JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Lipid Disorders in Children and Adolescents
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

IMPORTANCE Familial hypercholesterolemia and multifactorial dyslipidemia are 2 conditions that cause abnormally high lipid levels in children, which can lead to premature cardiovascular events (eg, myocardial infarction and stroke) and death in adulthood.

OBJECTIVE The US Preventive Services Task Force (USPSTF) commissioned a systematic review to evaluate the benefits and harms of screening for lipid disorders in asymptomatic children and adolescents.

POPULATION Asymptomatic children and adolescents 20 years or younger without a known diagnosis of a lipid disorder.

EVIDENCE ASSESSMENT The USPSTF concludes that the current evidence is insufficient and the balance of benefits and harms for screening for lipid disorders in asymptomatic children and adolescents 20 years or younger cannot be determined.

RECOMMENDATION The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for lipid disorders in children and adolescents 20 years or younger. (I statement)

JAMA. 2023;330(3):253-260. doi:10.1001/jama.2023.11330

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Supplemental content

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Group Information: The US Preventive Services Task Force (USPSTF) members are listed at the end of this article.

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Summary of Recommendation

Population	Recommendation	Grade
Asymptomatic children and adolescents 20 years or younger	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for lipid disorders in children and adolescents 20 years or younger. See the Practice Considerations section for additional information regarding the I statement.	I

USPSTF indicates US Preventive Services Task Force.

See the Summary of Recommendation figure.

Preamble

The US Preventive Services Task Force (USPSTF) makes recommendations about the effectiveness of specific preventive care services for patients without obvious related signs or symptoms to improve the health of people nationwide.

It bases its recommendations on the evidence of both the benefits and harms of the service and an assessment of the balance. The USPSTF does not consider the costs of providing a service in this assessment.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation. Similarly, the USPSTF notes that policy and coverage decisions involve considerations in addition to the evidence of clinical benefits and harms.

The USPSTF is committed to mitigating the health inequities that prevent many people from fully benefiting from preventive services. Systemic or structural racism results in policies and practices, including health care delivery, that can lead to inequities in health. The USPSTF recognizes that race, ethnicity, and gender are all social rather than biological constructs. However, they are also often important predictors of health risk. The USPSTF is committed to helping reverse the negative impacts of systemic and structural racism, gender-based discrimination, bias, and other sources of health inequities, and their effects on health, throughout its work.

Table. Summary of USPSTF Rationale

Rationale	Assessment
Detection	The USPSTF found inadequate evidence on the diagnostic yield of serum lipid screening for familial hypercholesterolemia or multifactorial dyslipidemia.

Benefits of early detection and intervention and treatment	The USPSTF found inadequate direct evidence on the benefits of screening for familial hypercholesterolemia or multifactorial dyslipidemia in children and adolescents.
	• Familial hypercholesterolemia:
	  • The USPSTF found inadequate evidence that lipid-lowering interventions in children and adolescents identified by screening the general pediatric population leads to reductions in cardiovascular events (eg, myocardial infarction or stroke) or all-cause mortality in adults.
	  • The USPSTF found adequate evidence from short-term trials (≤2 years) that pharmacotherapy interventions substantially reduce total cholesterol and low-density lipoprotein cholesterol levels in children and adolescents with familial hypercholesterolemia.
	  • The USPSTF found inadequate evidence on the association between changes in intermediate lipid outcomes in children and adolescents identified by screening the general pediatric population and a reduction in relevant adult health outcomes.
	• Multifactorial dyslipidemia:
	  • The USPSTF found inadequate evidence on the benefits of lipid-lowering interventions in children and adolescents with multifactorial dyslipidemia to improve intermediate lipid outcomes or reduce relevant health outcomes in children or adults.

