



### General Implementation January 1998

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These clinical guidelines are designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and are not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. A guideline will rarely establish the only approach to a problem.

A = Annotation  
D = Discussion

The ICSI Lipids Screening work group is a subgroup of the ICSI Preventive Services work group.

## **TARGET POPULATION**

Patients ages 19 years and younger.

## **POTENTIAL AIMS FOR MEDICAL GROUPS WHEN USING THIS GUIDELINE**

1. Increase appropriate cholesterol screening for children at risk for familial hypocholesterolemia.  
Possible measures of accomplishing this aim:
  - a. Percentage of children receiving serum cholesterol screening who are at risk for familial hypocholesterolemia.
  - b. Percentage of children who are at risk for familial hypocholesterolemia who receive serum cholesterol screening.
2. Increase the use of history and exercise and nutrition assessments in the context of lipid screening.  
Possible measures of accomplishing this aim:
  - a. Percentage of children with documented exercise and nutrition assessments.
  - b. Percentage of children with relevant history recorded for lipid screening.
  - c. Percentage of children with relevant history recorded and both exercise and nutrition assessments.
3. Decrease inappropriate cholesterol screening for children.  
Possible measures of accomplishing this aim:
  - a. Percentage of children with serum cholesterol screening.
  - b. Percent of children with serum cholesterol screening without increased risk for familial hypocholesterolemia.

## **EVIDENCE GRADING SYSTEM**

- Grade A: Conclusion based on a randomized, controlled trial that has been published in a peer-reviewed journal.
- Grade B: Conclusion based on one of the following study types published in a peer-reviewed journal (but not on a randomized, controlled trial):
- a trial using historical or other non-randomized controls;
  - a prospective cohort study;
  - a case-control study; or
  - a meta-analytic study.

Grade C: Conclusion based on one of the following (but not on any studies of the types mentioned above):

- an uncontrolled case series; or
- expert opinion.

Guidelines obtained from the Agency for Health Care Policy and Research (AHCPR) or other sources, position statements, panel consensus statements from the National Institutes of Health (NIH) or elsewhere, review articles, and textbook chapters that cite primary evidence are not assigned a grade because they are not primary evidence. The individual studies cited in such secondary sources can be graded according to the categories presented above.

### INTRODUCTION

The only need for lipid screening in children and adolescents is to identify pediatric patients with familial hypercholesterolemia (FH), since early disease detection is crucial in order to facilitate treatment to prevent coronary artery disease. FH is an autosomal dominant disorder, affecting about 1 in 500 individuals, and appears to be the only pediatric lipid disorder that requires treatment beyond the usual lifestyle counseling recommended for all children and adolescents.

Thus, this guideline focuses on patients whose family history includes a CHD event at a young age or profound hypercholesterolemia. Its goal is to identify children and adolescents with FH through targeted cholesterol measurement in subpopulations whose members carry a higher likelihood of disease.

### ALGORITHM ANNOTATIONS

#### **1. Preventive Health Encounter**

A preventive health encounter is a routinely scheduled well child visit in which the provider assesses the growth, development and lifestyle of the individual. The ICSI Preventive Counseling and Education and Preventive Services guidelines would be implemented at this point.

#### **2. Age Between 2 and 19 Years and No Prior Screening?**

This guideline applies to children and young adults between the ages of two and nineteen years. Children prior to the age of two years do not require lipid status assessment. Adults 20 years old or older should be screened for their lipid status under the ICSI Lipids Screening in Adults Guideline.

Once a child or adolescent has been screened any time between the ages of 2 and 19, they do not need to have the screening repeated.

#### **3. Nutrition and Exercise Assessment; Family History Risk Factors**

Please refer to the nutrition and physical activity sections of the ICSI Preventive Counseling and Education guideline.

Children and young adults at risk for familial hypercholesterolemia (FH) can be identified at any age by inquiring into the lipid status of their primary relatives. (Primary relatives include parents, adult siblings, and grandparents.)

### 4. Primary Relative with a CHD Event at an Early Age?

A primary relative is a parent, grandparent or sibling. CHD event at an early age includes occurrence prior to the age of 55 in men or prior to the age of 65 in women. If the family history is unobtainable clinicians may wish to test the patient.

**Strength of evidence for this recommendation: B.**

### 5. Parent with Pretreatment Total Cholesterol Greater Than 300?

Adult FH heterozygotes have pretreatment cholesterol levels in the 300-500 mg/dL range. Adult FH homozygotes have untreated cholesterol levels greater than 500 mg/dL.

**Strength of evidence for this recommendation: B.**

### 6. Measure Total Cholesterol

Measurement of a non-fasting serum total cholesterol is recommended for children and young adults who have either a primary relative with a history of CHD prior to the age of 55 years or a parent with a history of a total cholesterol > 300 mg/dL. The NCEP guideline recommends chemical screening if parental levels are  $\geq 240$  mg/dL.

### 7. Is Total Cholesterol Greater Than 200?

A total cholesterol of 200 mg/dL is the cutoff for individuals at risk for familial hypercholesterolemia. Total cholesterol  $\geq 200$  mg/dL requires further clinical assessment.

**Strength of evidence for this recommendation: C.**

### 8. Measure fasting total cholesterol, HDL, Triglycerides, and calculated LDL

A fasting lipoprotein analysis will provide confirmation of any prior questionable or high screening results from non-fasting tests.

A fasting lipid panel should include a total cholesterol, HDL, triglycerides and a calculated LDL.

Fasting should occur over a period of nine to twelve hours prior to the blood draw for the lipid panel.

### 9. Is LDL Greater Than or Equal To 164?

An LDL cholesterol of 164 mg/dl has been shown to be the most discriminating level for identifying FH. Borderline levels (155-175) should be repeated to obtain an average. Clinicians should also obtain cholesterol levels from the parents. A markedly elevated level from one parent supports the diagnosis, while normal levels from both parents rules out FH.

Once a child has been tested and found to not have FH, no further testing is necessary until the individual is age 20, at which time they enter the ICSI Lipid Screening in Adults guideline. Clinicians should continue to review and offer praise or advice concerning diet and lifestyle at each routine health visit.

**Strength of evidence for this recommendation: B.**

### **10. Case Management. Out of Guideline.**

Children and young adults with an LDL  $\geq$  164 mg/dL are considered to have FH and require individual management. These individuals are therefore no longer considered part of this guideline.

Additional follow-up with these individuals includes screening of the entire family and referral to a lipid specialty clinic for multidisciplinary management.

**Evidence grading system**

- Grade A: Conclusion based on a randomized, controlled trial that has been published in a peer-reviewed journal.
- Grade B: Conclusion based on one of the following study types published in a peer-reviewed journal (but not on a randomized, controlled trial):
- a trial using historical or other non-randomized controls;
  - a prospective cohort study;
  - a case-control study; or
  - a meta-analytic study.
- Grade C: Conclusion based on one of the following (but not on any studies of the types mentioned above):
- an uncontrolled case series; or
  - expert opinion.

Guidelines obtained from the Agency for Health Care Policy and Research (AHCPR) or other sources, position statements, panel consensus statements from the National Institutes of Health (NIH) or elsewhere, review articles, and textbook chapters that cite primary evidence are not assigned a grade because they are not primary evidence. The individual studies cited in such secondary sources can be graded according to the categories presented above.

Released in January 1998 for General Implementation.  
*The next revision will occur within one year.*

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## Introduction

The goal of this guideline is the reduction of coronary heart disease by the early detection and treatment of individuals at risk. No attempt is made to identify hypercholesterolemic children or young adults through universal screening. Universal screening is not recommended by the National Cholesterol Education Program expert panel or the United States Preventive Services Task Force, and has not been shown to be an effective or efficient means of identifying individuals at risk for development of coronary heart disease (CHD).

National Cholesterol Education Program. "Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents." *Pediatrics* 89:525-584, 1992.

U.S. Preventive Services Task Force. Section I Chapter 2: "Screening for High Blood Cholesterol and other Lipid Abnormalities." in Guide to clinical preventive services: an assessment of the effectiveness of 169 interventions. pp. 15-38. Baltimore, Maryland: Williams & Wilkins, 1996.

Childhood lipid levels are not good predictors of adult levels.

Stuhldreher WL. "Cholesterol Screening in Childhood: Sixteen-year Beaver County Lipid Study Experience." *Journal of Pediatrics* 119(4):551-556, 1991. (Evidence grade B)

Lauer RM. "Factors Affecting the Relationship Between Childhood and Adult Cholesterol Levels: The Muscatine Study." *Pediatrics* 82(3):309-318, 1988. (Evidence grade B)

Further, the benefits of lowering cholesterol levels appear to be achievable even if the cholesterol-lowering intervention does not occur until adulthood. This suggests that childhood cholesterol levels are relatively unimportant.

Lipids Research Clinics Program. "The Lipids Research Clinics Coronary Primary Prevention Trial Results." *JAMA* 251(3):365-374, 1984. (Evidence grade C)

Tyroler HA. "Review of lipid-lowering clinical trials in relation to observational epidemiologic studies." *Circulation* 76(3):515-522, 1987. (Evidence grade B)

Screening may be of some value in identifying individuals with diseases of lipid metabolism. Many types of dyslipidemia have been described, but most are difficult to diagnose in childhood.

One disorder that is amenable to screening is familial hypercholesterolemia (FH). This disease also happens to have the worst prognosis in either the heterozygous or homozygous forms. FH has an autosomal dominant pattern of inheritance and can be diagnosed at any age. FH occurs in about 0.2% of the population and accounts for about 5% of the cases of CHD events at a young age.

Kwiterovich PO. "Pediatric Implications of Heterozygous Familial Hypercholesterolemia." *Arteriosclerosis* 9:111-120, 1989. (Evidence grade B)

## 4. Primary Relative with a CHD Event at an Early Age?

Children affected by FH have an 88% positive family history of CHD.

Starc TJ et al. "Family History Fails to Identify Many Children with Severe Hypercholesterolemia." *American Journal of Diseases in Children* 145:61-64, 1991. (Evidence grade B)

### 5. Parent with Pretreatment Total Cholesterol Greater Than 300?

Current NCEP guidelines recommend testing all children who have at least one parent with a total cholesterol > 240 mg/dL. This recommendation would result in screening 25% of children, and would be unlikely to provide a better yield than a cutoff of 300 mg/dL. Therefore, the work group recommends the parameter be set at 300 mg/dL.

Kwiterovich PO. "Biochemical, Clinical, Epidemiologic, Genetic, and Pathologic Data in the Pediatric Age Group Relevant to the Cholesterol Hypothesis." *Pediatrics* 78(2):349-362, 1986. (Evidence grade C)

Yamamoto A. "Clinical Features of Familial Hypercholesterolemia." *Arteriosclerosis* 9:66-74, 1989. (Evidence grade B)

The NCEP recommends chemical screening when parental cholesterol levels are  $\geq 240$  mg/dL, with the goal of identifying children with LDL cholesterol levels of 130 mg/dL or greater - a subset of children likely to have a heritable lipid disorder. Because this guideline attempts to identify only those children with true Familial Hypercholesterolemia, the higher parental threshold of 300 mg/dL was chosen, with the goal of identifying children with LDL cholesterol levels  $\geq 164$  mg/dL. Individuals in this subpopulation likely have familial hypercholesterolemia and represent the only group in whom treatment other than lifestyle modification might be warranted.

Individual clinicians may choose to adhere to NCEP guidelines but are cautioned that the lower parental threshold may lead to identification and stigmatization of children as "abnormal" when in fact treatment other than diet and lifestyle counseling (as advised for all children) cannot clearly be recommended.

### 6. Measure Total Cholesterol

A total cholesterol is the second-level screening activity because it is reliable and has the advantage of being non-fasting. It can be done with minimal preparation at the first visit.

### 7. Is Total Cholesterol Greater Than 200?

Total cholesterol was chosen for the second level of screening because it has been shown that a cutoff of 200 mg/dL will miss no individuals in the FH range.

Kwiterovich PO. "Biochemical, Clinical, Epidemiologic, Genetic, and Pathologic Data in the Pediatric Age Group Relevant to the Cholesterol Hypothesis." *Pediatrics* 78(2):349-362, 1986. (Evidence grade C)

### 9. Is LDL Greater Than or Equal To 164?

LDL cholesterol of 164 mg/dL or above has been shown to be the most accurate marker for familial hypercholesterolemia. A single test will produce a false positive rate of about 7% and a false negative rate of about 10%. The average of two tests would be expected to improve the accuracy and should be done in borderline cases if the family history does not eliminate the diagnosis of FH. In its guideline, the NCEP strive to identify children with LDL cholesterol levels  $\geq 130$  at a reasonable cost, citing the high incidence of heritable lipid disorders in this subpopulation. Clinicians who choose to follow NCEP guidelines should recognize that management of many such individuals may not differ from that of the general pediatric population, but that such identification may result in the labeling of many more children as abnormal.

Kwiterovich PO. "Pediatric Implications of Heterozygous Familial Hypercholesterolemia." *Arteriosclerosis* 9:111-120, 1989. (Evidence grade C)

Gillman MW. "Impact of Within-Person Variability on Identifying Children with Hypercholesterolemia: Framingham Children's Study." *Journal of Pediatrics* 121(3):342-347, 1992. (Evidence grade B)

Magadam M. "Within-Person Fluctuation of Serum Cholesterol and Lipoproteins." *Archives of Internal Medicine* 150:1645-1648, 1990. (Evidence grade B)

Cholesterol levels in adolescent males will decrease between 15-20% from preadolescent levels. Levels in adolescent females will be slightly lower than preadolescent levels. This decrease has not been demonstrated to occur in FH individuals. If, however, it does, it could confuse the issue in this age group. Family history and parental cholesterol levels could help to clarify borderline cases.

Kwiterovich PO. "Biochemical, Clinical, Epidemiologic, Genetic, and Pathologic Data in the Pediatric Age Group Relevant to the Cholesterol Hypothesis." *Pediatrics* 78(2):349-362, 1986. (Evidence grade C)

Michel U and Riechers B. "Cardiovascular Risk Factors in School Children." *Journal of the American College of Nutrition* 11:365-405, 1992. (Evidence grade B)



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Specifications for Selected Measures:

## Lipid Screening in Children and Adolescents

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This document provides a descriptive account of selected measurement strategies to help close the gap between clinical practice and the guideline recommendations.

# Measurement –

## Overview, Aims and Possible Measures

*Lipid Screening in Children and Adolescents*

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### OVERVIEW OF IDEAS FOR MEASUREMENT

The following aims were identified by the guideline work group as key areas in which medical groups may receive benefits in implementing this guideline.

The measures associated with these aims are presented as suggested measures. Measures of aim help medical groups determine progress in achieving a particular aim. However, additional approaches may be customized by individual medical groups to ferret out improvement information important to the medical group's individual practice.

### PRIORITY AIMS FOR MEDICAL GROUPS WHEN USING THIS GUIDELINE

1. Increase appropriate cholesterol screening for children at risk for familial hypocholesterolemia.  
Possible measures of accomplishing this aim:
  - a. Percentage of children receiving serum cholesterol screening who are at risk for familial hypocholesterolemia.
  - b. Percentage of children who are at risk for familial hypocholesterolemia who receive serum cholesterol screening.
2. Increase the use of history and exercise and nutrition assessments in the context of lipid screening.  
Possible measures of accomplishing this aim:
  - a. Percentage of children with documented exercise and nutrition assessments.
  - b. Percentage of children with relevant history recorded for lipid screening.
  - c. Percentage of children with relevant history recorded and both exercise and nutrition assessments.
3. Decrease inappropriate cholesterol screening for children.  
Possible measures of accomplishing this aim:
  - a. Percentage of children with serum cholesterol screening.
  - b. Percent of children with serum cholesterol screening without increased risk for familial hypocholesterolemia.

# Measurement Plan - Specifics

## Possible Success Measurement #1

Percent of children with relevant history recorded and both exercise and nutrition assessments.

## Population Definition

Children ages 2-19 who had an encounter in the last month.

## Data of Interest

Number of those in denominator with documentation of family history of heart disease risk factors and appropriate assessments

Number of children whose charts are abstracted

## Numerator/Denominator Definitions

**Numerator:** Of those in the denominator, those who have documentation of that the family risk factors for heart disease has been checked. This needs to be in an easily accessible place in the medical record. Any comment, note, or form mentioning the heart disease history (either none or yes and who) is counted. Also review for both exercise and nutrition assessments.

**Denominator:** This includes a sample of all children 2-19 who were seen by the medical group in the last month.

## Method/Source of Data Collection

A random sample of at least 10 children (ages 2-19) per month is suggested. The children will be drawn from all children seen by the medical group in that time frame.

## PROBING MEASURES

Probing measures include: breaking the data out by age cohorts.