*

- Long-term follow-up studies have found that subjects who were breastfed have sustained cardiovascular health benefits, including lower cholesterol levels, lower BMI, reduced prevalence of type 2 DM, 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 cardiovascular 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% to 10% of calories, and dietary cholesterol limited to 300 mg/day. Under the guidance of qualified nutritionists, this dietary composition has been shown to result in lower TC and LDL cholesterol levels, less obesity, and

less insulin resistance (grade A). Under similar conditions and with ongoing follow-up, these levels of fat intake might have similar effects starting in infancy (grade B). Fats are important to infant diets because of their role in brain and cognitive development. Fat intake for infants younger than 12 months should not be restricted without medical indication.

- The remaining 20% of fat intake should comprise a combination of monosaturated and polyunsaturated fats (grade D). Intake of trans fats should be limited as much as possible (grade D).
- For adults, the current NCEP guidelines[9] recommend that adults consume 25% to 35% of calories from fat. The 2010 DGA supports the Institute of Medicine recommendations for 30% to 40% of calories from fat for ages 1 to 3 years, 25% to 35% of calories from fat for ages 4 to 18 years, and 20% to 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 2 years of age and through adolescence optimizes these benefits without compromising nutrient quality while avoiding excess saturated fat and calorie intake (grade A). Between the ages of 1 and 2 years, as children transition from breast milk or formula, reduced-fat milk (ranging from 2% milk to fat-free milk) can be used on the basis of 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% to 20% from protein and 50% to 55% from carbohydrate sources (no grade). These recommended ranges fall within the acceptable macronutrient distribution range specified by the 2010 DGA: 10% to 30% of calories from protein and 45% to 65% of calories from carbohydrate for children aged 4 to 18 years.
- Sodium intake was not addressed by the evidence review for this section on nutrition and diet. From the evidence review for the "High BP" section, lower sodium intake is associated with lower systolic and diastolic BP 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 100% fruit juice by infants was made by 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 according to gender and age group at 3 levels of physical activity from the dietary guidelines are shown in Table 5-2. For children of normal weight whose activity is minimal, most calories are needed to meet nutritional requirements, which leaves only ~5% to 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 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 up to 14 g/1000 kcal for older children and adolescents is recommended (grade D).
- The expert panel supports the 2008 AAP recommendation for vitamin D supplementation with 400 IU/day for all infants and children.[10] No other vitamin, mineral, or dietary supplements are recommended (grade D). The new recommended daily allowance for vitamin D for those aged 1 to 70 years is 600 IU/day.
- Use of dietary patterns modeled on those shown to be beneficial for adults (eg, Dietary Approaches to Stop Hypertension [DASH] pattern) is a promising approach to improving nutrition and decreasing cardiovascular 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).

3. INTEGRATED CARDIOVASCULAR HEALTH SCHEDULE

Risk Factor	Age					
	Birth to 12 mo	**1–4 y**	**5–9 y**	**9–11 y**	**12–17 y**	**18–21 y**
Family history of early CVD	—	At 3 y, evaluate family history for early CVD: parents, grandparents, aunts/uncles, men ≤55 y old, women ≤65 y old; review with parents and refer as needed; positive family history identifies children for intensive CVD RF attention	Update at each nonurgent health encounter	Reevaluate family history for early CVD in parents, grandparents, aunts/uncles, men ≤55 y old, women ≤65 y old	Update at each nonurgent health encounter	Repeat family-history 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	Obtain smoke exposure history from child 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 12 mo of age if possible; add formula if breastfeeding decreases or stops before 12 mo of age	At age 12–24 mo, may change to cow's milk with 2% percentage of fat decided by family and pediatric care provider; after 2 y of age, fat-free milk for all; juice ≤4 oz/d; transition to CHILD-1 diet by the age of 2 y	Reinforce CHILD-1 diet messages	Reinforce CHILD-1 diet messages 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 family history for obesity; discuss weight-for-height tracking, growth chart, and healthy diet	Chart height/weight/BMI; classify weight-by BMI from age 2 y; review with parent	Chart height/weight/BMI and review with parent; BMI ≥ 85th percentile, crossing percentiles: Intensify diet/ activity focus for 6 mo; if no change: RD referral, manage per obesity algorithms BMI ≥ 95th percentile, manage per obesity algorithms	Chart height/weight/BMI and review with parent and child; BMI ≥ 85th percentile, crossing percentiles: Intensify diet/activity focus for 6 mo; if no change: RD referral, manage per obesity algorithms; BMI ≥ 95th percentile: manage per obesity algorithms	Chart height/weight/BMI and review with child and parent; BMI ≥85th percentile, crossing percentiles: intensify diet/activity focus for 6 mo; if no change: RD referral, manage per obesity algorithms; BMI ≥ 95th percentile, manage per obesity algorithms	Review height/weight/BMI and norms for health with patient; BMI ≥ 85th percentile, crossing percentiles: intensify diet/activity focus for 6 mo; if no change: RD referral, manage per obesity algorithms; BMI ≥ 95th percentile, manage per obesity algorithms
Lipids	No routine lipid screening	Obtain FLP only if family history for CVD is positive, parent has dyslipidemia, child has any other RFs or high-risk condition	Obtain FLP only if family history for CVD is positive, parent has dyslipidemia, child has any other RFs or high-risk condition	Obtain universal lipid screen with nonfasting non-HDL = TC − HDL, or FLP: manage per lipid algorithms as needed	Obtain FLP if family history newly positive, parent has dyslipidemia, child has any other RFs or high-risk condition; manage per lipid algorithms as needed	Measure 1 nonfasting non–HDL or FLP in all: review with patient; manage with lipid algorithms per ATP as needed
BP	Measure BP in infants with renal/urologic/cardiac diagnosis or history of neonatal ICU	Measure BP annually in all from the age of 3 y; chart for age/ gender/height percentile and review with parent	Check BP annually and chart for age/gender/height: review with parent; workup and/or management per BP algorithm as needed	Check BP annually and chart for age/gender/height: review with parent, workup and/or management per BP algorithm as needed	Check BP annually and chart for age/gender/height: review with adolescent and parent, workup and/or management per BP algorithm as needed	Measure BP: review with patient; evaluate and treat per JNC guidelines
Physical activity	Encourage parents to model routine activity; no screen time before the age of 2 y	Encourage active play; limit sedentary/screen time to ≤2 h/d; no TV in bedroom	Recommend MVPA of ≥1 h/d; limit screen/sedentary time to ≤2 h/d	Obtain activity history from child: recommend MVPA of ≥1 h/d and screen/sedentary time of ≤2 h/d	Use activity history with adolescent to reinforce MVPA of ≥1 h/d and leisure screen time of ≤2 h/d	Discuss lifelong activity, sedentary time limits with patient
Diabetes	—	—	—	Measure fasting glucose level per ADA guidelines; refer to endocrinologist as needed	Measure fasting glucose level per ADA guidelines; refer to endocrinologist as needed	Obtain fasting glucose level if indicated; refer to endocrinologist as needed

All algorithms and guidelines in this schedule are included in this summary report. RF indicates risk factor; RD, registered dietitian; ATP, Adult Treatment Panel III ("Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults"); JNC, Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; MVPA, moderate-to-vigorous physical activity; ADA, American Diabetes Association.
The full and summary reports of the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents can also be found on the NHLBI Web site (www.nhlbi.nih.gov).

TABLE 4-1 Evidence-Based Recommendations for Use of Family History in Cardiovascular Health Promotion

Birth to 18 y	Take detailed family history of CVD at initial encounter and/or at 3, 9–11, and 18 y[a]	Grade B Recommend
	If positive family history identified, evaluate patient for other cardiovascular risk factors, including dyslipidemia, hypertension, DM, obesity, history of smoking, and sedentary lifestyle	
	If positive family history and/or cardiovascular risk factors identified, evaluate family, especially parents, for cardiovascular risk factors	Grade B Recommend
	Update family history at each nonurgent health encounter	Grade D Recommend
	Use family history to stratify risk for CVD risk as risk profile evolves	Grade D Recommend
	Supportive action: educate parents about the importance of family history in estimating future health risks for all family members	
18 to 21 y	Review family history of heart disease with young adult patient	Grade B Strongly recommend
	Supportive action: educate patient about family/personal risk for early heart disease, including the need for evaluation for all cardiovascular risk factors	

Grades reflect the findings of the evidence review; recommendation levels reflect the consensus opinion of the expert panel; and supportive actions represent expert consensus suggestions from the expert panel provided to support implementation of the recommendations (they are not graded).

[a] "Family" includes parent, grandparent, aunt, uncle, or sibling with heart attack, treated angina, coronary artery bypass graft/stent/angioplasty, stroke, or sudden cardiac death at <55 y in males and <65 y in females.

Graded, age-specific recommendations for pediatric care providers to use in optimizing cardiovascular health in their patients are summarized in Table 5-1. The Cardiovascular Health Integrated Lifestyle Diet (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 might ultimately require more intensive dietary change. CHILD-1 is also the recommended diet for children with a positive family history of early cardiovascular disease, dyslipidemia, obesity, primary hypertension, DM, or exposure to smoking in the home. Any dietary modification must provide nutrients and calories needed for optimal growth and development (Table 5-2). 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 diet has been modified for use in children aged 4 years and older on the basis of daily energy needs according to food group and is shown in Table 5-3 as an example of a heart-healthy eating plan using CHILD-1 recommendations.

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 cardiovascular 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 cardiovascular 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 linked increased time spent in sedentary activities with reduced overall activity levels, disadvantageous lipid profiles, higher systolic BP, higher levels of obesity, and higher levels of all the obesity-related cardiovascular risk factors including hypertension, insulin resistance, and type 2 DM.

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 BP, decreased measures of body fat, decreased BMI, improved fitness measures, lower TC level, lower LDL cholesterol level, lower triglyceride level, higher HDL cholesterol level, 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).

TABLE 5-1 Evidence-Based Recommendations for Diet and Nutrition: CHILD-1

Birth to 6 mo	Infants should be exclusively breastfed (no supplemental formula or other foods) until the age of 6 mo[a]	Grade B Strongly recommend
6 to 12 mo	Continue breastfeeding until at least 12 mo of age while gradually adding solids; transition to iron-fortified formula until 12 mo if reducing breastfeeding[a]	Grade B Strongly recommend
	Fat intake in infants <12 mo 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
12 to 24 mo	Transition to reduced-fat[b] (2% to fat-free) unflavored cow's milk[c] (see supportive actions)	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[d]	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 12–24 mo of age should be decided together by parents and health care providers on the basis of 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, and low-fat/fat-free milk and milk products and lower in sugar (Table 5-3)	
2 to 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 fats 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[e]	Grade B recommend
	Supportive actions: Teach portions based on EER for age/gender/age (Table 5-2) Encourage moderately increased energy intake during periods of rapid growth and/or regular moderate-to-vigorous physical activity Encourage dietary fiber from foods: age + 5 g/d[e] Limit naturally sweetened juice (no added sugar) to 4 oz/d Limit sodium intake Support DASH-style eating plan (Table 5-3)	
11 to 21 y	Primary beverage: fat-free unflavored milk	Grade A Strongly recommend
	Limit/avoid sugar-sweetened beverages; encourage water	Grade B Recommend

TABLE 5-1 Continued

Fat content:	
Total fat 25%–30% of daily kcal/EER[d]	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[e]	Grade B Recommend
Supportive actions:	
Teach portions based on EER for age/gender/activity (Table 5-2)	
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/1000 kcal[e]	
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 (Table 5-3)	

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. EER indicates estimated energy requirement.

[a] Infants who 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.

[b] For toddlers 12 to 24 mo of age with a family history of obesity, heart disease, or high cholesterol, parents should discuss transition to reduced-fat milk with pediatric care provider after 12 months of age.

[c] Continued breastfeeding is still appropriate and nutritionally superior to cow's milk. Reduced-fat milk should be used only in the context of an overall diet that supplies 30% of calories from fat.

[d] Estimated energy requirements per day for age/gender (Table 5-2).

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

TABLE 5-2 Estimated Calorie Needs per Day by Age, Gender, and Physical Activity Level[a]

Gender	Age (Years)	Calorie Requirements (kcals) by Activity Level[b]		
		Sedentary	Moderately Active	Active
Child	2–3	1000–1200	1000–1400[c]	1000–1400[c]
Female[d]	4–8	1200–1400	1400–1600	1400–1800
	9–13	1400–1600	1600–2000	1800–2200
	14–18	1800	2000	2400
	19–30	1800–2000	2000–2200	2400
Male	4–8	1200–1400	1400–1600	1600–2000
	9–13	1600–2000	1800–2200	2000–2600
	14–18	2000–2400	2400–2800	2800–3200
	19–30	2400–2600	2600–2800	3000

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.

[a] Based on Estimated Energy Requirements (EER) equations, using reference heights (average) and reference weights (health) 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.

[b] 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 ~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 >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.

[c] 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.

[d] Estimates for females do not include women who are pregnant or breastfeeding.

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- 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 healthy 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 cardiovascular health. Reported activity interventions ranged from 20 to 60 minutes, 2 to 5 times per week in children aged 3 to 17 years and included a wide variety of dynamic and isometric exercises. Extrapolating from these interventions, which 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

TABLE 5-3 DASH Eating Plan: Servings per Day According to Food Group and Total Energy Intake

Food Group	No. of Servings						Serving Size	Examples and Notes	Significance of Each Food Group to the DASH Eating Plan
	1200 cal	1400 cal	1600 cal	1800 cal	2000 cal	2600 cal			
Grains[a]	4–5/d	5–6/d	6/d	6/d	6–8/d	10–11/d	1 slice bread; 1 oz dry cereal[b]; ½ cup cooked rice, pasta, or cereal[b]	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/d	3–4/d	3–4/d	4–5/d	4–5/d	5–6/d	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/d	4/d	4/d	4–5/d	4–5/d	5–6/d	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/d	2–3/d	2–3/d	2–3/d	2–3/d	3/d	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
Lean meats, poultry, and fish	≤3/d	≤3–4/d	≤3–4/d	≤6/d	≤6/d	≤6/d	1 oz cooked meats, poultry, or fish; 1 egg[c]	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/wk	3/wk	3–4/wk	4/wk	4–5/wk	1/d	⅓ 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[d]	1/d	1/d	2/d	2–3/d	2–3/d	3/d	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% of calories as fat, including fat in or added to foods
Sweets and added sugars	≤3/wk	≤3/wk	≤3/wk	≤5/wk	≤5/wk	≤2/d	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

Table 5-2 provides estimated energy requirements according to age, gender, and activity level for use with this table. The FDA and the Environmental Protection Agency advise 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[hyphen]888-SAFEFOOD or visit www.cfsan.fda.gov/~dms/admehg3.html.

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

[b] Serving sizes vary between a ½ and 1¼ cups, depending on cereal type. Check the product's nutrition-facts label.

[c] Because eggs are high in cholesterol, limit egg yolk intake to no more than 4 per week; 2 egg whites have the same protein content as 1 oz of meat.

[d] Fat content changes serving amount for fats and oils. For example, 1 tbsp of regular salad dressing = 1 serving; 1 tbsp of low-fat dressing = ½ serving; 1 tbsp fat-free dressing = 0 servings.

older than 5 years (Table 6-1). In agreement with the "Physical Activity Guidelines Advisory Committee Report, 2008"[11] from the 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 with jogging or playing baseball and that vigorous physical activity could be compared with running, playing singles tennis, or playing soccer. Similarly, reducing sedentary time is convincingly associated with a favorable cardiovascular profile, and the expert panel agreed with the AAP recommendation for limiting leisure screen time to <2 hours/day.

7. TOBACCO EXPOSURE

Tobacco dependence is responsible for ~4 million deaths worldwide annually, 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. On the basis of 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; symptoms of tobacco dependence have been found after brief intermittent use. Cigarette use among high school students declined from 1997 to 2003. Rates were stable from 2003 to 2007 with >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 US Public Health Service published in May 2008[12] systematically reviewed almost 9000 publications and concluded that smoking prevention and cessation interventions are effective in adults. These same methods should be safely applicable in childhood and adolescence, because behavioral interventions to alter smoking behaviors have little if any morbidity and because 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, because 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 CVD, 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. That evidence grades in the recommendations are less than grade A reflects the lack of existing evidence on interventions that impact 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 had 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 by using the medical history (Table 7-1). 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, and arrange), providers can assess readiness to quit and assist in providing resources to support smoking-cessation efforts. Information about telephone quit lines (eg, 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 had mixed results. Nonetheless, the expert panel believes that pediatric care providers

TABLE 6-1 Evidence-Based Activity Recommendations for Cardiovascular Health

Newborn to 12 mo	Parents should create an environment that promotes and models physical activity and limits sedentary time	Grade D Recommend
	Supportive actions:	
	Discourage TV viewing altogether	
1 to 4 y	Allow unlimited active playtime in safe, supportive environments	Grade D Recommend
	Limit sedentary time, especially TV/video	Grade D Recommend
	Supportive actions:	
	Limit total media time to no more than 1-2 hours of quality programming per day	
	For children ≤2 y old, discourage TV viewing altogether	
	No TV in child's bedroom	
	Encourage family activity at least once per week	
	Counsel routine activity for parents as role models for children	
5 to 10 y	Moderate-to-vigorous physical activity every day[a]	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[a] with vigorous-intensity physical activity 3 d/wk[b]	
	Limit total media time to no more than 1–2 h/d of quality programming	
	No TV in child's bedroom	
	Take activity and screen-time history from child once per year	
	Match physical activity recommendations with energy intake	
	Recommend appropriate safety equipment relative to each sport	
	Support recommendations for daily physical education in schools	
11 to 17 y	Moderate-to-vigorous physical activity every day[a]	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[a] with vigorous intense physical activity[b] 3 d/wk	
	Encourage no TV in bedroom	
	Limit total media time to no more than 1–2 h/d of quality programming	
	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 per week and/or family support of adolescent's physical activity program	
	Endorse appropriate safety equipment relative to each sport	
18 to 21 y	Moderate-to-vigorous physical activity every day[a]	Grade A Strongly recommend
	Limit leisure time TV/video/computer	Grade B Strongly recommend
	Supportive actions:	
	Support goal of 1 h/d of moderate-to-vigorous activity with vigorous intense physical activity 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	

Grades reflect the findings of the evidence review; recommendation levels reflect the consensus opinion of the expert panel; and supportive actions represent expert consensus suggestions from the expert panel provided to support implementation of the recommendations (they are not graded).

[a] Examples of moderate-to-vigorous physical activities are jogging and playing baseball.

[b] Examples of vigorous physical activities are running, playing singles tennis, and playing soccer.

should identify parents and other caregivers who smoke and explicitly recommend that children not be exposed to tobacco smoke in the home, in automobiles, or 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 and referral to smoking-cessation care providers.

8. HIGH BP

In 2004, an NHLBI task force published "The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents."[13] This report included a complete review of the current evidence on this subject and detailed recommendations for managing BP throughout childhood. These recommendations were used as the basis for these guidelines, considered complete until 2003 when the review for the report ended. Therefore, this evidence review for BP for these guidelines was 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 as having met all the criteria for inclusion. Repeating the review performed by the task force was not felt to be necessary, given the short time since publication of that report, or a judicious use of the resources available for development of these guidelines. Recommendations regarding BP are all graded as expert opinion (grade D), because they are based on the expert consensus conclusions of this NHLBI task force.

Conclusions of the Evidence-Review Update for High BP (2003–2008)

- The evidence review for the defined time period resulted in no major changes in the approach to BP evaluation and management.
- According to epidemiologic surveys of children and adolescents over

TABLE 7-1 Evidence-Based Recommendations to Prevent Tobacco Exposure

Prenatal	Obtain 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	
0 to 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 to 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 to 21 y	Obtain personal smoking history at every nonurgent 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 5 A questions to assess readiness to quit Establish your health care practice as a resource for smoking cessation Provide quit-line phone number Identify community cessation resources Provide information about pharmacotherapy for cessation Advocate for school and community-based smoke-free interventions	

Grades reflect the findings of the evidence review; recommendation levels reflect the consensus opinion of the expert panel; and supportive actions represent expert consensus suggestions from the expert panel provided to support implementation of the recommendations (they are not graded).

the past 20 years, BP levels have been increasing, and the prevalence of hypertension and prehypertension are also increasing, explained partially by the rise in obesity rates.

- Prehypertension progresses to hypertension at a rate of ~7% 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 BP 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 BP. The CHILD-1 combined with the DASH eating plan described in "Diet and Nutrition" is an appropriate diet for children that meets the DASH study and 2010 DGA nutrient goals.
- Lower dietary sodium intake is associated with lower BP 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 BP in children from ages 6 to 17 years but are predominantly effective in adolescents. For black children, greater doses of fosinopril might be needed for effective BP control. Medications are shown in Table 8-5.
- In 1 study of small-for-gestational-age infants, a nutrient-enriched diet that promoted rapid weight gain was associated with higher BP on follow-up in late childhood. This potential risk should be considered when such diets are selected in the clinical setting.
- In another study, transcendental meditation effectively lowered BP in nonhypertensive adolescents.

Recommendations

In "The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents,"[13] an NHLBI task force provided an algorithm and flow diagram to assist clinicians in identifying hypertension in children. For these guidelines, the task force's 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 Figs 8-1 and 8-2). Conditions under which children

TABLE 8-1 Age-Specific Recommendations for BP Measurement and Diagnosis of Hypertension

Birth to 3 y	No routine BP measurement Measure BP if history (+) for neonatal complications, congenital heart disease, urinary/renal abnormality, solid-organ transplant, malignancy, drug prescription, or condition known to raise BP or increase intracranial pressure (Table 8-2) If BP ≥90th percentile by oscillometry, confirm by auscultation → If BP confirmed ≥90th percentile, initiate evaluation for etiology and treatment per algorithm (Figure 8-2)
3 to 11 y	Annual BP measurement in all, interpreted for age/gender/height per Tables 8-3 and 8-4 If BP <90th percentile, repeat in 1 y If BP ≥90th percentile: Repeat BP × 2 by auscultation Average replicate measurements and reevaluate BP category (Fig 8-1) If BP confirmed >90th percentile, <95th percentile = **prehypertension (HTN):** Recommend weight management if indicated Repeat BP in 6 mo If BP ≥95th percentile, <99th percentile + 5 mm Hg: Repeat BP in 1–2 wk, average all BP measurements and reevaluate BP category (Fig 8-1) If BP confirmed >95th percentile, <99th percentile + 5 mm Hg = **stage 1 HTN:** Basic work-up per Fig 8-2 If BP ≥99th percentile + 5 mm Hg Repeat BP by auscultation × 3 at that visit, average all BP measurements and reevaluate BP category If BP confirmed >99th percentile + 5 mm Hg = **stage 2 HTN:** **Refer to pediatric HTN expert within 1 wk OR** **Begin BP treatment and initiate basic work-up, per Fig 8-2**
12 to 17 y	Annual BP measurement in all, interpreted for age/gender/height per Tables 8-3 and 8-4 If BP <90th percentile, counsel on CHILD-1 diet, activity recommendations, and repeat BP in 1 y If BP ≥90th percentile or ≥120/80 mm Hg: Repeat BP × 2 by auscultation Average replicate measurements and reevaluate BP category (Fig 8-1) If BP confirmed >90th percentile, < 95th percentile or >120/80 = **pre-HTN:** CHILD-1 diet, activity recommendations, weight management if indicated Repeat BP in 6 mo If BP ≥95th percentile, <99th percentile + 5 mm Hg Repeat BP in 1–2 wk, average all BP measurements and reevaluate BP category (Fig 8-1) If BP confirmed ≥95th percentile, <99th percentile + 5 mm Hg = **stage 1 HTN:** Basic workup per Fig 2 If BP ≥99th percentile + 5 mm Hg: Repeat BP by auscultation × 3 at that visit, average all BP measurements and reevaluate BP category If BP confirmed >99th percentile + 5 mm Hg = **stage 2 HTN:** **Refer to pediatric HTN expert within 1 wk OR** **Begin BP treatment and initiate work-up per Fig 8-2**
18 to 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

BP recommendations are based on the NHLBI's "The Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents" with the evidence review updated from 2003. Recommendations are all graded as expert opinion (grade D) because they are based on the expert consensus conclusions of the Fourth Report.

younger than 3 years should have BP measured are shown in Table 8-2. The BP norms for age, gender, and height are shown in Tables 8-3 and 8-4 and were taken directly from the NHLBI task force's report. Age-specific percentiles of BP measurements from birth to 12 months are provided in the "Report of the Fourth Task Force on Blood Pressure Control in Children." For all age groups the assessment of left ventricular mass by echocardiography is recommended as the best method of assessing hypertensive target organ disease; this testing should be performed for patients with stage 2 hypertension and those with persistent stage 1 hypertension. Elevated left ventricular mass might be useful in establishing the need for pharmacologic treatment of hypertension. In Table 8-5, the medications used to achieve BP control in children and adolescents are listed. At present, there are no data to support the use of specific antihypertensive agents for specific age groups.

9. LIPIDS AND LIPOPROTEINS

Since the last NHLBI guidelines for lipid management in children and adolescents were published in 1992,[1] both the knowledge base surrounding dyslipidemia in childhood and the clinical picture have changed. A series of critical observational studies have found 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 an elevated LDL cholesterol level. Since then, the predominant dyslipidemic pattern in childhood is a combined pattern associated with obesity, moderate-to-severe elevation in triglyceride level, normal-to-mild elevation in LDL cholesterol level, and a reduced HDL cholesterol level. 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 lipid and lipoprotein levels.

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

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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.

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 familial hypercholesterolemia with markedly elevated LDL cholesterol levels 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. Lipid and lipoprotein results in childhood are 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 cholesterol levels decrease as much as 10% to 20% or more during puberty (grade B). On the basis of this normal pattern of change in lipid and lipoprotein levels with growth and maturation, 10 years of age (range: 9–11 years) is a stable time for lipid assessment in children (grade D). For most children, this age range will precede the onset of puberty.
- Significant evidence exists to indicate that using family history of premature CVD or cholesterol disorders as the primary factor in determining lipid screening for children misses ~30% to 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 cholesterol level has 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 cholesterol level seems to be more predictive of persistent dyslipidemia and, therefore, atherosclerosis and future events than TC, LDL cholesterol, or HDL cholesterol levels alone. A major advantage of non-HDL cholesterol is that it can be accurately calculated in a nonfasting state and is therefore practical to obtain in clinical practice. The expert panel felt that non-HDL cholesterol 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 have found that measurement of apolipoprotein B and apolipoprotein A-1 for universal screening provides no additional advantage over measuring non-HDL cholesterol, LDL cholesterol, and HDL cholesterol levels, (2) measurement of lipoprotein(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 apolipoprotein B, apolipoprotein A-1, and lipoprotein(a) have been noted, and (4) measurement of lipoprotein subclasses and their sizes by advanced lipoprotein testing has not been found 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 cholesterol levels, moderate-to-severe elevation in triglyceride level, and a low HDL cholesterol level. This is the most common dyslipidemic pattern seen in childhood, and lipid assessment in overweight

TABLE 8-3 BP Norms for Boys by Age and Height Percentile

Age, y	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
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

The 90th percentile is 1.28 SD, the 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.
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and obese children identifies an important proportion of those with significant lipid abnormalities (grade B).

- Dyslipidemias can be acquired genetically but also secondary to specific conditions such as DM, 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 have been designated accordingly as special risk diagnoses for accelerated atherosclerosis (Table 9-7); management of these conditions is described in "DM and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis." Lipid evaluation for these patients contributes to risk assessment and identifies an important proportion of those with dyslipidemia (grade B).
- The complete phenotypic expression of some inherited disorders such as familial combined hyperlipidemia may be delayed until adulthood. Therefore, evaluation of children and adolescents from high-risk families with familial combined hyperlipidemia (Table 9-4) should 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 Figs 9-1 and 9-2. Definitions of the risk factors and spe-

TABLE 8-4 BP Norms for Girls by Age and Height Percentile

Age, y	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
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

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

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

- A diet with total fat at 25% to 30% of calories, saturated fat at <10% of calories, and cholesterol intake at <300 mg/day, as recommended by the original NCEP Pediatric Panel,[1] has been shown to safely and effectively reduce the levels of TC and LDL cholesterol in healthy children (grade A). There is some evidence that this is also the case when the diet begins in infancy and is sustained throughout childhood and into adolescence (grade B). The CHILD-1, described in "Nutrition and Diet," has this composition.
- In children with identified hypercholesterolemia and an elevated LDL cholesterol level, a more stringent diet with saturated fat at ≤7% of calories and dietary cholesterol limited to 200 mg/day has been shown to be safe and modestly effective in lowering the LDL cholesterol level (grade A) (CHILD-2–LDL; Table 9-8).
- The use of dietary adjuncts such as plant sterol or stanol esters up to 20 g/day can safely enhance LDL cholesterol–lowering effects short-term in children with familial hypercholesterolemia (grade A). However, long-term studies on the safety and effectiveness of plant sterol and stanol esters have not been completed. Their use, therefore, is usually reserved for children with primary elevations of their LDL cholesterol level who do not achieve LDL cholesterol goals with dietary treatment alone. Such an approach

TABLE 8-5 Antihypertensive Medications With Pediatric Experience

Class	Drug	Initial Dose[a]	Maximal Dose	Dosing Interval	Evidence[b]	FDA[c]	Comments[d]
ACE inhibitors	Benazepril	0.2 mg/kg per d up to 10 mg/d	0.6 mg/kg per d up to 40 mg/d	QD	RCT	Yes	1. All ACE inhibitors are contraindicated in pregnancy; women of childbearing age should use reliable contraception
	Captopril	0.3–0.5 mg/kg per dose (>12 mo)	6 mg/kg per d	TID	RCT, CS	No	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
	Fosinopril[e]	Children >50 kg: 5–10 mg/d	40 mg/d	QD	RCT	Yes	4. Benazepril, enalapril, and lisinopril labels contain information on the preparation of a suspension; captopril may also be compounded into a suspension
	Lisinopril[e]	0.07 mg/kg per d up to 5 mg/d	0.6 mg/kg per d up to 40 mg/d	QD	RCT	Yes	5. FDA approval for ACE inhibitors with pediatric labeling is limited to children ≥6 y of age and to children with creatinine clearance rate of ≥30 mL/min per 1.73 m^2
	Quinapril	5–10 mg/d	80 mg/d	QD	RCT, EO	No	6. Initial dose of fosinopril of 0.1 mg/kg per d may be effective, although black patients might require a higher dose
ARBs	Irbesartan	6–12 y: 75–150 mg/d; ≥13 y: 150–300 mg/d	300 mg/d	QD	CS	Yes	1. All ARBs are contraindicated in pregnancy; women of childbearing age should use reliable contraception
	Losartan[e]	0.7 mg/kg per d up to 50 mg/d	1.4 mg/kg per d up to 100 mg/d	QD–BID	RCT	Yes	2. Check serum potassium and creatinine levels periodically to monitor for hyperkalemia and azotemia
	Valsartan[e]	5–10 mg/d; 0.4 mg/kg per d	40–80 mg/d; 3.4 mg/kg per d	QD	RCT	No	3. Losartan label contains information on the preparation of a suspension
							4. FDA approval for ARBs is limited to children ≥6 y of age and to children with creatinine clearance rate of ≥30 mL/min per 1.73 m^2
α- and β-antagonist	Labetalol	1–3 mg/kg per d	10–12 mg/kg per d up to 1200 mg/d	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 diabetic patients
β-antagonists	Atenolol	0.5–1 mg/kg per d	2 mg/kg per d up to 100 mg/d	QD–BID	CS	No	1. Noncardioselective agents (propranolol) are contraindicated in asthma and heart failure
	Bisoprolol/ hydrochlorothiazide	2.5–6.25 mg/d	10/6.25 mg/d	QD	RCT	No	2. Heart rate is dose-limiting
	Metoprolol[e]	Children >6 y: 1 mg/kg per d (12.5–50 mg/d)	2 mg/kg per d up to 200 mg/d	BID	CS	Yes[f]	3. May impair athletic performance in athletes
	Propranolol	1–2 mg/kg per d	4 mg/kg per d up to 640 mg/d	BID–TID	RCT, EO	Yes	4. Should not be used in insulin-dependent diabetic patients 5. A sustained-release, once-daily formulation of propranolol is available
Calcium-channel blockers	Amlodipine[e]	Children 6–17 y: 2.5 mg/d	5 mg/d	QD	RCT	Yes	1. Amlodipine and isradipine can be compounded into stable extemporaneous suspensions
	Felodipine	2.5 mg/d	10 mg/d	QD	RCT, EO	No	2. Felodipine and extended-release nifedipine tablets must be swallowed whole

TABLE 8-5 Continued

Class	Drug	Initial Dose[a]	Maximal Dose	Dosing Interval	Evidence[b]	FDA[c]	Comments[d]
	Isradipine	0.15–0.2 mg/kg per d	0.8 mg/kg per d up to 20 mg/d	TID–QID	CS, EO	No	3. Isradipine is available in both immediate- and sustained-release formulations; sustained release form is dosed QD or BID
	Extended-release nifedipine	0.25–0.5 mg/kg per d	3 mg/kg per d up to 120 mg/d	QD–BID	CS, EO	No	4. May cause tachycardia 5. Doses up to 10 mg of amlodipine have been evaluated in children 6. Contraindicated for children <1 y of age
Central α-agonist	Clonidine	Children ≥12 y: 0.2 mg/d	2.4 mg/d	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
Diuretics	Hydrochlorothiazide	1 mg/kg per d	3 mg/kg per d up to 50 mg/d	QD	EO	Yes	1. All patients treated with diuretics should have their electrolytes monitored shortly after initiating therapy and periodically thereafter
	Chlorthalidone	0.3 mg/kg per d	2 mg/kg per d up to 50 mg/d	QD	EO	No	2. Useful as add-on therapy in patients being treated with drugs from other drug classes
	Furosemide	0.5–2.0 mg/kg per dose	6 mg/kg per d	QD–BID	EO	No	3. Potassium-sparing diuretics (spironolactone, triamterene, amiloride) may cause severe hyperkalemia, especially if given with an ACE inhibitor or ARB
	Spironolactone	1 mg/kg per d	3.3 mg/kg per d up to 100 mg/d	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
	Triamterene	1–2 mg/kg per d	3–4 mg/kg per d up to 300 mg/d	BID	EO	No	5. Chlorthalidone may precipitate azotemia in patients with renal diseases and should be used with caution in those with severe renal impairment
	Amiloride	0.4–0.625 mg/kg per d	20 mg/d	QD	EO	No	
Peripheral α-antagonists	Doxazosin	1 mg/d	4 mg/d	QD	EO	No	1. May cause first-dose hypotension
	Prazosin	0.05–0.1 mg/kg per day	0.5 mg/kg per d	TID	EO	No	
	Terazosin	1 mg/d	20 mg/d	QD	EO	No	
Vasodilators	Hydralazine	0.75 mg/kg per d	7.5 mg/kg per d up to 200 mg/d	QID	EO	Yes	1. Tachycardia and fluid retention are common adverse effects
	Minoxidil	Children <12 y: 0.2 mg/kg per d; children >12 y: 5 mg/d	Children <12 y: 50 mg/d; children ≥12 y: 100 mg/d	QD–TID	CS, EO	Yes	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 that is resistant to multiple drugs

ACE indicates angiotensin-converting enzyme; QD, every day; BID, 2 times daily; TID, 3 times daily; QID, 4 times daily; CS, case series; EO, expert opinion; ARB, angiotensin-receptor blocker.

[a] The maximal recommended adult dose should not be exceeded in routine clinical practice.

[b] Level of evidence on which recommendations are based.

[c] 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.

[d] Comments apply to all members of each drug class except where otherwise stated.

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

[f] Study did not reach the primary end point (dose response for reduction in systolic BP). Some prespecified secondary end points demonstrated effectiveness.

Adapted from High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. *Pediatrics*. 2004;114(2 suppl 4th report):555–576.

TABLE 9-1 Acceptable, Borderline-High, and High Plasma Lipid, Lipoprotein, and Apolipoprotein Concentrations for Children and Adolescents

Category	Low, mg/dL[a]	Acceptable, mg/dL	Borderline-High, mg/dL	High, mg/dL[a]
TC	—	<170	170–199	≥200
LDL cholesterol	—	<110	110–129	≥130
Non-HDL cholesterol	—	<120	120–144	≥145
Apolipoprotein B	—	<90	90–109	≥110
Triglycerides				
0–9 y	—	<75	75–99	≥100
10–19 y	—	<90	90–129	≥130
HDL cholesterol	<40	>45	40–45	—
Apolipoprotein A-1	<115	>120	115–120	—

Values for plasma lipid and lipoprotein levels are from the NCEP Expert Panel on Cholesterol Levels in Children. Non-HDL cholesterol values from the Bogalusa Heart Study are equivalent to the NCEP Pediatric Panel cut points for LDL cholesterol. Values for plasma apolipoprotein B and apolipoprotein A-1 are from the National Health and Nutrition Examination Survey III. Note that values shown are in mg/dL; to convert to SI units, divide the results for TC, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol by 38.6; for triglycerides, divide by 88.6.

[a] Low cut points for HDL cholesterol and apolipoprotein A-1 represent approximately the 10th percentile. The cut points for high and borderline-high represent approximately the 95th and 75th percentiles, respectively.

TABLE 9-2 Recommended Cut Points for Lipid and Lipoprotein Levels in Young Adults

Category	Low, mg/dL	Borderline-Low, mg/dL	Acceptable, mg/dL	Borderline-High, mg/dL	High, mg/dL
TC	—	—	<190	190–224	≥225
LDL cholesterol	—	—	<120	120–159	≥160
Non-HDL cholesterol	—	—	<150	150–189	≥190
Triglycerides	—	—	<115	115–149	≥150
HDL cholesterol	<40	40–44	>45	—	—

Values provided are from the Lipid Research Clinics Prevalence Study. The cut points for TC, LDL cholesterol, and non-HDL cholesterol represent the 95th percentile for 20- to 24-year-old subjects and are not identical with the cut points used in the most recent NHLBI adult guidelines, Adult Treatment Panel III ("Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults"), which are derived from combined data on adults of all ages. The age-specific cut points given here are provided for pediatric care providers to use in managing this young adult age group. For TC, LDL cholesterol, and non-HDL cholesterol, borderline-high values are between the 75th and 94th percentiles, whereas acceptable value are at the <75th percentile. The high triglyceride cut point represents approximately the 90th percentile; borderline-high values are between the 75th and 89th percentiles, and acceptable values are at the <75th percentile. The low HDL cholesterol cut point represents approximately the 25th percentile; borderline-low values are between the 26th and 50th percentiles, and acceptable values are at the >50th percentile.

TABLE 9-3 Causes of Secondary Dyslipidemia

- Exogenous
  - Alcohol
  - Drug therapy: corticosteroids
    - Isoretinoin
    - β-blockers
    - Some oral contraceptives
    - Select chemotherapeutic agents
    - Select antiretroviral agents
- Endocrine/metabolic
  - Hypothyroidism/hypopituitarism
  - T1DM and T2DM
  - Pregnancy
  - Polycystic ovary syndrome
  - Lipodystrophy
  - Acute intermittent porphyria
- Renal
  - Chronic renal disease
  - Hemolytic uremic syndrome
  - Nephrotic syndrome
- Infectious
  - Acute viral/bacterial infection[a]
  - 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 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 syndrome

[a] Delay measurement until ≥3 weeks after infection.

might lower the LDL cholesterol level sufficiently to avoid the necessity of drug treatment. Food products that contain plant stanol esters, such as some margarines, are marketed directly to the general public. In 2 short-term trials, they have been shown to be safe and have minimal LDL-lowering effects in healthy children (grade B).

- Evidence for the use of other dietary supplements is insufficient for any recommendation (no grade).
- In children with an elevated triglyceride level, reduction of simple carbohydrate intake and weight loss are associated with decreased triglyceride levels (grade B). Reduction of simple carbohydrate intake needs to be associated with increased intake of complex carbohydrates and reduced saturated-fat intake. When triglyceride elevation is associated with obesity, decreased calorie intake and increased activity levels are of paramount importance. The CHILD-2–TG (shown 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.[1] 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 "Nutrition and Diet") is recommended as the first step; implementation should be guided by a registered dietitian. For obese children with identified dyslipidemia, additional age- and BMI-specific recommendations that

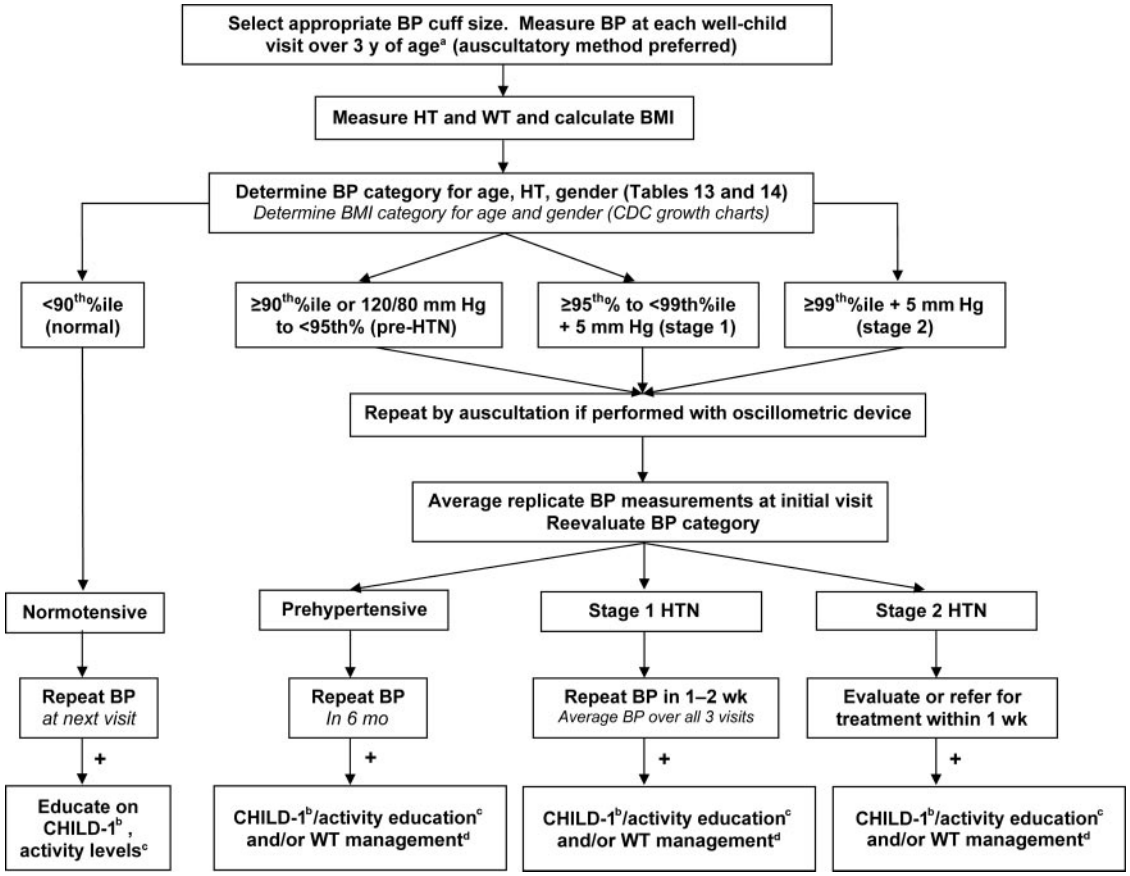


FIGURE 8-1

BP measurement and categorization. HT indicates height; WT, weight; HTN, hypertension; %ile, percentile. [a] See Table 8-2; [b] see "Nutrition and Diet"Table 5-1; [c] see "Physical Activity"; [c] see "Overweight and Obesity." Adapted from High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. *Pediatrics*. 2004;114(2 suppl 4th report):555–576.

address calorie restriction and increased activity appear in "Overweight and Obesity." If, after a 3-month trial of the CHILD-1/lifestyle management, fasting-lipid-profile (FLP) findings exceed the therapeutic goals listed in Tables 9-1 and 9-2, then the lipid parameter-specific diet changes outlined in Table 9-8 are recommended. Dyslipidemia management is also outlined in the algorithms in Figs 9-1 and 9-2.

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

When medication is recommended, it 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 that, in the following section, values given are in mg/dL; to convert to SI units, divide the results for TC, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol by 38.6; for triglycerides, divide by 88.6.

- Decisions regarding the need for medication therapy should be based on the average of results from at least 2 FLPs obtained at least 2 weeks but no more than 3 months apart (grade C) (Fig 9-1).
- The cut points used to define the level at which drug therapy should be considered from the 1992 NCEP pediatric guidelines[1] have been used as the basis for multiple drug safety and efficacy trials in dyslipidemic children (grade B):
  - LDL cholesterol ≥ 190 mg/dL after a 6-month trial of lifestyle management (CHILD-1 → CHILD-2–LDL) for children aged 10 years or older.
  - LDL cholesterol 160 to 189 mg/dL after a 6-month trial of lifestyle/diet management (CHILD-1 → CHILD-2–LDL) in a child aged 10 years or older with a positive family history of premature CVD/events in first-degree relatives (Table 9-6) or at least 1 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; Fig 9-1).
  - LDL cholesterol 130 to 190 mg/dL in a child aged 10 years or older with a negative family history of premature CVD in first-degree

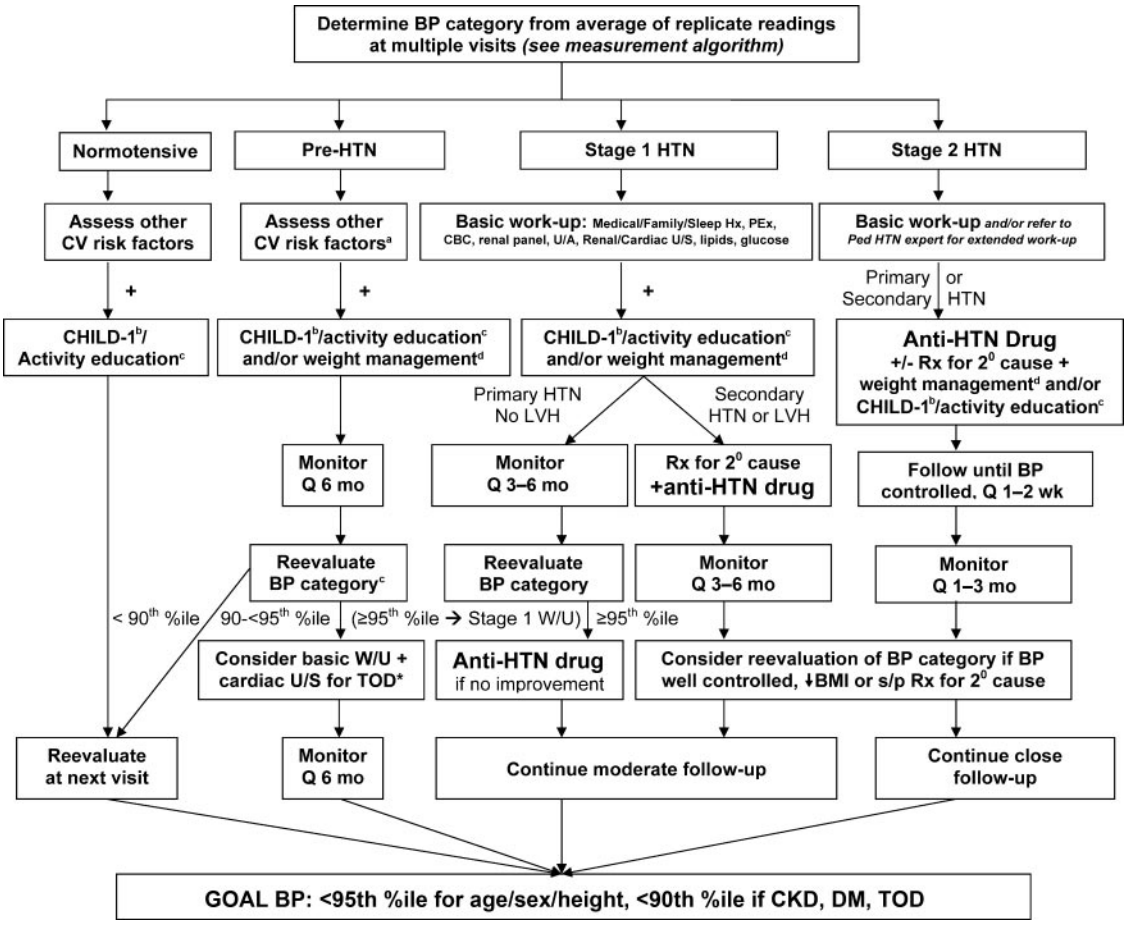


FIGURE 8-2

BP management according to category. HTN indicates hypertension; CV, cardiovascular; Hx, history; PEx, physical examination; CBC, complete blood count; U/A, urinalysis; U/S, ultrasound; Ped, pediatric; LVH, left ventricular hypertrophy; Q, every; Rx, prescription; 2°, secondary; W/U, workup; TOD, target organ damage; s/p, status post; CKD, chronic kidney disease; %ile, percentile. [a] Workup for target organ damage/left ventricular hypertrophy if obese or positive for other cardiovascular risk factors; [b] see "Nutrition and Diet"; [c] see "Physical Activity"; [d] see "Overweight and Obesity." Adapted from High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. *Pediatrics*. 2004;114(2 suppl 4th report):555–576.

relatives and no high- 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 (Fig 9-1) plus weight management if the BMI is at the ≥85th percentile.

- The goal of LDL-lowering therapy in childhood and adolescence is to decrease the LDL cholesterol level to the <95th percentile (≤130 mg/dL).

- Children with homozygous familial hypercholesterolemia and extremely elevated LDL cholesterol 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 have found 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 post–cardiac transplantation) should be considered for initiation of medication therapy (grade C) (see "DM and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis").

- Bile acid sequestrants are medications that bind bile salts within the intestinal lumen and prevent their enterohepatic reuptake in the terminal ileum, which results in a depletion of bile salts in the liver and signals for increased production. Because bile salts are synthesized from intracellular cholesterol in the liver, the intracellular pool of cholesterol becomes depleted, which signals increased production of LDL receptors and increased clearance of circulating LDL cholesterol to replenish the intracellular cholesterol

TABLE 9-4 Summary of Major Lipid Disorders in Children and Adolescents

Primary Lipid Disorders	Lipid/Lipoprotein Abnormality
Familial hypercholesterolemia	
Homozygous	↑ ↑ LDL cholesterol
Heterozygous	↑ LDL cholesterol[a]
Familial defective apolipoprotein B	↑ LDL cholesterol
Familial combined hyperlipidemia[a]	
Type IIa	↑ LDL cholesterol
Type IV	↑ VLDL cholesterol, ↑ triglycerides
Type IIb	↑ LDL cholesterol, ↑ VLDL cholesterol, ↑ triglycerides
Types IIb and IV	↓ HDL cholesterol (often)
Polygenic hypercholesterolemia	↑ LDL cholesterol
Familial hypertriglyceridemia (200–1000 mg/dL)	↑ VLDL cholesterol, ↑ triglycerides
Severe hypertriglyceridemia (≥1000 mg/dL)	↑ chylomicrons, ↑ VLDL cholesterol, ↑ ↑ triglycerides
Familial hypoalphalipoproteinemia	↓ HDL cholesterol
Dysbetalipoproteinemia (TC: 250–500 mg/dL; triglycerides: 250–600 mg/dL)	↑ IDL cholesterol, ↑ chylomicron remnants

↑ indicates increased; ↓, decreased; IDL indicates intermediate-density lipoprotein; VLDL, very low density lipoprotein.
[a] These are the 2 lipid and lipoprotein disorders seen most frequently in childhood and adolescence; familial combined hyperlipidemia most often manifests with obesity.

pool for increased production of bile salts. Studies of bile acid sequestrants in children and adolescents aged 6 to 18 years with LDL cholesterol levels from 131 to 190 mg/dL have resulted in TC reduction of 7% to 17% and reduction of LDL cholesterol of 10% to 20%, sometimes with a modest elevation in triglyceride level. Bile acid sequestrants commonly cause adverse gastrointestinal effects that can 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 inhibition results in a decrease in the intracellular pool of cholesterol, which signals upregulation of LDL receptors and increased clearance of circulating LDL cholesterol. As a group, statins have been shown to reduce LDL cholesterol in children and adolescents with marked LDL cholesterol elevation or familial hypercholesterolemia (defined as elevated LDL cholesterol in the child in conjunction with a family history of elevated LDL cholesterol and/or atherosclerosis or CAD) when used from 8 weeks to 2 years for children aged 8 to 18 years. The lower LDL cholesterol level for eligibility into the statin trials was ≥190 or ≥160 mg/dL with ≥2 additional risk factors after a trial period on diet. Trial subjects were monitored carefully throughout treatment; adverse effects 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 a 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 occurs 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, azole antifungal agents, macrolide antibiotics, antiarrhythmic agents, and protease inhibitors (grade A).
- Bile acid–binding sequestrants may be used in combination with a statin for patients who fail to meet LDL cholesterol target levels with either medication alone. One pediatric study assessed this combination and found no increase in adverse effects. The efficacy of the 2 agents together seems to be additive (grade B).
- There is limited published experience in children of 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 cholesterol therapeutic targets. Because their action is independent of and complementary to that of statins, the LDL cholesterol–lowering effect is additive. No pediatric studies of monotherapy with cholesterol absorption inhibitors had been published during the time period for this evidence review. The 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 triglyceride levels that respond well to weight loss and lifestyle changes (grade B) (Fig 9-2; Table 9-8). When triglyceride levels exceed 500 mg/

TABLE 9-5 Evidence-Based Recommendations for Lipid Assessment

Birth to 2 y	No lipid screening	Grade C Recommend
2 to 8 y	No routine lipid screening	Grade B Recommend
	Measure fasting lipid profile twice,[a] average results if:	
	Parent, grandparent, aunt/uncle, or sibling with	Grade B
	MI, angina, stroke, CABG/stent/angioplasty at <55 y in males, <65 y in females	Strongly recommend
	Parent with TC ≥ 240 mg/dL or known dyslipidemia	Grade B
	Parent with TC ≥ 240 mg/dL or known dyslipidemia	Strongly recommend
	Child has diabetes, hypertension, BMI ≥ 95th percentile or smokes cigarettes	Grade B Strongly recommend
	Child has a moderate- or high-risk medical condition (Table 5-2)	Grade B Strongly recommend
	Use Table 9-1 for interpretation of results, algorithms in Figs 9-1 and 9-2 for management.	
9 to 11 y	**Universal screening**	Grade B Strongly recommend
	Non-FLP: **Calculate non–HDL cholesterol:** **Non–HDL cholesterol = TC − HDL cholesterol** If non-HDL ≥ 145 mg/dL ± HDL < 40 mg/dL[b]: Obtain FLP twice,[a] average results OR FLP: If LDL cholesterol ≥ 130 mg/dL ± non-HDL cholesterol ≥ 145 mg/dL ± HDL cholesterol < 40 mg/dL ± triglycerides ≥ 100 mg/dL if <10 y, ≥130 mg/dL if ≥10 y: Repeat FLP, average results *Use Table 9-1 for interpretation of results, algorithms in Figs 9-1 and 9-2 for management.*	
12 to 16 y	No routine screening[c]	Grade B Recommend
	Measure FLP twice,[a] average results, if new knowledge of:	
	Parent, grandparent with MI, angina, stroke, CABG/stent/angioplasty, sudden death at <55 y in male, <65 y in female	Grade B Strongly recommend
	Parent with TC ≥ 240 mg/dL or known dyslipidemia	Grade B Strongly recommend
	Patient has diabetes, hypertension, BMI ≥ 85th percentile or smokes cigarettes	Grade B Strongly recommend
	Patient has a moderate- or high-risk medical condition (Table 5-2)	Grade B Strongly recommend
	Use Table 9-1 for interpretation of results, algorithms in Figs 9-1 and 9-2 for management.	
17 to 21 y	**Universal screening once in this time period:**	Grade B Recommend
	Non-FLP: Calculate non–HDL cholesterol: **Non–HDL cholesterol = TC − HDL cholesterol*** **17–19 y:** If non–HDL cholesterol ≥145 mg/dL ± HDL cholesterol < 40 mg/dL[b] Measure FLP twice,[a] average results OR FLP: If LDL cholesterol ≥ 130 mg/dL ± non–HDL cholesterol ≥ 145 mg/dL ± HDL cholesterol < 40 mg/dL ± triglycerides ≥ 130 mg/dL Repeat FLP, average results *Use Table 9-1 for interpretation of results, algorithms in Figs 9-1 and 9-2 for management.* **20–21 y:** Non–HDL cholesterol ≥ 190 mg/dL ± HDL cholesterol < 40 mg/dL Measure FLP twice, average results OR FLP: If LDL cholesterol ≥ 160 mg/dL ± non–HDL cholesterol ≥ 190 mg/dL ± HDL cholesterol < 40 mg/dL ± triglycerides ≥ 150 mg/dL Repeat FLP, average results *Use Table 9-2 for interpretation of results, Adult Treatment Panel (ATP III) algorithm for management.*	

Grades reflect the findings of the evidence review, recommendation levels reflect the consensus opinion of the expert panel. Note that the values given are in mg/dL. To convert to SI units, divide the results for TC, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol by 38.6; for triglycerides, divide by 88.6. MI indicates myocardial infarction; CABG, coronary artery bypass graft; ATP III, Adult Treatment Panel III.

[a] Interval between FLP measurements: after 2 weeks but within 3 months.

[b] Use Table 9-1 for interpretation of results; use lipid algorithms in Figs 9-1 and 9.2 for management of results.

[c] Disregard triglyceride and LDL cholesterol levels in nonfasting sample.

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

[e] Use Table 9-1 for interpretation of results of 7- to 19-year-olds and lipid algorithms in Figs 9-1 and 9-2 for management. Use Table 17 for interpretation of results of 20- to 21-year-olds and ATP III algorithms for management.

TABLE 9-6 Risk-Factor Definitions for Dyslipidemia Algorithms

Positive family history: myocardial infarction, angina, coronary artery bypass graft/stent/angioplasty, sudden cardiac death in parent, grandparent, aunt, or uncle at <55 y for males, <65 y for females
High-level RFs
Hypertension that requires drug therapy (BP ≥ 99th percentile + 5 mm Hg)
Current cigarette smoker
BMI at the ≥97th percentile
Presence of high-risk conditions (Table 9-7)
(DM is also a high-level RF, but it is classified here as a high-risk condition to correspond with Adult Treatment Panel III recommendations for adults that DM be considered a CVD equivalent.)
Moderate-level RFs
Hypertension that does not require drug therapy
BMI at the ≥95th percentile, <97th percentile
HDL cholesterol < 40 mg/dL
Presence of moderate-risk conditions (Table 9-7)

RF indicates risk factor.

TABLE 9-7 Special Risk Conditions

High risk
T1DM and T2DM
Chronic kidney disease/end-stage renal disease/post–renal transplant
Post–orthotopic heart transplant
Kawasaki disease with current aneurysms
Moderate risk
Kawasaki disease with regressed coronary aneurysms
Chronic inflammatory disease (systemic lupus erythematosus, juvenile rheumatoid arthritis)
HIV infection
Nephrotic syndrome

dL, patients are at risk for pancreatitis and require care in consultation with a lipid specialist (grade B). In adults, use of ω-3 fish oil has been shown to lower the triglyceride level by 30% to 40% and to raise the HDL level by 6% to 17%. Experience with fish oil in children has been limited to small case series, and 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

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

Children Younger Than 10 Years

- Children younger than 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 cholesterol level of ≥400 mg/dL; primary hypertriglyceridemia with a triglyceride level of ≥500 mg/dL; evident CVD in the first 2 decades of life; post–cardiac transplantation) (grade C).

Children Aged 10 to 21 Years

- Decisions regarding the need for medication therapy should be based on the average of results from at least 2 FLPs obtained at least 2 weeks but no more than 3 months apart (grade C) (Fig 9-1).
- Children with an average LDL cholesterol level of ≥250 mg/dL or average triglyceride level of ≥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 an LDL cholesterol level of ≥250 mg/dL or triglyceride level of >500 mg/dL) should be managed initially for 3 to 6 months with diet changes (CHILD-1 → CHILD-2–LDL or CHILD-2–TG) (Table 9-8) on the basis of specific lipid profile findings (Figs 9-1 and 9-2); if the BMI is at the ≥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, post–cardiac transplantation) should concomitantly be considered for initiation of medication therapy (grade C) (see "DM and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis").

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

- Children with an average LDL cholesterol level of ≥250 mg/dL should be referred directly to a lipid specialist (grade B).
- If the LDL cholesterol level remains ≥190 mg/dL after a 6-month trial of lifestyle/diet management (CHILD-1 → CHILD-2–LDL) for children aged 10 years and older, statin therapy should be considered (grade A) (Fig 9-1; Table 9-11 and 9-12).
- If the LDL cholesterol level remains ≥130 to <190 mg/dL in a child aged 10 years or older with a negative

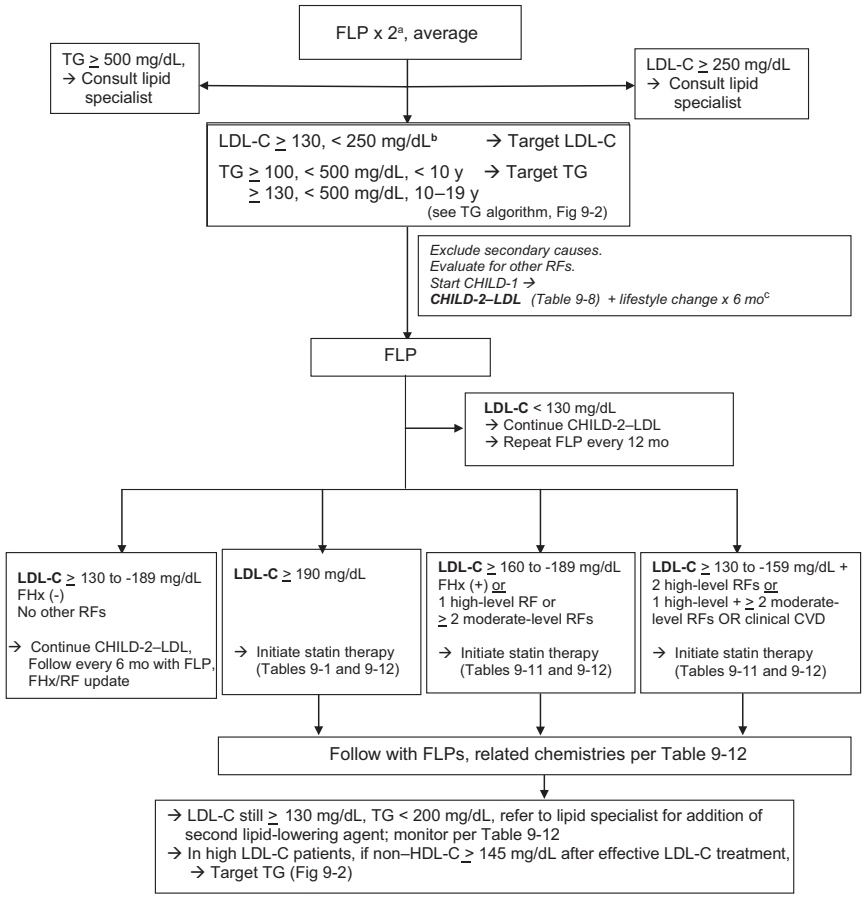


FIGURE 9-1

Dyslipidemia algorithm: target LDL cholesterol. Values given are in mg/dL. To convert to SI units, divide results for TC, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol by 38.6; for triglycerides, divide by 88.6. TG indicates triglycerides; C, cholesterol; RF, risk factor; FHx, family history; [a] Obtain FLPs at least 2 weeks but no more than 3 months apart. [b] Per Table 9-9, use of drug therapy is limited to children aged 10 years and older with defined risk profiles. [c] In a child with an LDL cholesterol level of >190 mg/dL and other risk factors, a trial of the CHILD-2–LDL may be abbreviated.

family history of premature CVD in first-degree relatives and no high- or moderate-level risk factor or risk condition (Tables 9-6 and 9-7), management should continue to be focused on diet changes (CHILD-2–LDL) on the basis of lipid profile findings (Fig 9-1) plus weight management if BMI is at the ≥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 the LDL cholesterol level remains ≥160 to 189 mg/dL after a trial of lifestyle/diet management (CHILD-1 → CHILD-2–LDL) in a child aged 10 years or older with a positive family history of premature CVD/events in first-degree relatives (Table 9-6) or at least 1 high-level risk factor or risk condition or at least 2 moderate-level risk factors or risk conditions (Tables 9-6 and 9-7), then statin therapy should be considered (grade B) (Fig 3; Table 27).
- If the LDL cholesterol level remains ≥130 to 159 mg/dL after a trial of lifestyle/diet management (CHILD-1 → CHILD-2–LDL) in a child aged 10 years or older with at least 2 high-level risk factors or risk conditions or at least 1 high-level risk factor or risk condition together with at least 2 moderate-level risk factors or risk conditions (Tables 21 and 22), then statin therapy should be considered (grade C) (Fig 9-1; Table 9-12).
- For children aged 8 or 9 years with an LDL cholesterol level 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 1 high-level risk factor or risk condition or the presence of at least 2 moderate-level risk factors or risk conditions (Fig 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 cholesterol target levels are not achieved with at least 3 months of compliant use, then the dose may be increased by 1 increment (usually 10 mg). If LDL cholesterol target levels are still not achieved with at least 3 months of compliant use, then the dose may be further increased by 1 increment. The risk and effectiveness of dose escalation have been explored in several of the clinical trials of statins in children, and no additional safety issues have been 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

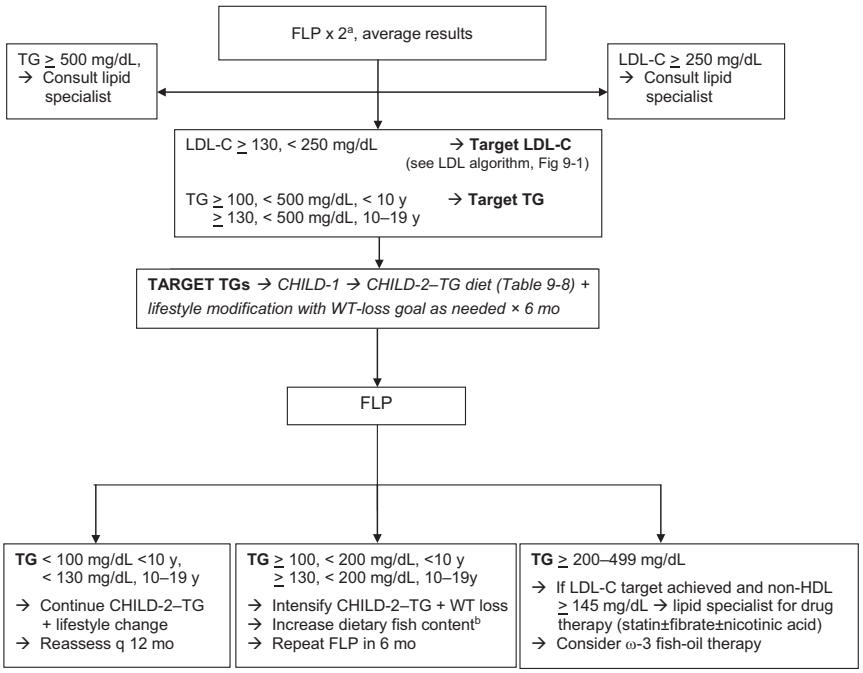


FIGURE 9-2

Dyslipidemia algorithm: target triglycerides. Values given are in mg/dL. To convert to SI units, divide results for TC, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol by 38.6; for triglycerides, divide by 88.6. C indicates cholesterol; [a] Obtain FLPs at least 2 weeks but no more than 3 months apart. [b] The FDA and the Environmental Protection Agency advise women of childbearing age who may become pregnant, pregnant women, nursing mothers, and young children to avoid some types of fish and shellfish and to 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 ~dms/admehg3.html;/Border [0 0 0]?>www.cfsan.fda.gov/~dms/admehg3.html.

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).

Children with elevated triglyceride or non-HDL cholesterol after control of LDL cholesterol are managed on the basis of lipid levels (Fig 9-2):

- Children with average fasting triglyceride levels of ≥500 mg/dL or any single measurement of ≥1000 mg/dL related to a primary hypertriglyceridemia should be treated in conjunction with a lipid specialist; the CHILD-2–TG (Table 9-8) should be started, and use of fish oil, fibrate, or niacin to prevent pancreatitis should be considered (grade D) (Fig 9-2) (Tables 9-10 and 9-11).
- Children with fasting triglyceride levels of ≥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 level of <145 mg/dL (grade D).
- Children with fasting triglyceride levels of ≥200 to 499 mg/dL, non-HDL levels of >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 aged 10 years or older with non-HDL cholesterol levels of ≥145 mg/dL after the LDL cholesterol goal has been 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) (Fig 9-1) (Tables 9-10 and 9-11).
- Children with severe or complex mixed dyslipidemias, particularly when multiple medications are being considered, should be referred for consultation with a lipid specialist (grade D) (Figs 9-1 and 9-2).

10. OVERWEIGHT AND OBESITY

The 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 the National Health and Nutrition Examination Survey[14] show sustained high prevalence; 17% of children and adolescents have a BMI at 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 cardiovascular disease, obesity is even more powerfully correlated with atherosclerosis; this association has been shown for BP, 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 subclinical vascular changes. Higher BMI during childhood is directly associated with increased coronary heart disease in adult life. Extrapolation

TABLE 9-8 Evidence-Based Recommendations for Dietary Management of Elevated LDL Cholesterol, Non-HDL Cholesterol, and Triglyceride Levels

2 to 21 y	Elevated LDL cholesterol: CHILD-2–LDL	
	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 fats as much as possible	Grade A Recommend
	Supportive actions:	
	Plant sterol esters and/or plant stanol esters[a] up to 2 g/d as replacement for usual fat sources can be used after 2 y of age in children with familial hypercholesterolemia	
	Plant stanol esters as part of a regular diet are marketed directly to the public; short-term studies have found 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 y of age and 12 g/d for those ≥12 y of age	
	As for all children, 1 h/d of moderate-to-vigorous physical activity and <2 h/d of sedentary screen time are recommended.	
	Elevated triglycerides or non-HDL cholesterol: CHILD-2–TG	
	Refer to a registered dietitian for family medical nutrition therapy[b]	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 fats as much as possible	Grade A Recommend
	Decrease sugar intake	Grade B Recommend
	Replace simple with complex carbohydrates	
	No sugar-sweetened beverages	
	Increase dietary fish to increase ω-3 fatty acids[c]	Grade D Recommend

Grades reflect the findings of the evidence review; recommendation levels reflect the consensus opinion of the expert panel; and supportive actions represent expert consensus suggestions from the expert panel provided to support implementation of the recommendations (they are not graded). Values given are in mg/dL. To convert to SI units, divide the results for TC, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol by 38.6; for triglycerides, divide by 88.6.

[a] Can be found added to some foods, such as some margarines.

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

[c] The FDA and the Environmental Protection Agency advise 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[hyphen]888-SAFEFOOD or visit ~dms/admehg3.html;/Border [0 0 0]?>www.cfsan.fda.gov/~dms/admehg3.html.

from current data suggests that adolescent obesity will likely increase adult coronary heart disease by 5% to 16% over the next 25 years with >100 000 excess cases of coronary heart disease attributable to increased obesity in childhood. The evidence review included RCTs, systematic reviews, meta-analyses, and observational studies that assessed 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 United States, BMI percentile distributions relative to gender and age on the Centers for Disease Control and Prevention (CDC) 2000 growth charts[15] 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 National Health and Nutrition Examination 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 US population in 2000. These BMI percentile growth charts provide the best reference data available for describing normal growth in US 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 (US Department of Health and Human Services)[16] 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 those 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, because parents recognize a child's overweight status in fewer than half of the cases. The AMA/CDC/MCHB expert committee[16] defined a BMI at the ≥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 cardiovascular risk factors

TABLE 9-9 Evidence-Based Recommendations for Pharmacologic Treatment of Dyslipidemia

Birth to 10 y	Pharmacologic treatment is limited to children with severe primary hyperlipidemia (homozygous familial hypercholesterolemia, primary hypertriglyceridemia [triglycerides ≥ 500 mg/dL]), 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
≥10 to 21 y	Detailed family history and RF assessment required before initiation of drug therapy[a] (high- to moderate-level RFs and RCs are listed in Tables 9-6 and 9-7)	Grade C Strongly recommend
	LDL cholesterol	
	If average LDL cholesterol ≥ 250 mg/dL[a], consult lipid specialist	Grade B Strongly recommend
	If average LDL cholesterol ≥ 130–250 mg/dL, or non-HDL ≥ 145 mg/dL:	
	Refer to dietitian for medical nutrition therapy with CHILD-1 → CHILD-2–LDL (Table 9-8) for 6 mo; repeat FLP	Grade A Strongly recommend
	Repeat FLP	
	LDL cholesterol < 130 mg/dL, continue CHILD-2–LDL, reevaluate in 12 mo	Grade A Strongly recommend
	LDL cholesterol ≥ 190 mg/dL,[b] consider initiation of statin therapy per Tables 9-11 and 9-12	Grade A Strongly recommend
	LDL cholesterol ≥ 130–189 mg/dL, negative family history, no other RF or RC, continue CHILD-2–LDL, reevaluate every 6 mo	Grade B Recommend
	LDL cholesterol = 160–189 mg/dL + positive family history 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 cholesterol ≥ 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
≥10 to 21 y	Detailed family history and RF/RC assessment required before initiation of drug therapy[a] (high- and moderate-level RFs/RCs in Tables 9-6 and 9-7[c])	Grade C Strongly recommend
	Triglycerides	
	If average triglycerides ≥ 500 mg/dL, consult lipid specialist	Grade B Recommend
	If average triglycerides ≥ 100 mg/dL in a child aged <10 y, ≥130 mg/dL in a child aged 10–19 y, or <500 mg/dL:	
	Refer to dietitian for medical nutrition therapy with CHILD-1 → CHILD-2–TG (Table 9-8) for 6 mo	Grade B Strongly recommend
	Repeat FLP	
	Triglycerides < 100 (130) mg/dL, continue CHILD-2–TG, monitor every 6–12 mo	Grade B Strongly recommend
	Triglycerides > 100 (130) mg/dL, reconsult dietitian for intensified CHILD-2–TG diet counseling	Grade C Recommend
	Triglycerides ≥ 200–499 mg/dL, non-HDL ≥ 145 mg/dL, consider fish oil ± consult lipid specialist	Grade D Recommend
	Non-HDL cholesterol	
	Children aged ≥10 y with non-HDL cholesterol ≥ 145 mg/dL after LDL cholesterol goal is achieved may be considered for additional treatment with statins, fibrates, or niacin in conjunction with a lipid specialist consultation	Grade D Optional

Grades reflect the findings of the evidence review, and recommendation levels reflect the consensus opinion of the expert panel. When medication is recommended, it should always be in the context of the complete cardiovascular risk profile of the patient and in consultation with the patient and the family. Values given are in mg/dL. To convert to SI units, divide the results for TC, LDL cholesterol, HDL cholesterol, and non-HDL cholesterol by 38.6; for triglycerides, divide by 88.6. RF indicates risk factor; RC, risk condition.

[a] Consideration of drug therapy is based on the average of ≥2 FLPs, obtained at least 2 weeks but no more than 3 months apart.

[b] If average LDL cholesterol ≥ 190 mg/dL after CHILD-2–LDL and child is 8 to 9 years old with a positive family history or ≥1 high-level risk factor/risk condition or ≥2 moderate-level risk factors/risk conditions, statin therapy may be considered.

[c] If the child is obese, nutrition therapy should include calorie restriction and increased activity beyond that recommended for all children. See "Overweight and Obesity" for additional age-specific recommendations.

associated with body adiposity. The expert panel also concluded that the scientific evidence linking elevated BMI to cardiovascular risk factors and morbidity is strong and well supported.

The expert panel therefore recommends that children and adolescents aged 2 to 18 years with a BMI at the ≥95th percentile be described as "obese" and identified as needing assessment for cardiovascular 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 important to follow the pattern of growth over time by using these cut points to identify children who require more frequent follow-up and further assessment rather than to assign a diagnosis. Some might 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 and to provide 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 that result in lower saturated fat intake, reduced

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)	Inhibits cholesterol synthesis in hepatic cells; decreases cholesterol pool, resulting in upregulation of LDL receptors	Mainly lowers LDL cholesterol; some decrease in triglycerides and modest increase in HDL cholesterol	Atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin	Raised hepatic enzymes, raised creatine kinase, myopathy possibly progressing to rhabdomyolysis	All statins listed are approved as an adjunct to diet to lower LDL cholesterol in adolescent boys and postmenarcheal girls aged 10–18 y (≥8 y for pravastatin) with heFH and LDL cholesterol ≥190 mg/dL, or ≥160 mg/dL with family history of premature CVD and ≥2 CVD risk factors in the pediatric patient
Bile acid sequestrants	Binds intestinal bile acids, interrupting enterohepatic recirculation; more cholesterol converted into bile acids; decreases hepatic cholesterol pool; upregulates LDL receptors	Lowers LDL cholesterol; small increase in HDL cholesterol; raises triglycerides	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 cholesterol reduction in boys and postmenarcheal girls aged 10–17 y with family history after diet trial if LDL cholesterol ≥ 190 mg/dL or if LDL cholesterol ≥ 160 mg/dL with family history of premature CVD or ≥2 CVD risk factors in the pediatric patient
Cholesterol absorption inhibitors	Inhibits intestinal absorption of cholesterol and plant sterols; decreases hepatic cholesterol pool; upregulates LDL receptors	Mainly lowers LDL cholesterol; some decrease in triglycerides and small increase in HDL cholesterol	Ezetimibe	Myopathy, gastrointestinal upset, headache	Not approved
Fibric acid derivatives	Agonist for PPAR-α nuclear receptors that upregulate LPL and downregulate apolipoprotein C-III, both increasing degradation of VLDL cholesterol and triglycerides; hepatic synthesis of VLDL cholesterol may also be decreased	Mainly lowers triglycerides and raises HDL cholesterol; little effect on LDL cholesterol	Fenofibrate, gemfibrozil	Dyspepsia, constipation, myositis, anemia	Not approved
Nicotinic acid (extended release)	Inhibits release of FFA from adipose tissue; decreases VLDL and LDL cholesterol production and HDL cholesterol degradation	Lowers triglycerides and LDL cholesterol and raises HDL cholesterol; can decrease lipoprotein(a)	Niacin, extended release	Flushing, hepatic toxicity, can increase fasting blood glucose, uric acid; can cause hyperacidity	Use not recommended in children <2 y old
ω-3 fish oil	Decreases hepatic FA and triglycerides synthesis while enhancing FA degradation/oxidation, with subsequent reduced VLDL cholesterol release	Lowers triglycerides; raises HDL cholesterol; increases LDL cholesterol and LDL cholesterol particle size	ω-3 acid ethyl esters	Occasional adverse gastrointestinal effects but no adverse effect on glucose levels or muscle or liver enzymes or bleeding	Only 1 fish-oil preparation is FDA-approved for adults, but many generic fish-oil capsules are commercially available

HMG-CoA indicates hydroxymethylglutaryl coenzyme A; heFH, heterozygous hypercholesterolemia; PPAR-α, peroxisome proliferator-activated receptor; LPL, lipoprotein lipase; VLDL, very low density lipoprotein; FFA, free fatty acid; FA, fatty acid.

Adapted from McCrindle BW, Urbina EM, Dennison BA, et al; American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee; American Heart Association, Council of Cardiovascular Disease in the Young; American Heart Association, Council on Cardiovascular Nursing. *Circulation*. 2007;115(14):1948–1967.

intake of sweetened beverages, and increased fruit and vegetable consumption. In a small number of studies, these changes were 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

TABLE 9-11 Clinical Trials of Lipid-Lowering Medication Therapy in Children and Adolescents

Study Authors, Type, and Duration	Medication	No. of Subjects, Gender, Condition	Daily Dose	Effect on Lipid Profile, %			
				TC	LDL Cholesterol	HDL Cholesterol	Triglycerides
Bile acid–binding resins							
Tonstad et al, RCT, 1 y	Cholestyramine	72, male and female, FH (LDL ≥ 190 mg/dL without family history of premature CVD or LDL ≥ 160 with family history after 1-y diet; ages 6–11 y)	8 g	−12	−17	8	NA
McCrindle et al, RCT crossover, 2 × 8 wk	Cholestyramine	40, male and female, FH (1 parent with FH; LDL cholesterol ≥ 131 mg/dL; on diet; ages 10–18 y)	8 g	−7 to −11	−10 to −15	2 to 4	6 to 9
Tonstad et al, RCT, 8 wk; open label, 44–52 wk	Colestipol	66, male and female, FH (TC ≥ 239 mg/dL and triglycerides ≤ 115 mg/dL; ages 10–16 y)	2–12 g	−17	−20	−7	−13
McCrindle et al, RCT crossover, 2 × 18 wk	Colestipol	36, male and female, FH/FCHL (LDL ≥ 160 mg/dL after 6 mo of diet counseling; ages 8–18 y)	10 g	−7	−10	2	12
Stein et al , RCT, 8 wk; open label, 18 wk	Colesevelam	191, male and female, FH (LDL ≥ 190 mg/dL or LDL ≥ plus 2 additional risk factors after 6 mo of diet counseling; ages 10–17 y	1.87 g	−3	−6	5	6
			3.75 g	−7	−13	8	5
HMG-CoA reductase inhibitors (statins)							
McCrindle et al, RCT; open label, 26 wk	Atorvastatin	187, male and female, FH/severe hyperlipidemia (LDL cholesterol ≥ 190 mg/dL or LDL cholesterol ≥ 160 mg/dL with family history; triglycerides < 400 mg/dL; ages 10 – 17 y)	10–20 mg	−30	−40	6	−13
Van der Graaf et al, open label, 2 y	Fluvastatin	85, male and female, FH (LDL cholesterol ≥ 190 mg/dL or LDL cholesterol ≥ 160 mg/dL and ≥1 risk factor or LDL receptor mutation; ages 10–16 y)	80 mg	−27	−34	5	−5
Lambert et al, RCT, 8 wk	Lovastatin	69, male, FH (LDL cholesterol > 95th percentile, family history of atherosclerosis and hyperlipidemia; on diet; mean age: 13 y)	10 mg	−17	−21	9	−18
			20 mg	−19	−24	2	9
			30 mg	−21	−27	11	3
			40 mg	−29	−36	3	−9
Stein et al, RCT, 48 wk	Lovastatin	132, male, FH (LDL 189–503 mg/dL + family history of high LDL; or 220–503 mg/dL + family history of CAD death; AHA diet ≥4 mo; ages 10–17 y)	10 mg	−13	−17	4	4
			20 mg	−19	−24	4	8
			40 mg	−21	−27	5	6
Clauss et al, RCT, 24 wk	Lovastatin	54, female, FH (family history of FH; LDL 160–400 mg/dL and triglycerides < 350 mg/dL; 4-wk diet placebo run-in and 20-wk treatment; ages 10–17 y, postmenarcheal)	40 mg	−22	−27	3	−23
Knipscheer et al, RCT, 12 wk	Pravastatin	72, male and female, FH (family history hypercholesterolemia or premature atherosclerosis; LDL > 95th percentile; diet for 8 wk; ages 8–16 y)	5 mg	−18	−23	4	2
			10 mg	−17	−24	6	7
			20 mg	−25	−33	11	3
Wiegman et al, RCT, 2 y	Pravastatin	214, male and female, FH (LDL cholesterol ≥ 155 mg/dL and triglycerides ≤ 350 mg/dL; diet for 3 mo; ages 8–18 y)	20–40 mg	−19	−24	6	−17
Rodenburg et al, open-label, 2-y RCT; 4.5-y open-label follow-up	Pravastatin	186, male and female, FH (LDL cholesterol ≥ 154 mg/dL and triglycerides < 154 mg/dL; diet for 3 mo; ages 8–18 y)	20 mg (ages <14 y) or 40 mg (ages ≥ 14 y)	−23	−29	3	−2
de Jongh et al, RCT, 48 wk	Simvastatin	173, male and female, FH (LDL cholesterol = 158–397 mg/dL; ages 10–17 y)	10–40 mg	−31	−41	3	−9
de Jongh et al, RCT, 28 wk	Simvastatin	50, male and female, FH (LDL cholesterol > 95th percentile, family history of hyperlipidemia, or LDL receptor mutation; ages 9–18 y)	40 mg	−30	−40	5	−17

TABLE 9-11 Continued

Study Authors, Type, and Duration	Medication	No. of Subjects, Gender, Condition	Daily Dose	Effect on Lipid Profile, %			
				TC	LDL Cholesterol	HDL Cholesterol	Triglycerides
Avis et al, RCT, 12 wk; then, 40-wk open-label follow-up	Rosuvastatin	177, male and female, FH (LDL cholesterol ≥ 190 mg/dL or LDL cholesterol > 160 mg/dL plus positive family history of early CVD or ≥2 other risk factors for CVD)	5 mg 10 mg 20 mg	−30 −34 −39	−38 −45 −50	4 10 9	−13 −15 −16
Other agents							
Wheeler et al, RCT, 26 wk	Bezafibrate	14, male and female, FH (TC > 269 mg/dL, normal triglycerides + family history of FH or premature CAD; ages 4–15 y)	10–20 mg	−22	NC	15	−23
Colletti et al, open label, 1–19 mo	Niacin	21, male and female, FH (mean LDL = 243 ± 45 mg/dL on low-fat diet; mean triglycerides = 87 ± 39 mg/dL; ages 4–14 y)	500–2200 mg	−13	−17	4	13
McCrindle et al, RCT crossover, 2 × 18 wk	Pravastatin and colestipol	36, male and female, FH/FCHL (LDL > 160 mg/dL + family history of FH or premature CAD; triglycerides > 177 mg/dL in 10 of the 36; ages 10–18 y)	Pravastatin, 10 mg (with colestipol, 5g)	−13	−17	4	8
van der Graaf et al, RCT, 6 and 27 wk; open label to 53 wk	Simvastatin and ezetimibe	248, male and female, 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 + family history of hypercholesterolemia; ages 10–17 y)	Simvastatin 10–40 mg (with ezetimibe, 10 mg)	−38	−49	7	−17
Addendum							
Goldberg et al, ω-3 fatty acid review in adults; no RCTs in children	ω-3 fish oils (1 g per capsule)[a]	—	1–4 g/d	NC	17 to 31	6 to 17	−30 to −40

FH indicates heterozygous familial hypercholesterolemia; NA, not available; FCHL, familial combined hyperlipidemia; HMG-CoA, hydroxymethylglutaryl coenzyme A; CAD, coronary artery disease; NC, not calculated.

[a] 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 (www.heartdecision.org). The fish-oil section includes information about the content of various preparations. The Web site is updated every 6 months (www.heartdecision.org/chdrisk/v_hd/patient_edu_docs/Fish_Oil_11[hyphen]2007.pdf).

Adapted from McCrindle BW, Urbina EM, Dennison BA, et al; American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee; American Heart Association, Council of Cardiovascular Disease in the Young; American Heart Association, Council on Cardiovascular Nursing. *Circulation*. 2007;115(14):1948–1967.

separate benefits related to diet change alone. Although calorie balance is generally seen as a key issue for weight control, intervention studies that addressed both diet and physical activity had mixed results, perhaps because most of them 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; "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 healthy 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 on the basis of 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 studies, the intervention was effective. It should be noted that these successful interventions often addressed reduction in sedentary behavior rather than attempts to increase physical activity. In a majority of the studies there was no significant difference in body-size measures. Sample sizes were often small, and follow-up was often short (frequently <6 months). It is suggested that gender-specific programs might be more successful in changing activity behavior. Overall, the expert panel concluded that on the basis of

TABLE 9-12 Recommendations for Use of 3-Hydroxy-3-Methylglutaryl-Coenzyme A Reductase Inhibitors (Statins) in Children and Adolescents

Patient selection

1. Use algorithm (Fig 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 the age of 10 y (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 y).
4. Precaution/contraindication with potentially interactive medications (cyclosporine, niacin, fibric acid derivatives, erythromycin, azole antifungal agents, nefazodone, many HIV protease inhibitors); check for potential interaction with all current medications at baseline.
5. Conduct baseline hepatic panel and 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, ALT, and 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 antifungal agents, nefazodone, and HIV protease inhibitors.

Check for potential interaction whenever any new medication is initiated.

1. Whenever potential myopathy symptoms are 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 level. Consideration can be given to restarting the medication once symptoms and laboratory abnormalities have resolved.
2. After 4 wk, measure 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 cholesterol: minimal, <130 mg/dL; ideal, <110 mg/dL.
3. If target LDL cholesterol levels are achieved and there are no potential myopathy symptoms or laboratory abnormalities, continue therapy and recheck FLP, ALT, and AST in 8 wk and then in 3 mo.
4. If laboratory abnormalities are noted or symptoms are reported, temporarily withhold the medication and repeat the blood work in 2 wk. When abnormalities resolve, the medication may be restarted with close monitoring.
5. If target LDL cholesterol levels are not achieved, increase the dose by 1 increment (usually 10 mg) and repeat the blood work in 4 wk. If target LDL cholesterol levels are still not achieved, dose may be further increased by 1 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 FLP, ALT, and AST every 3–4 mo in the first year, every 6 mo 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 girls 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.

CK indicates creatine kinase; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

the evidence review, increasing activity in isolation is of little benefit in preventing obesity. By contrast, the review suggests that reducing sedentary behavior might 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 "Physical Activity." On the basis of this evidence review, no additional specific recommendations addressing physical activity in preventing obesity are indicated.

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 that 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:

- children with a BMI between the 85th and 95th percentiles;
- children in whom there is a positive family history of obesity in 1 or both parents;
- early onset of increasing weight beyond that appropriate for increase in height, which can be identified early (beginning in the first year of life);
- excessive increase in weight during adolescence, particularly in black girls; and
- children who have been very active and then become inactive or adolescents who are inactive in general (an example would be a child who previously participated in organized sports and has stopped, particularly in adolescence).

No RCTs that addressed these populations were identified. Despite this fact, 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 ("Nutrition and Diet"; "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 6 years with a BMI at the ≥95th percentile and no comorbidities (grade A). However, such programs have been effective primarily in a comprehensive weight-loss program or in research settings; only a small number have been shown to be effective in primary care settings.
- No data were identified on weight-loss programs for children younger than 6 years.
- No single negative-energy diet plan was identified from the evidence review. Dietary plans should be determined for each child on the basis of 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, including low-glycemic-load diets, low-carbohydrate diets, fiber supplements, and protein-sparing modified fasts, have not been adequately studied as to their effects on obesity in children and adolescents.
- For children aged 6 to 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 resulted in 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 insulin resistance, reduced BP, normalized dyslipidemia, and normalized subclinical measures of atherosclerosis (grade A).
  - In children aged 7 to 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 and a BMI at the >95th percentile and for adolescents with a BMI of >35 who have failed to lose weight in 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 levels and significantly reduced weight and BMI (grade B). (Metformin is currently approved by the US Food and Drug Administration [FDA] for pediatric patients aged 10 years or older with T2DM but is not approved for weight loss for either children or adults.)
- For obese adolescents older than 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 adverse gastrointestinal effects. (Orlistat [under the trade name Xenical (Roche Pharmaceuticals, Nutley, NJ)] is approved by the FDA for weight loss in pediatric patients 12 years of age 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 postmarketing cases of severe liver injury, including hepatic failure that resulted 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[8] recommends slowing weight gain while allowing normal growth and development. For those with a BMI at the >95th percentile without comorbidities, both the AMA/CDC/MCHB expert committee and the AAP[16] recommend weight maintenance resulting in decreasing BMI as age increases. With a BMI at the >95th percentile with comorbidities, the AMA/CDC/MCHB expert committee and the AAP[16] recommend gradual weight loss not to exceed 1 lb/month in children aged 2 to 11 years or 2 lb/week in adolescents (no grade).
- For adolescents with a BMI far above 35 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 insulin resistance, glucose tolerance, and cardiovascular measures in small case series (grade D).

The recommendations for management of overweight and obesity are listed in Table 10-1.

11. DM AND OTHER CONDITIONS PREDISPOSING TO THE DEVELOPMENT OF ACCELERATED ATHEROSCLEROSIS

DM is an established risk factor for early CVD. Metabolically, DM is characterized by hyperglycemia caused by defects in insulin secretion (T1DM) and insulin function and/or secretion (T2DM). Both T1DM and T2DM are associated with vascular disease. Results of 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 2 types differ significantly. T1DM presents at a younger age; 25% of patients are diagnosed between the ages of 5 and 10 years and another 40% between the ages of 10 and 15 years. If not treated adequately, the degree of hyperglycemia is severe, and patients are highly symptomatic. By contrast, with 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 DM, type 1 or 2, are at significantly increased risk for accelerated atherosclerosis and early CVD.

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).[17] The expert panel elected to use the AHA guideline as a template for developing recommendations for children with conditions such as DM that predispose them to very accelerated atherosclerosis, because the evidence review identified only a small number of studies that addressed these conditions in an RCT.

Conclusions of the Evidence Review for DM and Other Predisposing Conditions

Children with DM, T1DM or T2DM, 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[18] is recommended for screening in all children (Table 11-1).

Limited high-quality studies that addressed cardiovascular risk reduction in children with conditions predisposing them to accelerated atherosclerosis were found, so the expert panel elected to modify the recommenda-

TABLE 11-1 American Diabetes Association (ADA) Screening Recommendations for Type 2 DM in Childhood

Criteria:

- Overweight, defined by:
  - –BMI ≥ 85th percentile for age and gender, or
  - –Weight for height ≥ 85th percentile, or
  - –Weight > 120% of ideal for height

Plus any two of the following risk factors:

- Family history of type 2 DM 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)

Screening procedure:

Age of initiation:

≥10 y, or at onset of puberty, if puberty occurs at a younger age

Frequency:

Every 2 y

Test:

Fasting plasma glucose

Reproduced with permission from American Diabetes Association. *Diabetes Care.* 2000;23(3):386.

TABLE 11-2 Special Risk Pediatric Conditions: Stratification by Risk Category

High risk
Manifest coronary artery disease at ≤30 y of age: clinical evidence
T1DM or T2DM
Chronic kidney disease/end-stage renal disease/post–renal transplant
Post–orthotopic heart transplantation
Kawasaki disease with current coronary aneurysms
Moderate risk
Accelerated atherosclerosis: pathophysiologic evidence
Kawasaki disease with regressed coronary aneurysms
Chronic inflammatory disease (systemic lupus erythematosus, juvenile rheumatoid arthritis)
HIV infection
Nephrotic syndrome

Adapted from Kavey RE, Allada V, Daniels SR, et al; American Heart Association, Expert Panel on Population and Prevention Science; American Heart Association, Council on Cardiovascular Disease in the Young; American Heart Association, Council on Epidemiology and Prevention; American Heart Association, Council on Nutrition, Physical Activity and Metabolism; American Heart Association, Council on High Blood Pressure Research; American Heart Association, Council on Cardiovascular Nursing; American Heart Association, Council on the Kidney in Heart Disease; Interdisciplinary Working Group on Quality of Care and Outcomes Research. *Circulation.* 2006;114(24):2710–2738.

tions of an expert pediatric panel convened by the AHA that published its recommendations for risk-factor management in 2006; these recommendations have been endorsed by the AAP and are included in the guideline database for these guidelines.[17]

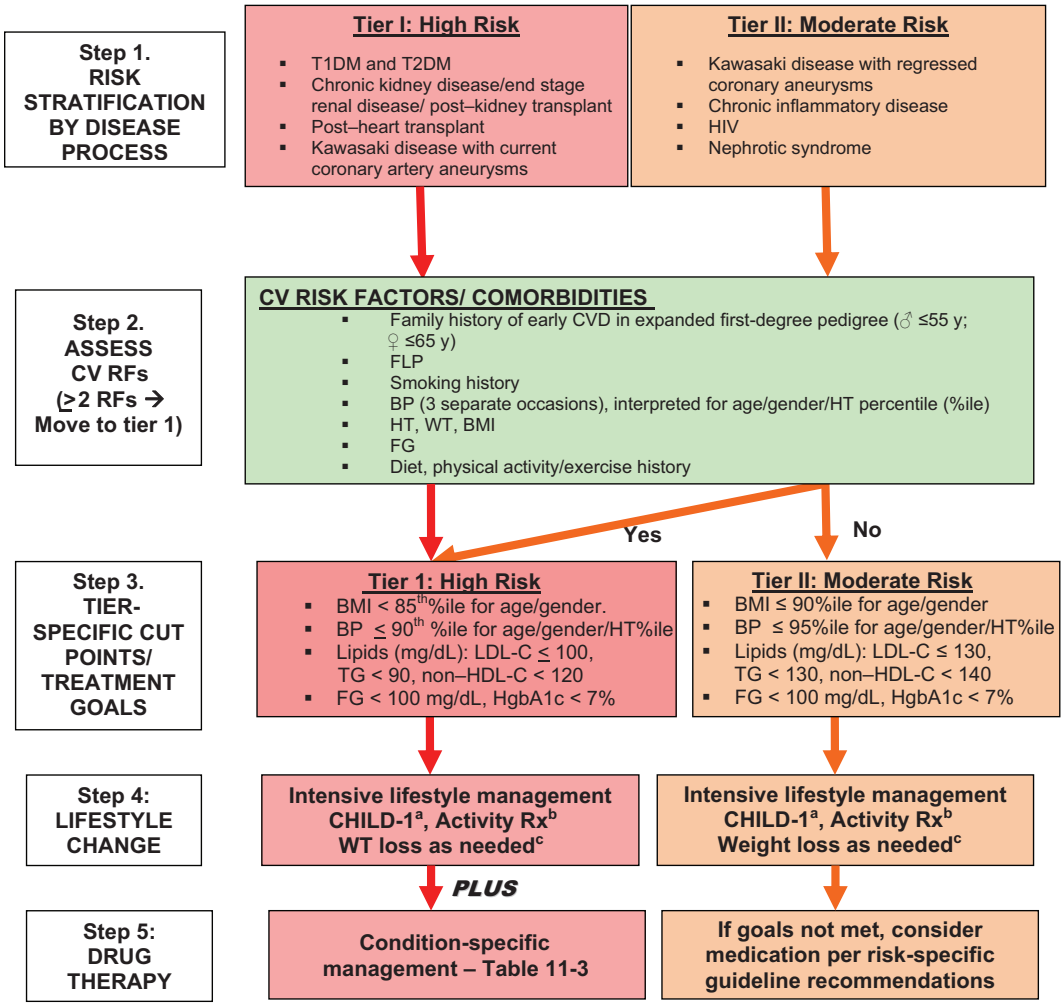
The authors of the AHA statement recommended specific risk identification and management stratified according to risk on the basis of defined other conditions that parallel the recommendations for adults with DM or other CVD equivalents. For those in the high-risk category (Table 11-2), the disease process has been associated with clinical coronary disease before 30 years of age. For those in 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 the management of children and adolescents with DM and other predisposing conditions as outlined in the algorithm in Fig 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 that it was prudent to include both T1DM and T2DM in the high-risk category. With increasing evidence of vascular dysfunction in children with HIV infection and nephrotic syndrome, these 2 conditions have been 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.

12. RISK-FACTOR CLUSTERING AND THE METABOLIC SYNDROME

Traditional cardiovascular risk factors such as obesity, hypertension, and dyslipidemia demonstrate clustering in youth. Risk behaviors such as 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 of the following risk factors: elevated waist circumference, triglyceride levels, BP, and/or fasting glucose level and reduced HDL cholesterol level. 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, systematic reviews, 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[19] 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



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/cut points 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.

FIGURE 11-1

Risk stratification and management for children with conditions predisposing to accelerated atherosclerosis and early CVD. CV indicates cardiovascular; RF, risk factor; HT, height; WT, weight; TG, triglycerides; %ile, percentile; C, cholesterol; FG, fasting glucose; Rx, recommendation. [a] See "Nutrition and Diet"; [b] see "Physical Activity"; [c] see "Overweight and Obesity." Adapted from Kavey RE, Allada V, Daniels SR, et al; American Heart Association, Expert Panel on Population and Prevention Science; American Heart Association, Council on Cardiovascular Disease in the Young; American Heart Association, Council on Epidemiology and Prevention; American Heart Association, Council on Nutrition, Physical Activity and Metabolism; American Heart Association, Council on High Blood Pressure Research; American Heart Association, Council on Cardiovascular Nursing; American Heart Association, Council on the Kidney in Heart Disease; Interdisciplinary Working Group on Quality of Care and Outcomes Research. *Circulation.* 2006;114(24):2710–2738.

is higher in older (12- to 14-year-old) compared with younger (8- to 11-year-old) children. The specific etiology of 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 in which the metabolic syndrome cluster was present in childhood identified an increased incidence of both T2DM and clinical cardiovascular events over a follow-up period of 25 years.[4] 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 cardiovascular risk-factor clustering in youth has not been thoroughly evaluated, but maintenance of low levels of cardiovascular risk factors starting in

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 BP, LDL cholesterol, glucose, and HbA1c goals indicated for each tier, as outlined in algorithm; timing individualized for each patient and diagnosis
DM regardless of type:
For T1DM, intensive glucose management per endocrinologist with frequent glucose monitoring/insulin titration to maintain optimal plasma glucose and HbA1c levels for age
For T2DM, intensive weight management and glucose control in consultation with an endocrinologist as needed to maintain optimal plasma glucose and HbA1c levels for age
Assess BMI and fasting lipid levels: step 4 lifestyle management of weight and lipid levels for 6 mo
If LDL goals are not achieved, consider statin therapy if age is ≥10 y to achieve tier 1 treatment goals for LDL cholesterol
Initial BP ≥ 90th percentile: step 4 lifestyle management plus no added salt, increased activity for 6 mo
If BP is consistently at the ≥95th percentile for age/gender/height, initiate angiotensin-converting enzyme inhibitor therapy with a BP goal of <90th percentile for gender/height or <120/80 mm Hg, whichever is lower
Chronic kidney disease/end-stage renal disease/post–renal transplant:
Optimization of renal-failure management with dialysis/transplantation per nephrology
Assess BMI, BP, and lipid and FG levels: step 4 lifestyle management for 6 mo
If LDL goals are not achieved, consider statin therapy if age is ≥10 y to achieve tier 1 treatment goals for LDL cholesterol
If BP is consistently at the ≥95th percentile for age/gender/height, initiate angiotensin-converting enzyme inhibitor therapy with a BP goal of <90th percentile for gender/height or <120/80 mm Hg, 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, and lipid and FG levels: initiate step 5 therapy, including statins, immediately for all patients aged ≥1 y to achieve tier 1 treatment goals
Kawasaki disease with current coronary aneurysms:
Antithrombotic therapy, activity restriction, ongoing myocardial perfusion evaluation per cardiologist
Assess BMI, BP, and lipid and FG levels: step 4 lifestyle management for 6 mo
If goals are not achieved, consider pharmacologic therapy for LDL cholesterol and BP if age is ≥10 y to achieve tier 1 treatment goals

FG indicates fasting glucose.

Adapted from Kavey RE, Allada V, Daniels SR, et al; American Heart Association, Expert Panel on Population and Prevention Science; American Heart Association, Council on Cardiovascular Disease in the Young; American Heart Association, Council on Epidemiology and Prevention; American Heart Association, Council on Nutrition, Physical Activity and Metabolism; American Heart Association, Council on High Blood Pressure Research; American Heart Association, Council on Cardiovascular Nursing; American Heart Association, Council on the Kidney in Heart Disease; Interdisciplinary Working Group on Quality of Care and Outcomes Research. *Circulation.* 2006;114(24):2710–2738.

childhood is associated with a lower prevalence of CVD and increased longevity in adult life.

RECOMMENDATIONS FOR MANAGEMENT OF RISK-FACTOR CLUSTERING AND THE METABOLIC SYNDROME

The metabolic-syndrome concept is important, because it identifies a common multiple cardiovascular-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 for lowering the prevalence of metabolic syndrome in adults, and this seems strongly applicable in childhood (see "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. Because of the paucity of evidence available, the recommendations are a consensus of the expert panel (grade D).

- The 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.
- The presence of obesity should prompt specific evaluation for all other cardiovascular risk factors including family history of premature CVD, hypertension, dyslipidemia, DM, and tobacco exposure.
- The coexistence of obesity with any other major cardiovascular risk factor should be recognized by clinicians as a setting in which:
  - intensive weight reduction should be undertaken per the recommendations in "Overweight and Obesity," along with management of identified risk factors including initiation of pharmacologic therapy, per the risk-factor–specific sections in these guidelines ("High BP"; "Lipids and Lipoproteins"; "DM and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis"; "Tobacco Exposure"); and
  - prompt evaluation for DM, liver-function abnormalities, left ventricular hypertrophy, and sleep apnea should be undertaken.

These recommendations are supported by the knowledge that cardiovascular morbidity has a continuous relationship across the risk-distribution spectrum and that a youth with multiple borderline risk factors might, in fact, have risk equivalent to a person with extreme abnormality of a single major risk factor. A presentation such as 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	Cut Point	Reference
Obesity, percentile		
BMI	≥85th to <95th	CDC growth charts
Waist circumference	≥90th to <95th	NHANES
BP, percentile	≥90th to <95th	"The Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents"
Dyslipidemia, mg/dL		See "Lipids and Lipoproteins" for normative values
HDL cholesterol	≥40 to ≤45	
Triglycerides		
0–9 y	≥75 to <100	
≥10 y	≥90 to <130	
Non-HDL cholesterol	≥120 to <144	
Glycemia, mg/dL		ADA screening recommendations
Fasting glucose	≥100 to <126	
Fasting insulin	Elevated fasting insulin level, above normal for gender, race, and pubertal status, is considered evidence of insulin resistance	

NHANES indicates National Health and Nutrition Examination Survey; ADA, American Diabetes Association.

TABLE 13-1 Evidence-Based Recommendations for Maternal Smoking Cessation

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 the "Tobacco Exposure" section	

Grades reflect the findings of the evidence review; recommendation levels reflect the consensus opinion of the expert panel; and supportive actions represent expert consensus suggestions from the expert panel provided to support implementation of the recommendations (they are not graded).

13. PERINATAL FACTORS

Increasing evidence links prenatal exposures to adverse health outcomes. Perinatal risk reduction is an area in which pediatric care providers can potentially be effective, because they are often the only physicians whom a mother sees between pregnancies. The expert panel identified 3 potential areas for consideration: maternal obesity; choice of neonatal feeding method; and maternal smoking cessation. Maternal obesity is associated with gestational DM, higher birth weight, childhood obesity measured by increased BMI, and increased risk of the metabolic syndrome and T2DM in offspring. However, the expert panel could not identify any prepregnancy or postpartum studies that addressed 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 "Overweight and Obesity." With regard to choice of neonatal feeding method, the cardiovascular advantages of breastfeeding as the primary source of nutrition for infants are emphasized in "Nutrition and Diet." Therefore, the evidence review for this section is focused on maternal smoking cessation.

Conclusions and Grading of the Evidence Review on Maternal Smoking Cessation

- The expert panel found 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 after delivery. Trials of cessation in the postpartum period, which would be the most applicable to pediatric providers, have been 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 have resulted in any reported 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 the early first trimester of any subsequent pregnancy. The pediatric well-child schedule calls for ~10 visits in the first 2 years of life, and mothers attend most of those 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 the mother and her infant, 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).

Recommendations for maternal smoking cessation are listed in Table 13-1.

TABLE 10-1 Evidence-Based Recommendations for Management of Overweight and Obesity

Birth to 24 mo	No weight-for-height–specific recommendations	
	CHILD-1 diet is recommended for pediatric care providers to use with their child and adolescent patients to reduce cardiovascular risk	
2 to 5 y	Identify children at high risk for obesity because of parental obesity and excessive BMI increase	Grade B Recommend
	Focused CHILD-1 diet and physical activity education	
	BMI percentile stable: reinforce current program, follow-up in 6 mo	
	Increasing BMI percentile: RD counseling for energy-balanced diet, intensify physical activity change; 6-mo follow-up	
	BMI = 85th–95th percentile	
	Excess weight-gain prevention with parents as focus for energy-balanced diet; reinforce physical activity recommendations for 6 mo	Grade D Recommend
	Improvement in BMI percentile: continue current program	
	Increasing BMI percentile: RD counseling for energy-balanced diet; intensify physical activity recommendations; 6-mo follow-up	
	BMI ≥ 95th percentile	
	Specific assessment for comorbidities[a]	Grade B Strongly recommend
	Family-based weight-gain prevention with parents as focus; RD counseling and follow-up for energy-balanced diet; MVPA prescription; limit sedentary screen time; 3-mo follow-up	Grade B Recommend
6 to 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 diet/physical activity education	Grade B Recommend
	BMI percentile stable: reinforce current program, 6-mo follow-up	
	Increasing BMI percentile: RD counseling for energy-balanced CHILD-1 diet, intensified physical activity, 3 mo follow-up	
	BMI = 85th–95th percentile	
	Excessive weight-gain prevention with parents as focus for energy-balanced diet; reinforce physical activity recommendations, 6-mo follow-up	Grade D Recommend
	Stable/improving BMI percentile: reinforce current program, 6-mo follow-up	
	Increasing BMI percentile: RD counseling for energy-balanced CHILD-1 diet, intensified physical activity recommendations, 3-mo follow-up	
	BMI ≥ 95th percentile	
	Specific assessment for comorbidities[a]	Grade B Strongly recommend
	BMI ≥ 95th percentile with no comorbidities	
	Office-based weight-loss plan: family-centered program with parents as focus for behavior modification, (−) energy-balanced diet, counseling by RD, prescription for increased MVPA, decreased sedentary time for 6 mo	Grade A Strongly recommend
	Improvement in BMI percentile/comorbidities: continue current plan	
	No improvement in BMI percentile: refer to comprehensive multidisciplinary lifestyle weight-loss program	
	BMI ≥ 95th percentile with comorbidities, BMI > 97th percentile, or progressive rise in BMI despite therapy	Grade A Strongly recommend
	Refer to comprehensive multidisciplinary weight-loss program for intensive management for 6 mo	
	Improvement in BMI percentile: continue current program	
	No improvement in BMI percentile: consider referral to another comprehensive multidisciplinary weight-loss program	
12 to 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 education for 6 mo	Grade B Recommend
	BMI/BMI percentile stable: reinforce current program, 6-mo follow-up	
	Increasing BMI/BMI percentile: RD counseling for energy-balanced CHILD-1 diet, intensified physical activity for 3 mo	
	BMI = 85th–95th percentile	
	Excess weight-gain prevention with adolescent as change agent for energy-balanced CHILD-1 diet, reinforced physical activity recommendations for 6 mo	Grade B Recommend
	Improvement in BMI percentile: continue current program	
	Increasing BMI percentile: RD counseling for energy-balanced weight-control diet, intensified physical activity, 3-mo follow-up	
	BMI ≥ 95th percentile	
	Specific assessment for comorbidities[a]	Grade B
	BMI ≥ 95th percentile with no comorbidities	Strongly recommend
	Office-based weight-loss plan: family-centered with adolescent as change agent for behavior-modification counseling, RD counseling for (−) energy-balanced diet, prescription for increased MVPA, decreased sedentary time for 6 mo	Grade B Strongly recommend
	Improvement in BMI/BMI percentile: continue current program	
	No improvement in BMI/BMI percentile: refer to comprehensive multidisciplinary weight-loss program with peers	
	No improvement in BMI/BMI percentile: consider initiation of medication (orlistat) under care of experienced clinician for 6–12 mo	
	BMI ≥ 95th percentile with comorbidities or BMI > 35	
	Refer to comprehensive lifestyle weight-loss program for intensive management for 6–12 mo	Grade A
	Improvement in BMI/BMI percentile: continue current program	Strongly recommend
	No improvement in BMI/BMI percentile: consider initiation of orlistat under care of experienced clinician for 6–12 mo	
	If BMI is far above 35 and comorbidities unresponsive to lifestyle therapy for >1 y, consider bariatric surgery/referral to center with experience/expertise in procedures	

Grades reflect the findings of the evidence review, and recommendation levels reflect the consensus opinion of the expert panel. RD indicates registered dietitian; MVPA, moderate-to-vigorous physical activity.

[a] Comorbidities: hypertension, dyslipidemia, and T2DM.

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