Harms of early detection and intervention and treatment	• The USPSTF found inadequate evidence to assess the harms of screening for familial hypercholesterolemia or multifactorial dyslipidemia. • The USPSTF found adequate evidence that the harms of treatment of familial hypercholesterolemia or multifactorial dyslipidemia in children and adolescents are no greater than small.
USPSTF assessment	Due to a lack of available data, the USPSTF found that the evidence is insufficient, and the balance of benefits and harms for screening for lipid disorders in asymptomatic children and adolescents 20 y or younger cannot be determined.

Abbreviation: USPSTF, US Preventive Services Task Force.

Importance

Familial hypercholesterolemia (FH) and multifactorial dyslipidemia are 2 conditions that cause abnormally high lipid levels in children, which can lead to premature cardiovascular events (eg, myocardial infarction and stroke) and death in adulthood. The prevalence of FH in US children and adolescents ranges from 0.2% to 0.4% (1 of every 250 to 500 children and adolescents). Multifactorial dyslipidemia is much more common than FH, with prevalence in children and adolescents ranging from 7.1% to 9.4%.[1]

USPSTF Assessment of Magnitude of Net Benefit

The USPSTF concludes that the current evidence is insufficient and that the balance of benefits and harms for screening for lipid disorders in asymptomatic children and adolescents 20 years or younger cannot be determined.

See the **Table** for more information on the USPSTF recommendation rationale and assessment and the eFigure in the Supplement for information on the recommendation grade. See the **Figure** for a summary of the recommendation for clinicians. For more details on the methods the USPSTF uses to determine the net benefit, see the USPSTF Procedure Manual.[2]

Practice Considerations

Patient Population Under Consideration

This statement applies to asymptomatic children and adolescents 20 years or younger without a known diagnosis of a lipid disorder.

Definitions

Familial hypercholesterolemia is a genetic disorder of cholesterol metabolism characterized by very high levels of low-density lipoprotein cholesterol (LDL-C) early in life. This cumulative exposure to abnormal lipid levels over time can lead to early atherosclerotic changes and premature cardiovascular morbidity and mortality. Diagnosis of FH is variably defined but generally includes substantially elevated lipid levels, a monogenic mutation, or both. There are several variants that can individually lead to the FH phenotype, so genetic testing includes examination for each of these variants.[1]

Multifactorial dyslipidemia is a condition of elevated lipid levels primarily associated with environmental factors such as excessive intake of saturated fat, sedentary lifestyle, and obesity; polygenic variants with small additive effects may also contribute to the condition. Abnormal lipid values associated with multifactorial dyslipidemia are generally lower than those associated with FH.[1]

Screening Tests

Although there is insufficient evidence to recommend for or against screening in young patients without signs or symptoms, a serum lipid panel is the most commonly proposed screening test for FH and multifactorial dyslipidemia. Lipid panels measure different components of cholesterol metabolism, including total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), non–HDL-C, and triglycerides.[1]

Treatment

Treatment interventions to lower lipid levels generally include lifestyle modification (eg, changes in diet and physical activity), pharmacotherapy (eg, statins, bile acid sequestering agents, or cholesterol absorption inhibitors), and dietary supplements (eg, plant sterols or fish oil). Statins are approved by the US Food and Drug Administration for use in children 8 years or older and are the first-line pharmacotherapy treatment for children with elevated LDL-C levels.

Figure. Clinician Summary: Screening for Lipid Disorders in Children and Adolescents

What does the USPSTF recommend?	For children and adolescents 20 years or younger: The USPSTF found that the current evidence is insufficient to assess the balance of benefits and harms of screening for lipid disorders. Grade: I statement
To whom does this recommendation apply?	This recommendation statement applies to children and adolescents who do not have signs or symptoms of a lipid disorder.
What's new?	This recommendation statement is consistent with the 2016 USPSTF recommendation.
How to implement this recommendation?	• There is insufficient evidence to recommend for or against screening for lipid disorders in children and adolescents. The USPSTF is calling for more long-term data on the effectiveness of screening for and treatment of lipid disorders in the general pediatric population to prevent premature cardiovascular events or death in adulthood. • In the absence of evidence, clinicians are encouraged to use their judgment when deciding whether to screen for lipid disorders in children and adolescents.
What additional information should clinicians know about this recommendation?	• There are 2 main types of lipid disorders seen in children and adolescents: familial hypercholesterolemia (FH) and multifactorial dyslipidemia. FH is a genetic disorder of cholesterol metabolism that causes very high levels of low-density lipoprotein cholesterol early in life. Multifactorial dyslipidemia is much more common than FH and is primarily associated with environmental factors such as excessive intake of saturated fat, sedentary lifestyle, and obesity. • The evidence review for FH focused on heterozygous FH, because it is the most common type of FH. Dyslipidemia due to homozygous FH or secondary causes (such as diabetes, nephrotic syndrome, or hypothyroidism), and targeted screening based on family history of premature cardiovascular events, are outside the scope of this review.
Why is this recommendation and topic important?	• Cumulative exposure to abnormal lipid levels over time can lead to early atherosclerotic changes and premature cardiovascular events or death in adulthood. • Interventions to lower lipid levels are available, including lifestyle modification (eg, changes in diet and physical activity), medication (eg, statins), and dietary supplements (eg, plant sterols or fish oil).
What are other relevant USPSTF recommendations?	The USPSTF has recommendation statements on screening for obesity and high blood pressure in children and adolescents. These recommendation statements are available at https://www.uspreventiveservicestaskforce.org/uspstf/
What are additional tools and resources?	• The National Heart, Lung, and Blood Institute's Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents developed evidence-based guidelines to assist primary care professionals in promoting cardiovascular health and identifying and managing specific cardiovascular risk factors from infancy into young adult life (https://www.nhlbi.nih.gov/node/80308). • The US Department of Health and Human Services published the "Physical Activity Guidelines for Americans," which provide evidence-based recommendations for how physical activity can help promote health and reduce the risk of chronic disease for Americans 3 years or older (https://health.gov/our-work/nutrition-physical-activity/physical-activity-guidelines). • The US Departments of Agriculture and Health and Human Services published the "Dietary Guidelines for Americans," which provide advice on what to eat and drink at every stage of life to build a healthy diet that can help prevent chronic diseases (https://www.dietaryguidelines.gov/). • The Community Preventive Services Task Force recommends interventions promoting physical activity and healthy eating across the life span, including specific recommendations for youth (https://www.thecommunityguide.org/).
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org/uspstf/) or the *JAMA* website (https://jamanetwork.com/collections/44068/united-states-preventive-services-task-force) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

USPSTF indicates US Preventive Services Task Force.

Treatment algorithms for FH and multifactorial dyslipidemia differ because of the substantially higher lipid levels associated with FH.[1]

Suggestions for Practice Regarding the I Statement

Potential Preventable Burden

Familial hypercholesterolemia is generally asymptomatic in childhood and adolescence and is rarely associated with cardiovascular events in the first 2 decades of life. However, FH can cause early cardiovascular morbidity and mortality in adulthood from cumulative exposure to high LDL-C levels and atherosclerotic changes starting as early as age 8 years.[1]

Robust evidence from studies conducted primarily before statins were commonly used show that a diagnosis of FH substantially increases risk for cardiovascular events in adulthood. A meta-analysis of 68 565 adults from 6 US cohorts found that the FH phenotype, defined by an LDL-C level of 190 mg/dL or greater (to convert LDL-C values to mmol/L, multiply by 0.0259), was associated with an adjusted hazard ratio (HR) of 4.1 (95% CI, 1.2-13.4) for cardiovascular disease events over 30 years of follow-up, compared with a reference group defined by an LDL-C level of less than 130 mg/dL. Investigators also found that the FH phenotype accelerated coronary heart disease risk by 10 to 20 years in men and 20

to 30 years in women.[3] Observational studies in adults with FH recruited from lipid clinics suggest that the prognosis of FH has improved substantially with the advent of statin treatment.[4,5]

Prognostic data for FH as determined by genotype (rather than LDL-C levels) are more limited. Data suggest that carriers of the FH genetic variant are at increased risk for coronary artery disease at any level of LDL-C. For example, the odds ratio for coronary artery disease was 5.2 (95% CI, 4.4-6.2) for an individual with an LDL-C level of 190 to 220 mg/dL or greater but without a genetic variant (compared with an individual with an LDL-C level <130 mg/dL and no genetic variant). However, the odds ratio for coronary heart disease was 17.0 (95% CI, 5.3-77.9) among individuals with this level of LDL-C in the presence of an FH genetic variant.[6]

Multifactorial dyslipidemia in adulthood is widely established as a risk factor for cardiovascular disease based on evidence showing strong associations between cholesterol levels in adulthood and ischemic heart disease mortality.[7] Linking elevated lipid levels in children to adult cardiovascular outcomes requires long follow-up. A 2022 publication from the International Childhood Cardiovascular Cohorts (i3C) Consortium suggests that elevated lipid levels in childhood (ages 3 to 19 years) are associated with fatal cardiovascular events in adulthood with 35 years of follow-up; however, the evidence is complicated by childhood risk factors tracking into adulthood and the lack of control for other risk factors.[8]

Potential Harms

Available pharmacotherapy trials and observational follow-up studies in children and adolescents showed no significant differences in harms between control and intervention groups. Abnormal liver and musculoskeletal laboratory values were reported with statin use; however, most trials were short term and small with few events, leading to imprecise estimates. Additionally, the clinical importance of transient elevations in these laboratory values is unknown.[1]

Current Practice

Lipid screening practices in US pediatric populations vary. Recent studies investigating screening practices in large US health care organizations found universal screening rates of 2% to 9% in children aged 9 to 11 years. Higher weight status, non-White race or ethnicity, and the presence of comorbid conditions were associated with higher screening rates in these studies.[1]

Screening based on risk factors can be unreliable, leading to underdiagnosis and undertreatment. The genetic disorder that causes FH is not related to obesity, and studies show that patient reports of family history of lipid disorders or premature cardiovascular events are inaccurate. Higher body mass index is a risk factor for multifactorial dyslipidemia; however, screening guided by weight status alone could miss a significant number of children with multifactorial dyslipidemia who do not have overweight or obesity. Another approach sometimes used is universal screening in certain age groups.[1,9,10]

There are no universally accepted criteria for the diagnosis of FH. A combination of elevated lipid levels, physical findings, family history, or genetic tests are used to establish the diagnosis. Abnormal lipid value cut points for defining multifactorial dyslipidemia are based on population norms and correspond to approximately the 95th percentile of population-based cohorts. These thresholds, however, have not been validated as predictors for cardiovascular disease events and are not age- and sex-specific.[1]

Additional Tools and Resources

The National Heart, Lung, and Blood Institute's Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents developed comprehensive, evidence-based guidelines addressing the known risk factors for cardiovascular disease to assist all primary care professionals in both the promotion of cardiovascular health and the identification and management of specific risk factors from infancy into young adult life (https://www.nhlbi.nih.gov/node/80308).[9]

The US Department of Health and Human Services published the "Physical Activity Guidelines for Americans," which provide evidence-based recommendations for how physical activity can help promote health and reduce the risk of chronic disease for Americans 3 years or older (https://health.gov/our-work/nutrition-physical-activity/physical-activity-guidelines).[11]

The US Departments of Agriculture and Health and Human Services published the "Dietary Guidelines for Americans," which provide advice on what to eat and drink at every stage of life to build a healthy diet that can help prevent chronic diseases (https://www.dietaryguidelines.gov/).[12]

The Community Preventive Services Task Force recommends interventions promoting physical activity and healthy eating across the life span, including specific recommendations for youth (https://www.thecommunityguide.org/).[13]

Other Related USPSTF Recommendations

The USPSTF recommends that clinicians screen for obesity in children 6 years or older and offer them or refer them to a comprehensive, intensive behavioral intervention to promote improvements in weight status (B recommendation).[14] The USPSTF found insufficient evidence on screening for high blood pressure in children and adolescents to prevent subsequent cardiovascular disease in childhood or adulthood (I statement).[15]

Update of Previous USPSTF Recommendation

In 2016, the USPSTF found insufficient evidence to assess the balance of benefits and harms of screening for lipid disorders in children and adolescents 20 years or younger (I statement).[16] This recommendation concurs with the previous I statement.

Supporting Evidence

Scope of Review

The USPSTF commissioned a systematic review to evaluate the benefits and harms of screening for lipid disorders in asymptomatic children and adolescents.[1,17] In 2016, separate reports were issued for FH and multifactorial dyslipidemia. The current systematic evidence review presents updated evidence in a single report that clearly delineates the evidence specific to each condition. The review on FH focuses on heterozygous FH because it is the most common monogenic cause of dyslipidemia. Dyslipidemia due to homozygous FH or secondary causes (such as diabetes,

nephrotic syndrome, or hypothyroidism), and targeted screening based on family history of premature cardiovascular events, are outside the scope of the review.

Accuracy of Screening Tests and Risk Assessment

No studies performed a confirmatory lipid or genetic test; thus, evidence is limited to screen positivity (prevalence) rather than diagnostic yield of lipid screening for identifying FH and multifactorial dyslipidemia. Prevalence of any lipid abnormality in 6- to 19-year-olds was 19.2% based on 2013 to 2016 data from the National Health and Nutrition Examination Survey (n = 4381).[1,17]

Familial Hypercholesterolemia

The USPSTF reviewed 3 fair-quality US studies (n = 395 465) reporting prevalence of FH ranging from 0.2% to 0.4% (1/250 to 1/500) using diagnostic criteria exclusively based on lipid levels (LDL-C ≥190 mg/dL or total cholesterol ≥270 mg/dL [to convert total cholesterol values to mmol/L, multiply by 0.0259]).[1,17] One study screening for cardiovascular risk factors among fifth graders (n = 20 266) found that among 14 468 students with a positive family history of premature cardiovascular disease, 1.2% had a fasting LDL-C level of 160 mg/dL or greater; 1.7% of 5798 students without a family history of premature cardiovascular disease had a fasting LDL-C level of 160 mg/dL or greater.[18] These results show that targeted screening in children with a family history of hypercholesterolemia or premature cardiovascular disease would miss many cases of children with an elevated LDL-C level of 160 mg/dL or greater.

Multifactorial Dyslipidemia

The USPSTF reviewed 5 fair-quality studies (n = 142 257) reporting prevalence of multifactorial dyslipidemia. Prevalence ranged from 7.1% to 9.4% for elevated total cholesterol level (≥200 mg/dL), 6.4% to 7.4% for elevated LDL-C level (≥130 mg/dL), 12.1% to 22.2% for low HDL-C level (<40 mg/dL [to convert HDL-C values to mmol/L, multiply by 0.0259]), 8.0% to 17.3% for elevated triglyceride level (using various thresholds), and 6.4% to 13.0% for elevated non–HDL-C level (≥145 mg/dL [to convert non–HDL-C values to mmol/L, multiply by 0.0259]). Older age and higher body mass index were associated with higher prevalence of multifactorial dyslipidemia.[1,17]

Benefits of Early Detection and Treatment

No studies directly assessed the effectiveness of screening for FH or multifactorial dyslipidemia in children and adolescents to delay or reduce poor health outcomes (eg, myocardial infarctions, strokes, or cardiovascular-related or all-cause deaths) or improve intermediate outcomes (eg, serum lipid levels or atherosclerotic markers).[1,17]

Familial Hypercholesterolemia

The USPSTF reviewed 22 fair- to good-quality trials (n = 2257) examining the effectiveness of lipid-lowering treatments in individuals with FH, including pharmacotherapy, behavioral counseling, and dietary supplements. Trials were generally small and short term, and none reported effects on cardiovascular events or mortality. The evidence was strongest for statins causing the highest reductions in total cholesterol and LDL-C levels. Pharmacological effect on triglyceride and HDL-C levels was mixed. The review included 10 fair- to good-quality randomized clinical trials (n = 1230) of statins, with follow-up for up to 2 years. Pooled analyses demonstrated that statins were associated with an 81- to 82-mg/dL greater mean reduction in total cholesterol and LDL-C levels compared with placebo (total cholesterol: 7 studies [n = 706]; mean difference in change, −82.1 mg/dL [95% CI, −101.1 to −63.2 mg/dL]; LDL-C: 8 studies [n = 742]; mean difference in change, −81.3 mg/dL [95% CI, −97.6 to −65.0 mg/dL]). Other studies reporting lipid-lowering effects from bile acid sequestrant, ezetimibe, proprotein convertase subtilisin/kexin type 9 inhibitor, and statin plus ezetimibe combination drugs showed statistically significant reductions, but none as substantial as from statins alone; mean reduction in total cholesterol and LDL-C levels from nonstatin drugs peaked around −69 mg/dL. Despite large changes in LDL-C levels associated with statins, many children with FH do not achieve LDL-C goals due to high baseline values. No more than 60% of participants in the statin group achieved goal in 4 trials reporting this metric.[1,17]

Evidence from a very small, fair-quality behavioral counseling trial in an FH population (n = 21) showed that this intervention was not effective in lowering lipid levels or changing physical activity or diet behaviors. Supplements showed mixed results, with the best evidence supporting plant sterol spreads. Two fair-quality plant sterol supplement trials (n = 82) in FH populations showed statistically significant reductions of 20.5 to 30.5 mg/dL in total cholesterol level and 22.4 to 30.1 mg/dL in LDL-C level at 4 to 8 weeks. Two trials of omega-3 fatty acids did not show a statistically significant difference in lipid level changes between the intervention and control groups.[1,17]

Multifactorial Dyslipidemia

No trials of drug interventions in children and adolescents with multifactorial dyslipidemia met inclusion criteria. The USPSTF reviewed 4 fair- to good-quality trials (n = 1008) examining the effectiveness of various nonpharmacologic lipid-lowering treatments for multifactorial dyslipidemia. Two behavioral counseling trials (n = 934) with dietary interventions varying in intensity, duration, and follow-up showed a 3- to 6-mg/dL statistically significant reduction in total cholesterol and LDL-C levels and improvements in dietary intake in the intervention group compared with the control group; however, these findings did not persist at longer follow-up. Two small, fair-quality supplement intervention trials (n = 74) examining flaxseed and fish oil in populations with multifactorial dyslipidemia showed that these supplements did not improve lipid outcomes at 4 to 8 weeks.[1,17]

Familial Hypercholesterolemia or Multifactorial Dyslipidemia

The USPSTF reviewed 7 fair- to good-quality short-term supplement trials (n = 288) in populations of children and adolescents with FH or multifactorial dyslipidemia. Results for various supplement interventions were limited, inconsistent, or showed no difference between intervention and control groups.[1,17]

Harms of Screening and Treatment

No studies reported on the harms of screening for FH or multifactorial dyslipidemia in children and adolescents.[1,17]

Familial Hypercholesterolemia

Overall, harms reported in pharmacotherapy trials were similar in the intervention and control groups; however, most studies were relatively short term and small, with few events, leading to imprecise estimates. Further, the clinical importance of transient elevations in liver enzyme or creatine kinase levels is unknown.[1,17]

In the statin trials discussed above, elevated liver enzyme levels of 3 times or more the upper limit of normal occurred in 0% to 4.5% of participants in intervention groups and 0% to 1.9% of participants in control groups. The largest trial (n = 214), with 2-year follow-up, reported no cases in the statin group and only 2 cases meeting the more than 3 times the upper limit of normal threshold in the control group. In the 10-year observational follow-up of this trial, elevated liver enzyme levels at this threshold were similarly rare.[1,17] