Dyslipidemia Prevention and Management

Figure 9-1. Dyslipidemia Algorithm: TARGET LDL-C (Low-Density Lipoprotein Cholesterol) [Return to Top**]**

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

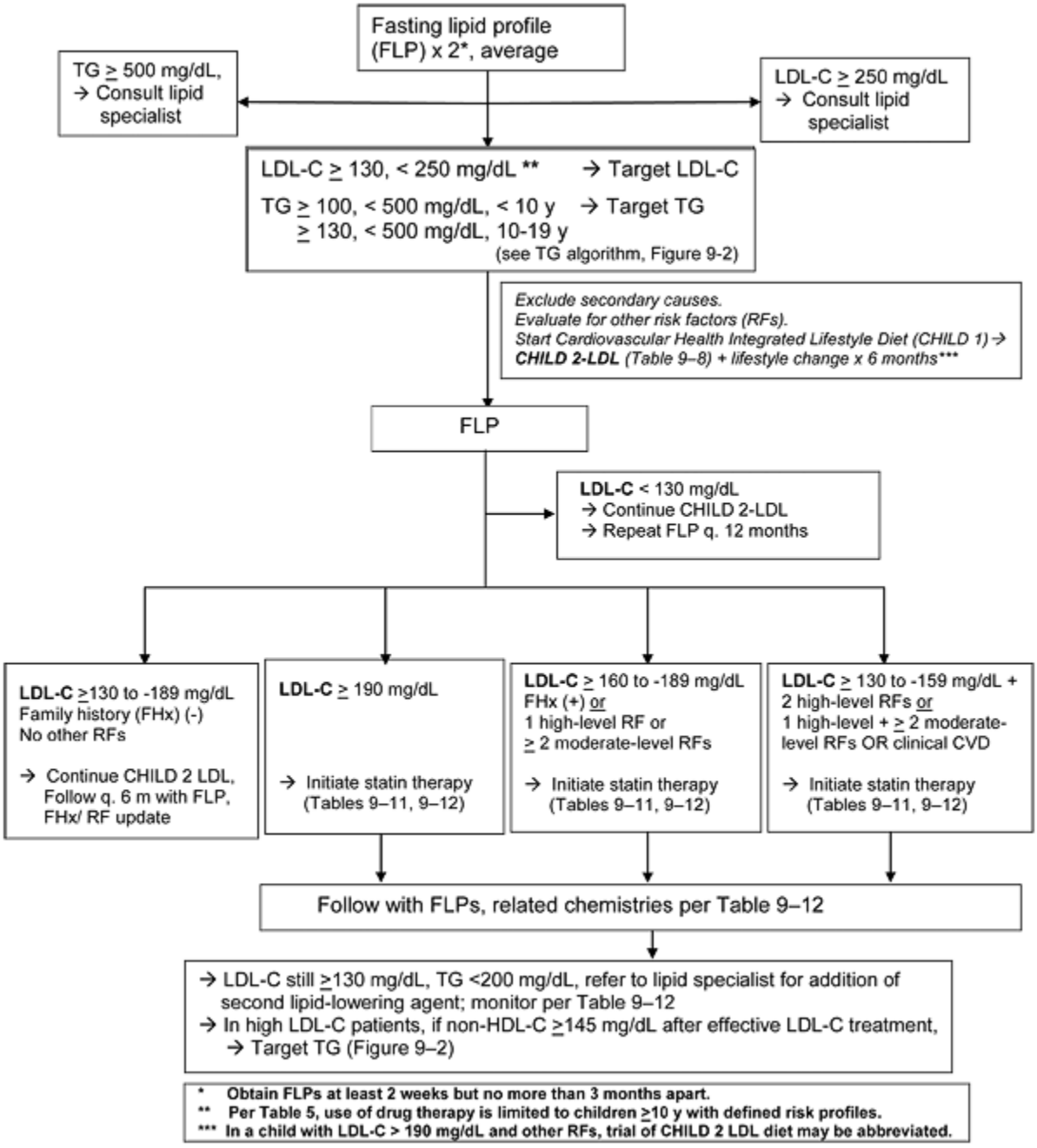


Figure 9-1 Description

The figure is a flow chart with 13 labeled boxes linked by arrows. The chart flows in one direction with arrows pointing downward and lateral arrows to one or more boxes.

Below the flow chart is described as lists in which the possible next steps are listed beneath each box label.

1. Fasting lipid profile (FLP) x 2[*], average
    a. Forward to LDL-C > 130, < 250 mg/dL [**] → Target LDL-C TG > 100, < 500 mg/dL, < 10 y → Target TG > 130, < 500 mg/dL, 10-19 y
2. TG ≥ 500 mg/dL,
   → Consult lipid specialist
    a. Lateral to LDL-C ≥ 250 mg/dL → Consult lipid specialist
3. LDL-C ≥ 250 mg/dL
   → Consult lipid specialist
    a. Lateral to TG ≥ 500 mg/dL, → Consult lipid specialist
4. LDL-C ≥ 130, < 250 mg/dL [**] → Target LDL-C
   TG≥ 100, < 500 mg/dL, < 10 y → Target TG
   ≥ 130, < 500 mg/dL, 10-19 y (see TG algorithm, Figure 9-2)
    a. Forward to FLP
    b. Boxed text with no arrow between the two boxes: Exclude secondary causes. Evaluate for other risk factors (RFs). Start Cardiovascular Health Integrated Lifestyle Diet (CHILD 1) → **CHILD 2-LDL** (Table 9-8) + lifestyle change x 6 months[***]
5. FLP
    a. Forward to **LDL-C** < 130 mg/dL
    b. Forward to **LDL-C** ≥130 to -189 mg/dL Family history (FHx) (-) No other RFs
    c. Forward to **LDL-C** ≥ 190 mg/dL
    d. Forward to **LDL-C** ≥ 160 to -189 mg/dL FHx (+) or 1 high-level RF or ≥ 2 moderate-level RFs
    e. Forward to **LDL-C** ≥ 130 to -159 mg/dL + 2 high-level RFs or 1 high-level + ≥ 2 moderate-level RFs OR clinical CVD
6. **LDL-C** < 130 mg/dL
   → Continue CHILD 2-LDL
   → Repeat FLP q. 12 months
7. **LDL-C** ≥130 to -189 mg/dL Family history (FHx) (-) No other RFs
   → Continue CHILD 2 LDL, Follow q. 6 m with FLP, FHx/ RF update
8. **LDL-C** ≥ 190 mg/dL
   → Initiate statin therapy (Tables 9-11, 9-12)
    a. Forward to Follow with FLPs, related chemistries per Table 9-12
9. **LDL-C** ≥ 160 to -189 mg/dL FHx (+) or 1 high-level RF or ≥ 2 moderate-level RFs
   →Initiate statin therapy (Tables 9-11, 9-12)
    a. Forward to Follow with FLPs, related chemistries per Table 9-12
10. **LDL-C** ≥ 130 to -159 mg/dL + 2 high-level RFs or 1 high-level + ≥ 2 moderate-level RFs OR clinical CVD
    → Initiate statin therapy (Tables 9-11, 9-12)
    a. Forward to Follow with FLPs, related chemistries per Table 9-12
11. Follow with FLPs, related chemistries per Table 9-12
    a. Forward to → LDL-C still≥130 mg/dL, TG <200 mg/dL, refer to lipid specialist for addition of second lipid-lowering agent; monitor per Table 9-12 → In high LDL-C patients, if non-HDL-C ≥145 mg/dL after effective LDL-C treatment, → Target TG (Figure 9-2)
12. → LDL-C still ≥130 mg/dL, TG <200 mg/dL, refer to lipid specialist for addition of second lipid-lowering agent; monitor per Table 9-12
    → In high LDL-C patients, if non-HDL-C ≥145 mg/dL after effective LDL-C treatment,
    → Target TG (Figure 9-2)

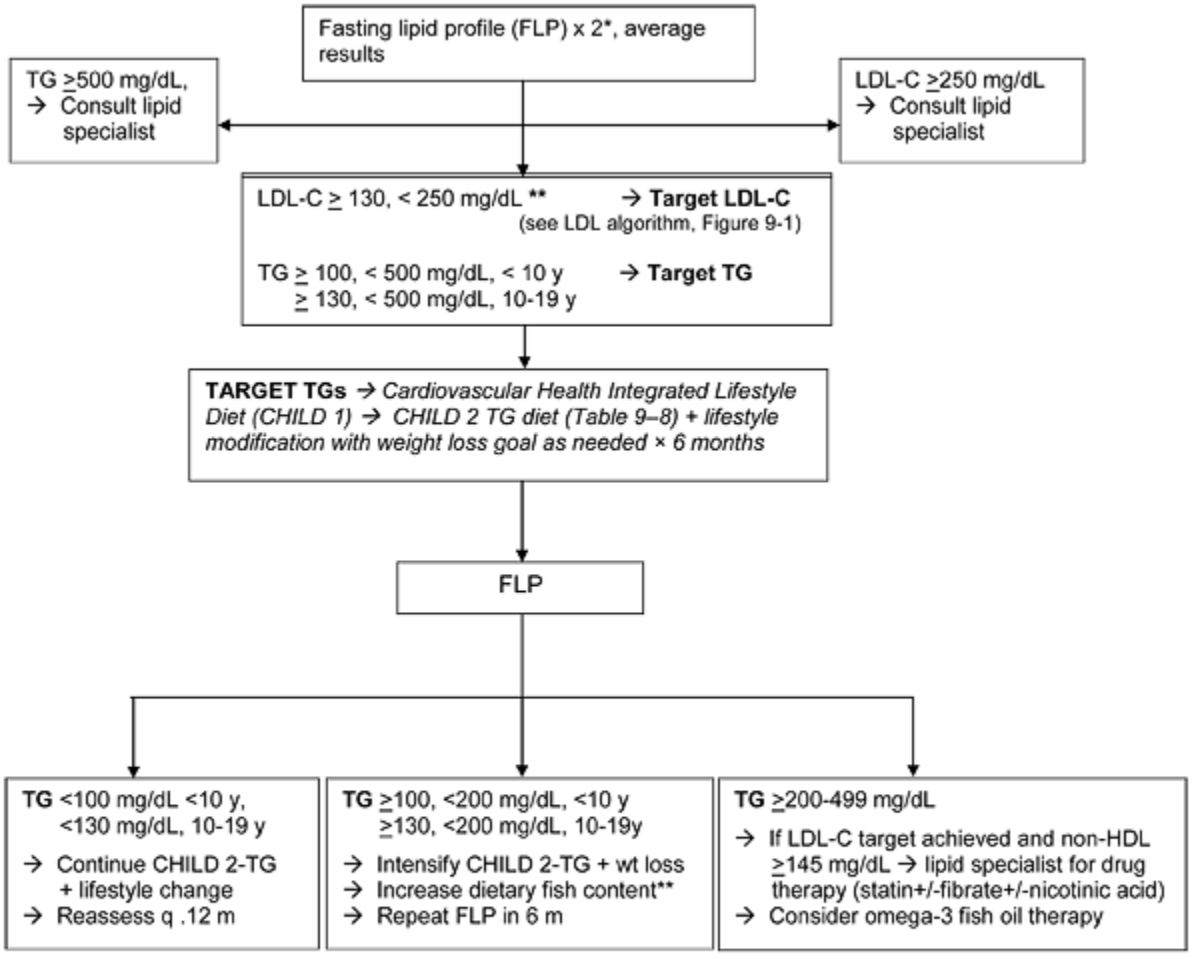
Figure 9-1 Footnotes:

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

Figure 9-2. Dyslipidemia Algorithm: TARGET TG (Triglycerides) [Return to Top]

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

.6.



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

**The Food and Drug Administration (FDA) and the Environmental Protection Agency are advising women of childbearing age who may become pregnant, pregnant women, nursing mothers, and young children to avoid some types of fish and shellfish and eat fish and shellfish that are lower in mercury. For more information, call the FDA's food information line toll free at 1-888-SAFEFOOD or visit http://www.cfsan.fda.gov/~dms/admehg3.html.

Figure 9-2 Description

The figure is a flow chart with 9 labeled boxes linked by arrows. The chart flows in one direction with arrows pointing downward and lateral arrows to one or more boxes.

Below the flow chart is described as lists in which the possible next steps are listed beneath each box label.

1. Fasting lipid profile (FLP) x 2[*], average results
    a. Forward to LDL-C ≥ 130, < 250 mg/dL [**] → **Target LDL-C** TG≥ 100, < 500 mg/dL, < 10 y → **Target TG** ≥ 130, < 500 mg/dL, 10-19 y
2. TG ≥ 500 mg/dL,
   → Consult lipid specialist
    a. Lateral to LDL-C ≥ 250 mg/dL → Consult lipid specialist
3. LDL-C ≥ 250 mg/dL
   → Consult lipid specialist
    a. Lateral to TG ≥ 500 mg/dL, → Consult lipid specialist
4. LDL-C ≥ 130, < 250 mg/dL [**] → **Target LDL-C** (see LDL algorithm, Figure 9-1)
   TG≥ 100, < 500 mg/dL, < 10 y → **Target TG**
   ≥ 130, < 500 mg/dL, 10-19 y
    a. Forward to **TARGET TGs** → Cardiovascular Health Integrated Lifestyle Diet (CHILD 1) → CHILD 2 TG diet (Table 9-8) + lifestyle modification with weight loss goal as needed × 6 months
5. **TARGET TGs** → Cardiovascular Health Integrated Lifestyle Diet (CHILD 1) → CHILD 2 TG diet (Table 9-8) + lifestyle modification with weight loss goal as needed × 6 months
    a. Forward to FLP
6. FLP
    a. Forward to **TG** <100 mg/dL <10 y, <130 mg/dL, 10-19 y
    b. Forward to**TG** ≥100, <200 mg/dL, <10 y ≥130, <200 mg/dL, 10-19y
    c. Forward to **TG** ≥200-499 mg/dL
7. **TG** <100 mg/dL <10 y,
   <130 mg/dL, 10-19 y
   → Continue CHILD 2-TG + lifestyle change
   →Reassess q .12 m
8. **TG** ≥100, <200 mg/dL, <10 y
   ≥130, <200 mg/dL, 10-19y
   → Intensify CHILD 2-TG + wt loss ' Increase dietary fish content**
   → Repeat FLP in 6 m
9. **TG** ≥200-499 mg/dL
   → If LDL-C target achieved and non-HDL ≥145 mg/dL → lipid specialist for drug therapy (statin+/-fibrate+/-nicotinic acid)
   → Consider omega-3 fish oil therapy

Figure 9-2 Footnotes:

[*] Obtain FLPs at least 2 weeks but no more than 3 months apart.
[**] The Food and Drug Administration (FDA) and the Environmental Protection Agency are advising women of childbearing age who may become pregnant, pregnant women, nursing mothers, and young children to avoid some types of fish and shellfish and eat fish and shellfish that are lower in mercury. For more information, call the FDA's food information line toll free at 1-888-SAFEFOOD or visit http://www.cfsan.fda.gov/~dms/admehg3.html.

Table 5–1. Evidence-Based Recommendations for Diet and Nutrition: Cardiovascular Health Integrated Lifestyle Diet (CHILD 1) [Return to Top]

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

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

Birth - 6 m	Infants should be exclusively breast fed (no supplemental formula or other foods) until age 6 m.[a]	Grade B Strongly recommend
6 - 12 m	Continue breast-feeding[a] until at least age 12 m while gradually adding solids; transition to iron-fortified formula until 12 m if reducing breast-feeding	Grade B Strongly recommend
6 - 12 m (cont.d)	Fat intake in infants less than 12 months of age should not be restricted without medical indication.	Grade D Recommend
6 - 12 m (cont.d)	Limit other drinks to 100% fruit juice < 4 oz/d; No sweetened beverages; encourage water.	Grade D Recommend
12 - 24 months	Transition to reduced-fat[b] (2% to fat-free) unflavored cow's milk[c] (see Supportive Actions bullet 1)	Grade B Recommend
12 - 24 months (cont.d)	Limit/avoid sugar-sweetened beverage intake; encourage water	Grade B Strongly recommend
12 - 24 months (cont.d)	Transition to table food with:	
12 - 24 months (cont.d)	• Total fat 30% of daily kcal/EER[d]	Grade B Recommend
12 - 24 months (cont.d)	• Saturated fat 8-10% of daily kcal/EER	Grade B Recommend
12 - 24 months (cont.d)	• Avoid trans fat as much as possible	Grade D Strongly recommend
12 - 24 months (cont.d)	• Monounsaturated and polyunsaturated fat up to 20% of daily kcal/EER	Grade D Recommend
12 - 24 months (cont.d)	• Cholesterol < 300 mg/d	Grade B Strongly recommend
12 - 24 months (cont.d)	*Supportive actions:* • The fat content of cow's milk to introduce at age 12-24 m should be decided together by parents and health care providers based on the child's growth, appetite, intake of other nutrient dense foods, intake of other sources of fat, and	

	potential risk for obesity and CVD • 100 percent fruit juice (from a cup) no more than 4 oz/d • Limit sodium intake • Consider DASH-type diet rich in fruits, vegetables, whole grains, low-fat/fat-free milk and milk products; lower in sugar (Table 5-3)	
2 -10 years	Primary beverage: Fat-free unflavored milk	Grade A Strongly recommend
2 -10 years (cont.d)	Limit/avoid sugar sweetened beverages; encourage water.	Grade B Recommend
2 -10 years (cont.d)	Fat content:	
2 -10 years (cont.d)	• Total fat 25-30% of daily kcal/EER[d]	Grade A Strongly recommend
2 -10 years (cont.d)	• Saturated fat 8-10% of daily kcal/ EER	Grade A Strongly recommend
2 -10 years (cont.d)	• Avoid trans fats as much as possible	Grade D Recommend
2 -10 years (cont.d)	• Monounsaturated and polyunsaturated fat up to 20% of daily kcal/EER	Grade D Recommend
2 -10 years (cont.d)	• Cholesterol < 300 mg/d	Grade A Strongly recommend
2 -10 years (cont.d)	Encourage high dietary fiber intake from foods[e]	Grade B Recommend
2 -10 years (cont.d)	*Supportive actions:* • Teach portions based on EER for age/sex/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 plus 5 g/d[e] • Limit naturally sweetened juice (no added sugar) to 4 oz/d • Limit sodium intake • Support DASH-style eating plan as outlined below (Table 5-3)	
11 - 21 y	Primary beverage: Fat-free unflavored milk	Grade A Strongly recommend
11 - 21 y (cont.d)	Limit/ avoid sugar sweetened beverages; encourage water.	Grade B Recommend
11 - 21 y (cont.d)	Fat content:	

11 - 21 y (cont.d)	• Total fat 25-30% of daily kcal/EER[d]	Grade A Strongly recommend
11 - 21 y (cont.d)	• Saturated fat 8-10% of daily kcal/ EER	Grade A Strongly recommend
11 - 21 y (cont.d)	• Avoid trans fat as much as possible	Grade D Recommend
11 - 21 y (cont.d)	• Monounsaturated and polyunsaturated fat up to 20% of daily kcal/ EER	Grade D Recommend
11 - 21 y (cont.d)	• Cholesterol < 300 mg/d	Grade A Strongly recommend
11 - 21 y (cont.d)	Encourage high dietary fiber intake from foods[e]	Grade B Recommend
11 - 21 y (cont.d)	*Supportive actions:* • Teach portions based on EER for age/sex/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/1,000 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 as outlined below (Table 5-3)	

[a] Infants that cannot be fed directly at the breast should be fed expressed milk. Infants for whom expressed milk is not available should be fed iron-fortified infant formula.
[b] Toddlers 12-24 m of age with a family history of obesity, heart disease, or high cholesterol, should discuss transition to reduced-fat milk with pediatric care provider after 12 months of age.
[c] Continued breast-feeding is still appropriate and nutritionally superior to cow's milk. Milk reduced in fat should be used only in the context of an overall diet that supplies 30% of calories from fat.
[d] EER = Estimated Energy Requirements/d 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 9–8. Evidence-Based Recommendations for Dietary Management of Elevated LDL–C, non-HDL-C and TG [Return to Top]

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

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

ELEVATED LDL–C: CHILD 2 - LDL

2–21 years	Refer to a registered dietitian for family medical nutrition therapy:	Grade B Strongly recommend
2–21 years (cont.d)	• 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 *Supportive actions:* • Plant sterol esters and/or plant stanol esters* up to 2 g/d as replacement for usual fat sources can be used after age 2 years in children with familial hypercholesterolemia. • Plant stanol esters as part of a regular diet are marketed directly to the public. Short-term studies show no harmful effects in healthy children. • The water-soluble fiber psyllium can be added to a low-fat, low saturated fat diet as cereal enriched with psyllium at a dose of 6 g/d for children 2–12 years, and 12 g/d for those ≥12 years. • As in all children, 1 hour/day (h/d) of moderate to vigorous physical activity and <2 h/d of sedentary screen time are recommended.	Grade A Recommend

* Can be found added to some foods, such as some Margarins

ELEVATED TG OR NON-HDL–C: CHILD 2 - TG

2–21 years	Refer to a registered dietitian for family medical nutrition therapy:*	Grade B Strongly recommend
2–21 years (cont.d)	• 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

2–21 years (cont.d)	• Decrease sugar intake:
	  • Replace simple with complex carbohydrates
	  • No sugar sweetened beverages
		Grade B
		Recommend

2–21 years (cont.d)	• Increase dietary fish to increase omega-3 fatty acids**	Grade D Recommend

* If child is obese, nutrition therapy should include calorie restriction, and increased activity (beyond that recommended for all children) should be prescribed. See Section X. Overweight and Obesity for additional age-specific recommendations.
** The Food and Drug Administration (FDA) and the Environmental Protection Agency are advising women of childbearing age who may become pregnant, pregnant women, nursing mothers, and young children to avoid some types of fish and shellfish and eat fish and shellfish that are low in mercury. For more information, call the FDA's food information line toll free at 1–888–SAFEFOOD or visit http://www.cfsan.fda.gov/~dms/admehg3.html.

Conclusions and Grading of the Evidence Review for Use of Medication to Treat Dyslipidemia [Return to Top]

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

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

- Decisions regarding the need for medication therapy should be based on the average of results from at least two fasting lipid profiles obtained at least 2 weeks but no more than 3 months apart (Grade C) (Figure 9–1).
- The cut points used to define the level at which drug therapy should be considered from the 1992 *NCEP Pediatric Guidelines* have been used as the basis for multiple drug safety and efficacy trials in dyslipidemic children (Grade B):
  - LDL–C ≥ 190 mg/dL after a 6-month trial of lifestyle management (CHILD 1 → CHILD 2-LDL) for children ≥10 years.
  - LDL–C 160–189 mg/dL after a 6-month trial of lifestyle/diet management (CHILD 1 → CHILD 2-LDL) in a child ≥10 years with a positive family history of premature CVD/events in first-degree relatives (Table 9–6) or at least one high-level risk factor

or risk condition or at least 2 moderate-level risk factors or risk conditions (Tables 9–6, 9–7, and 9–12) (Figure 9–1).

- LDL–C 130–190 mg/dL in a child ≥ 10 years with a negative family history of premature CVD in first-degree relatives and no high-level or moderate-level risk factor or risk condition: Management should continue to focus on lifestyle changes (CHILD 1→ CHILD 2-LDL) based on lipid profile findings (Figure 9–1) plus weight management if BMI ≥ 85th percentile.
- **The goal of LDL-lowering therapy in childhood and adolescence is LDL–C below the 95th percentile (≤130 mg/dL).**

- Children with homozygous FH and extremely elevated LDL–C levels (>500 mg/dL) have undergone effective LDL-lowering therapy with biweekly LDL apheresis under the care of lipid specialists in academic medical centers (Grade C).
- Multiple cohort studies series have shown that the benefits of LDL-lowering therapy in children at high risk for accelerated atherosclerosis (such as those with chronic kidney disease, T1DM or T2DM, Kawasaki disease with coronary aneurysms, or postcardiac transplantation) should be considered for initiation of medication therapy (Grade C) (see Section XI. Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis).
- The bile acid sequestrants are medications that bind bile salts within the intestinal lumen and prevent their enterohepatic reuptake in the terminal ileum, resulting in a depletion of bile salts in the liver and a signal for increased production. Since bile salts are synthesized from intracellular cholesterol in the liver, the intracellular pool of cholesterol becomes depleted, signaling increased production of LDL receptors and increased clearance of circulating LDL–C to replenish the intracellular cholesterol pool for increased production of bile salts. Studies of bile acid sequestrants in children and adolescents ages 6–18 years with LDL–C levels from 131 to 190 mg/dL show TC reduction of 7-17 percent and reduction of LDL–C of 10–20 percent, sometimes with a modest elevation in TG levels. The bile acid sequestrants commonly have gastrointestinal side effects, and these significantly affect compliance. However, they are safe and moderately effective (Grade A).
- Statin medications inhibit hydroxymethylglutaryl coenzyme A reductase, which is a rate-limiting enzyme in the endogenous cholesterol synthesis pathway. This results in a decrease in the intracellular pool of cholesterol, which signals upregulation of LDL receptors and increased clearance of circulating LDL–C. As a group, statins have been shown to reduce LDL–C in children and adolescents with marked LDL–C elevation or FH (defined as elevated LDL–C in the child in conjunction with a family history of elevated LDL–C and/or atherosclerosis or CAD) when used from 8 weeks to 2 years for children ages 8–18 years. The lower LDL–C level for eligibility into the statin trials was ≥190 mg/dl or ≥ 160 mg/dl with 2 or more additional risk factors, after a trial period on diet. Trial subjects were monitored carefully throughout treatment; adverse impacts on growth, development, or sexual maturation were not seen, and adverse event profiles and efficacy were similar to those in studies of adults (Grade A).
- Adverse effects from statins are rare at standard doses but include myopathy and hepatic enzyme elevation. In the meta-analysis of statin use in children, evidence of hepatic enzyme elevation and muscle toxicity did not differ between the statin and placebo groups. Routine monitoring of hepatic enzymes and clinical assessment for muscle toxicity are strongly recommended for children and adolescents on statin therapy (Table 9–12). The risk of adverse events increases with use of higher doses and interacting drugs, the latter occurring primarily with drugs that are metabolized by the cytochrome P–450 system, which is the primary mode of metabolism for the majority of statins. Drugs that potentially interact with statins include fibrates, azol antifungals, macrolide antibiotics, antiarrhthymics, and protease inhibitors (Grade A).
- Bile acid-binding sequestrants may be used in combination with a statin for patients who fail to meet LDL–C target levels with either medication alone. One pediatric study assessed this combination and showed no increase in adverse effects. The efficacy of the two agents together appears to be additive (Grade B).
- There is limited published experience in children with use of niacin and fibrates, which have been useful in treating adult patients with combined dyslipidemias. Efficacy and safety data are limited, and no data are available regarding newer formulations. In adults, cholesterol absorption inhibitors have been advocated as an adjunct to statin therapy for patients who do not reach LDL–C therapeutic targets. Since their action is independent of and complementary

to that of statins, the LDL–C-lowering effect is additive. No pediatric studies of monotherapy with cholesterol absorption inhibitors had been published during the time period for this evidence review. Use of niacin, fibrates, and cholesterol absorption inhibitors should be instituted only in consultation with a lipid specialist (Grade C).

- Medication therapy is rarely needed for children with elevated TG who respond well to weight loss and lifestyle changes (Grade B) (Figure 2) (Table 9-8). When TG levels exceed 500 mg/dL, patients are at risk for pancreatitis and require care in consultation with a lipid specialist (Grade B). In adults, use of omega-3 fish oil has been shown to lower TG by 30–40 percent and to raise HDL by 6–17 percent. Experience with fish oil in children is limited to small case series with no safety concerns identified; there have been no RCTs of fish oil in children (Grade D).

Age-Based Recommendations For Medication Therapy of Children With Dyslipidemia [Return to Top]

Children Younger Than Age 10 Years

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

Children Ages 10-21 Years (see algorithms, Figures 9–1 and 9–2)

- Decisions regarding the need for medication therapy should be based on the average of results from at least two FLPs obtained at least 2 weeks apart but no more than 3 months apart. (Grade C) (Figure 9–1).
- Children with average LDL-C ≥ 250 mg/dL or average TG ≥ 500 mg/dL should be referred directly to a lipid specialist (Grade B).

- Children with lipid abnormalities should have a detailed family history taken and be assessed for causes of hyperlipidemia, additional risk factors, and risk conditions (Grade C) (Tables 9–3, 9–6, and 9–7).
- Children with lipid abnormalities (other than LDL-C ≥ 250 mg/dL or TG > 500 mg/dL) should be initially managed for 3-6 months with diet changes (CHILD 1→CHILD 2-LDL or CHILD 2-TG, Table 9–8) based on specific lipid profile findings (Figures 9–1 and 9–2); if BMI is ≥85th percentile, add increased physical activity, reduced screen time, and calorie restriction. Assessment for associated secondary causes (Table 9–3), additional risk factors, or high-risk conditions (Tables 9–6 and 9–7) is recommended. Children at high risk who are unlikely to achieve lipid targets with this strategy alone (severe primary dyslipidemia, cardiac transplantation) should concomitantly be considered for initiation of medication therapy (Grade C) (Section XI. Diabetes Mellitus and Other Conditions Predisposing to the Development of Accelerated Atherosclerosis).

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

- Children with average LDL-C ≥ 250 mg/dL should be referred directly to a lipid specialist (Grade B).
- If LDL-C remains ≥ 190 mg/dL after a 6-month trial of lifestyle/diet management (CHILD 1→CHILD 2-LDL) for children ages 10 years and older, statin therapy should be considered (Grade A) (Figure 9–1) (Table 12).
- If LDL-C remains ≥ 130 mg/dL to < 190 mg/dL in a child age 10 years or older with a negative family history of premature CVD in first-degree relatives and no high-level or moderate-level risk factor or risk condition (Tables 9–6 and 9–7), management should continue to focus on diet changes (CHILD 2-LDL) based on lipid profile findings (Figure 9–1) plus weight management if BMI ≥ 85th percentile. Pharmacologic therapy is not generally indicated, but treatment with bile acid sequestrants might be considered, the latter in consultation with a lipid specialist (Grade B).
- If LDL-C remains ≥ 160 to 189 mg/dL after a trial of lifestyle/diet management (CHILD 1àCHILD 2- LDL) in a child age 10 years or older with a positive family history of premature CVD/events in first-degree relatives (Table 9–6) or at least one high-level risk factor or risk

condition or at least two moderate-level risk factors or risk conditions (Tables 9–6 and 9–7), then statin therapy should be considered (Grade B)(Figure 9–1) (Table 9–12).

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

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

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

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

Table 9–9. Evidence-Based Recommendations for Pharmacologic Treatment of Dyslipidemia [Return to Top]

Grades reflect the findings of the evidence review.
Recommendation levels reflect the consensus opinion of the Expert Panel.
When medication is recommended, this should always be in the context of the complete cardiovascular risk profile of the patient and in consultation with the patient and the family.

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

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

(cont.d)	per Tables 9–11 and 9–12	
≥10–21 years (cont.d)	• → LDL–C ≥130–159 mg/dL + ≥2 high-level RFs/RCs OR 1 high-level + 2 moderate-level RFs/RCs, consider statin therapy per Tables 9–11 and 9–12	Grade B Recommend
≥10–21 years (cont.d)	**Children on statin therapy should be counseled and carefully monitored per Table 9–12.**	Grade A Strongly recommend
≥10–21 years	Detailed FHx and RF/RC assessment required before initiation of drug therapy.*** High- and moderate-level RFs/RCs in Tables 9–6 and 9–7†	Grade C Strongly recommend
≥10–21 years (cont.d)	**TG:**	
≥10–21 years (cont.d)	If average TG ≥500 mg/dL, consult lipid specialist	Grade B Recommend
≥10–21 years (cont.d)	If average TG ≥100 mg/dL in a child <10 years, ≥130 mg/dL in a child age 10–19 years, <500 mg/dL:	
≥10–21 years (cont.d)	• Refer to dietitian for medical nutrition therapy with CHILD 1 → CHILD 2-TG (Table 9–8) × 6 months	Grade B Strongly recommend
≥10–21 years (cont.d)	Repeat fasting lipid profile:	
≥10–21 years (cont.d)	• → TG <100 (130) mg/dL, continue CHILD 2-TG, monitor q. 6–12 months	Grade B Strongly recommend
≥10–21 years (cont.d)	• → TG >100 (130) mg/dL, reconsult dietitian for intensified CHILD 2 TG diet counseling	Grade C Recommend
≥10–21 years (cont.d)	• → TG ≥200–499 mg/dL, non-HDL ≥145 mg/dL, consider fish oil +/- consult lipid specialist	Grade D Recommend
≥10–21 years (cont.d)	**Non-HDL-C:**	
≥10–21 years (cont.d)	Children ≥10 years with non-HDL–C ≥145 mg/dL after LDL–C goal achieved may be considered for additional treatment with statins, fibrates, or niacin in conjunction with a lipid specialist.	Grade D Optional

* Consideration of drug therapy based on the average of ≥2 FLPs, obtained at least 2 weeks but no more than 3 months apart.
** If average LDL–C ≥190 mg/dL after CHILD 2-LDL and child is age 8–9 years with + FHx OR ≥1 high-level RF/RC OR ≥ 2 moderate-level RFs/RCs, statin therapy may be considered.
*** Consideration of drug therapy based on the average of ≥2 fasting lipid profiles obtained at least 2

weeks but no more than 3 months apart.

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

Table 9–10. Medications for Managing Hyperlipidemia [Return to Top]

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-C; some decrease in TG and modest increase in HDL-C	Atorvastatin Fluvastatin Lovastatin Pravastatin Rosuvastatin Simvastatin	Raised hepatic enzymes, raised creatine kinase, myopathy possibly progressing to rhabdomyolysis	All statins listed approved as an adjunct to diet to lower LDL-C in adolescent boys and postmenarchal girls ages 10-18 years (8+ years for pravastatin) with heFH and LDL-C ≥190 mg/dL, or ≥160 mg/dL with FHx of premature CVD and 2+ CVD risk factors in the pediatric patient
Bile acid sequestrants	Binds intestinal bile acids interrupting enterohepatic recirculation, more cholesterol converted into bile acids, decreases hepatic cholesterol pool, upregulates LDL receptors	Lowers LDL-C; small increase in HDL; raises TG	Cholestyramine Colestipol Colesevelam	Limited to gastrointestinal tract: gas, bloating constipation, cramps	No pediatric indication listed for cholestyramine or colestipol; colesevelam indicated as monotherapy or with statin for LDL-C reduction in boys and postmenarchal girls ages 10-17 years with FH after diet trial if LDL-C ≥190 mg/dL or if LDL-C ≥160 mg/dL with FHx premature CVD or 2+ more CVD risk factors in the pediatric patient
Cholesterol absorption inhibitors	Inhibits intestinal absorption of cholesterol and plant sterols, decreases hepatic cholesterol pool, upregulates LDL receptors	Mainly lowers LDL-C; some decrease in TG and small increase in HDL-C	Ezetimibe	Myopathy, gastrointestinal upset, headache	No
Fibric acid derivatives	Agonist for PPAR alpha nuclear receptors that upregulate LPL and downregulate apoC-III,	Mainly lowers TG and raises	Fenofibrate Gemfibrozil	Dyspepsia, constipation, myositis, anemia	No

	both increasing degradation of VLDL-C and TG. Hepatic synthesis of VLDL-C may also be decreased.	HDL-C, with little effect on LDL-C			
Nicotinic acid (extended release)	Inhibits release of FFA from adipose tissue; decreases VLDL-C and LDL-C production and HDL-C degradation	Lowers TG and LDL-C and raises HDL-C; can decrease Lp(a)	Niacin, extended release	Flushing, hepatic toxicity, can increase fasting blood glucose, uric acid; hyperacidity	Use not recommended in children < age 2 years
Omega-3 fish oil	Decreases hepatic FA and TG synthesis while enhancing FA degradation/oxidation, with subsequent reduced VLDL-C release	Lowers TG, raises HDL-C, increases LDL-C and LDL-C particle size	Omega-3 acid ethyl esters	Occasional gastrointestinal side effects but no adverse effect on glucose levels or muscle or liver enzymes or bleeding	Only one FDA-approved fish oil preparation for adults, but many generic fish oil capsules commercially available

References:

Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents:Summary Report. National Heart, Blood, and Lung Institute, 2011. vhttp://www.nhlbi.nih.gov/guidelines/cvd_ped/