



Complete Summary

GUIDELINE TITLE

Drug therapy of high-risk lipid abnormalities in children and adolescents. A scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee, Council of Cardiovascular Disease in the Young, with the Council on Cardiovascular Nursing.

BIBLIOGRAPHIC SOURCE(S)

McCordle BW, Urbina EM, Dennison BA, Jacobson MS, Steinberger J, Rocchini AP, Hayman LL, Daniels SR, American Heart Association Atherosclerosis, Hypertension, and Obesity in, American Heart Association Council of Cardiovascular Disease in the Young, American Heart Association Council on Cardiovascular Nursing. Drug therapy of high-risk lipid abnormalities in children and adolescents: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee, Council of Cardiovascular Disease in the Young. *Circulation* 2007 Apr 10;115(14):1948-67. [149 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released

- [March 2, 2005, Crestor \(rosuvastatin calcium\)](#): Revisions to the WARNINGS, DOSAGE AND ADMINISTRATION, CLINICAL PHARMACOLOGY, and PRECAUTIONS sections of the labeling.

COMPLETE SUMMARY CONTENT

** REGULATORY ALERT **

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis

RECOMMENDATIONS

EVIDENCE SUPPORTING THE RECOMMENDATIONS

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

CONTRAINDICATIONS

QUALIFYING STATEMENTS

IMPLEMENTATION OF THE GUIDELINE

SCOPE

DISEASE/CONDITION(S)

High-risk lipid abnormalities, defined as: primary and secondary conditions associated with extreme lipid abnormalities or conditions with an underlying high risk of premature cardiovascular disease and accelerated atherosclerosis whereby the presence and severity of lipid abnormalities may further exacerbate that risk

GUIDELINE CATEGORY

Management
Treatment

CLINICAL SPECIALTY

Cardiology
Endocrinology
Family Practice
Gastroenterology
Nursing
Pediatrics
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To examine new evidence on the association of lipid abnormalities with early atherosclerosis, discuss challenges with previous guidelines, and highlight results of clinical trials with statin therapy in children and adolescents with familial hypercholesterolemia or severe hypercholesterolemia

TARGET POPULATION

Children and adolescents with high-risk lipid abnormalities

INTERVENTIONS AND PRACTICES CONSIDERED

Assessment

1. Risk factor assessment
2. Fasting lipid profile (in overweight and obese children)
3. Screening for other aspects of the metabolic syndrome (i.e., insulin resistance and type 2 diabetes, hypertension, or central adiposity [in overweight and obese children])

Treatment

Drug Therapy

1. 3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitors (statins)
2. Bile acid-reducing resins
3. Fibric acid derivatives
4. Nicotinic acid (extended release)
5. Cholesterol absorption inhibitors

Adjuvant Therapies

1. Physical activity
2. Nonpharmacologic therapies including fat- and cholesterol-restricted diets and dietary supplements

Management

1. Patient selection, initiation and titration, and monitoring of HMG CoA reductase inhibitors in children and adolescents with hyperlipidemia
2. Drug therapy of high-risk hyperlipidemia in children and adolescents

MAJOR OUTCOMES CONSIDERED

Change in levels of:

- Total cholesterol
- Low-density lipoprotein
- High-density lipoprotein
- Triglycerides
- Non-invasive vascular markers

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

This statement was approved by the American Heart Association (AHA) Science Advisory and Coordinating Committee on February 9, 2007. Expert peer review of AHA Scientific Statements is conducted at the AHA National Center.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations for Drug Therapy of High-Risk Hyperlipidemia in Children and Adolescents

Original Recommendations of the National Cholesterol Education Program (NCEP) Expert Panel

1. Consider drug therapy in children ≥ 10 years of age (usually wait until menarche for females) and after a 6- to 12-month trial of fat- and cholesterol-restricted dietary management.
2. Consider drug therapy if

LDL level remains ≥ 4.90 mmol/L (190 mg/dL) or

LDL remains > 4.10 mmol/L (160 mg/dL) and

- There is a positive family history of premature cardiovascular disease ≥ 2 other risk factors are present in the child or adolescent after vigorous attempts to control these risk factors.

3. Referral to specialized lipid center may be deemed appropriate.
4. Treatment goal

Minimal, LDL < 3.35 mmol/L (130 mg/dL)

Ideal, LDL < 2.85 mmol/L (110 mg/dL)

Current Modifications

1. In addition to family history, overweight and obesity should trigger screening with a fasting lipid profile.
2. Overweight and obese children with lipid abnormalities should be screened for other aspects of the metabolic syndrome (i.e., insulin resistance and type 2 diabetes, hypertension, or central adiposity).
3. For children meeting criteria for starting lipid-lowering drug therapy, a statin is recommended as first-line treatment.
4. For children with high-risk lipid abnormalities, the presence of additional risk factors or high-risk conditions may also lower the recommended cutpoint LDL cholesterol level for initiation of drug therapy, lower the desired target LDL cholesterol levels, and in selected cases, may prompt consideration for initiation below the age of 10 years. These risk factors and high-risk conditions may include:

Male gender

Strong family history of premature cardiovascular disease or events

Presence of associated low high-density lipoprotein (HDL), high triglycerides, small dense LDL

Presence of overweight or obesity and aspects of the metabolic syndrome

Presence of other medical conditions associated with an increased atherosclerotic risk such as diabetes, human immunodeficiency virus (HIV) infection, systemic lupus erythematosus, organ transplantation, survivors of childhood cancer

Presence of hypertension

Current smoking and passive smoke exposure

Presence of novel and emerging risk factors and markers, e.g., elevated lipoprotein(a), homocysteine, C-reactive protein

5. Ongoing research of drug therapy of high-risk lipid abnormalities in children is needed, particularly with regard to long-term efficacy and safety, and impact on the atherosclerotic disease process.

Recommendations for the Use of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) Reductase Inhibitors (Statins) in Children and Adolescents With Hyperlipidemia

Patient Selection

1. Begin with the present criteria of the expert panel of the National Cholesterol Education Program (NCEP) for drug initiation.
2. The age and low-density lipoprotein (LDL) level at which statin therapy is initiated may be influenced by the presence, magnitude, and number of other cardiovascular risk factors, as well as by the presence of cutaneous xanthomas.
3. Include the preferences of patient and family in the decision making.
4. In general, do not start before 10 years of age in boys and preferably after onset of menses in girls. Patients should ideally be at Tanner stage II or higher.
5. Ensure that there are no contraindications for statin therapy (e.g., important hepatic disease).

Initiation and Titration

1. The choice of the particular statin is a matter of preference.
2. Start with the lowest dose given once daily, usually at bedtime. Measure baseline creatine kinase (CK), alanine aminotransferase (ALT), and aspartate aminotransferase (AST).
3. Instruct the patient to report all potential adverse effects, especially myopathy (muscle cramps, weakness, asthenia, and more diffuse symptoms), immediately. If myopathy is present, its relation to recent physical activity

should be assessed, the medication stopped, and CK assessed. The patient should be monitored for resolution of the myopathy and any associated increases in CK. Consideration can be given to restarting the medication once symptoms and laboratory abnormalities have resolved.

4. Advise female patients about concerns with regard to pregnancy and the need for appropriate contraception if warranted.
5. Advise about drug interactions, especially cyclosporine, fibric acid derivatives, niacin, erythromycin,azole antifungals, nefazodone, and many human immunodeficiency virus (HIV) protease inhibitors.
6. After 4 weeks, measure fasting lipoprotein profile, CK, ALT and AST and compare with laboratory-specific reported normal values.

The threshold for worrisome level of CK is 10 times above the upper limit of reported normal; consider impact of physical activity

The threshold for worrisome level of ALT and AST is 3 times above the upper limit of reported normal

- Target levels for LDL: minimal, <3.35 mmol/L (130 mg/dL); ideal, <2.85 mmol/L (110 mg/dL)

7. If target LDL levels are achieved and there are no laboratory abnormalities, continue therapy and recheck in 8 weeks and then 3 months.
8. If laboratory abnormalities are noted or symptoms are reported, temporarily withhold the drug and repeat the blood work in approximately 2 weeks. When abnormalities return to normal, the drug may be restarted with close monitoring.
9. If target LDL levels are not achieved, double the dose, and repeat the blood work in 4 weeks. Continue stepped titration up to the maximum recommended dose until target LDL levels are achieved or there is evidence of toxicity.

Monitoring

1. Monitor growth (height, weight, and body mass index and relate to normal growth charts), sexual maturation, and development (Tanner staging).
2. Monitor fasting lipoprotein profile, CK, ALT, and AST every 3 to 6 months.
3. Monitor and encourage compliance with lipid-lowering dietary and drug therapy. Serially assess and counsel for other risk factors, such as weight gain, smoking, and inactivity.
4. Counsel adolescent females about statin contraindications in pregnancy and the need for abstinence or use of appropriate contraceptive measures. Seek referral to an adolescent medicine or gynecologic specialist as appropriate

Adjuvant Therapies

The Role of Physical Activity in Management

From current pediatric data, it would appear that an exercise program should be included as part of a comprehensive risk factor modification program for the

prevention of cardiovascular disease in children and adolescents. Emphasis on regular physical activity rather than improvement in aerobic capacity appears to be the best approach for structuring such a program. More long-term data are needed to completely assess the role of physical activity in risk factor modification for the pediatric population.

Nonpharmacological Therapies

In general, dietary recommendations should be consistent with good nutrition, aimed at a proper caloric balance to ensure optimal growth and development while preventing obesity.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Drug therapy of high-risk lipid abnormalities, particularly lowering of low-density (LDL) cholesterol levels, has resulted in great advances in the prevention and treatment of atherosclerotic cardiovascular disease.

POTENTIAL HARMS

3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitors (statins)

- Raised hepatic enzymes
- Raised creatine phosphokinase (CPK)
- Myopathy possibly progressing to rhabdomyolysis

Bile acid-binding resins

- Limited to gastrointestinal tract: gas, bloating, constipation, cramps

Fibric acid derivatives

- Dyspepsia
- Constipation
- Myositis
- Anemia

Nicotinic acid (extended release)

- Flushing
- Hepatic toxicity

Cholesterol absorption inhibitors

- Myopathy
- Gastrointestinal upset

CONTRAINDICATIONS

CONTRAINDICATIONS

- Patients should be advised of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG CoA) reductase inhibitors, or statins, and their contraindication with pregnancy, and care should be taken to prevent drug interactions that might increase the risk of rhabdomyolysis such as the concomitant use of cyclosporine, gemfibrozil, and erythromycin.
- Contraindications for statin therapy include important hepatic disease

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This statement is not meant to imply advocacy of widespread use of medications to treat the epidemic of lipid abnormalities associated with childhood obesity, for which strategies aimed at achieving sufficient weight loss are the cornerstone of therapy.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

McCordle BW, Urbina EM, Dennison BA, Jacobson MS, Steinberger J, Rocchini AP, Hayman LL, Daniels SR, American Heart Association Atherosclerosis, Hypertension, and Obesity in, American Heart Association Council of Cardiovascular Disease in the Young, American Heart Association Council on Cardiovascular Nursing. Drug therapy of high-risk lipid abnormalities in children and adolescents: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee, Council of Cardiovascular Disease in the Young. *Circulation* 2007 Apr 10;115(14):1948-67. [149 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Apr 10

GUIDELINE DEVELOPER(S)

American Heart Association - Professional Association

SOURCE(S) OF FUNDING

American Heart Association

GUIDELINE COMMITTEE

Atherosclerosis, Hypertension, and Obesity in Youth Committee
Council of Cardiovascular Disease in the Young
Council on Cardiovascular Nursing

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Brian W. McCordle, MD, MPH, *Chair*; Elaine M. Urbina, MD; Barbara A. Dennison, MD, FAHA; Marc S. Jacobson, MD, FAHA; Julia Steinberger, MD, MS; Albert P. Rocchini, MD, FAHA; Laura L. Hayman, PhD, RN, FAHA; Stephen R. Daniels, MD, PhD, FAHA

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit

a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

Writing Group Disclosures

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Ownership Interest	Consultant/Advisory Board
Brian W. McCrindle	Hospital for Sick Children (Toronto, Canada)	Schering-Plough*; AstraZeneca*; Sankyo*	None	AstraZeneca*; Merck*	None	None
Stephen R. Daniels	University of Colorado	Schering-Plough	None	None	None	None
Barbara A. Dennison	Columbia University	None	None	None	None	None
Laura L. Hayman	New York University	None	None	None	None	None
Marc S. Jacobson	Schneider Children's Hospital	None	None	None	None	None
Albert P. Rocchini	University of Michigan	None	None	None	None	None
Julia Steinberger	University of Minnesota	None	None	None	None	None
Elaine M. Urbina	University of Cincinnati	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "Significant" if (1) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "Modest" if it is less than "Significant" under the preceding definition.

*Modest

Reviewer Disclosures

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board
Robyn Barst	Columbia University	None	None	None	None	None	None
Evan Stein	Metabolic and Atherosclerosis Research Center, Cholesterol Treatment Center	None	None	None	None	None	None

Reviewer	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Board
	(Cincinnati, Ohio)						
Serena Tonstad	Ullevål University Hospital	None	None	None	None	None	None
Reginald Washington	Rocky Mountain Pediatric Cardiology	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the [American Heart Association Web site](#).

Print copies: Available from the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596; Phone: 800-242-8721

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI Institute on July 27, 2007. The information was verified by the guideline developer on August 24, 2007.

COPYRIGHT STATEMENT

Copyright to the original guideline is owned by the American Heart Association, Inc. (AHA). Reproduction of the AHA Guideline without permission is prohibited. A single reprint is available by calling 800-242-8721 (US only) or writing the American Heart Association, Public Information, 7272 Greenville Ave, Dallas, TX 75231-4596. Ask for reprint No. 71-0406. To purchase additional reprints, call 843-216-2533 or e-mail kelle.ramsay@wolterskluwer.com.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2008 National Guideline Clearinghouse

Date Modified: 11/3/2008

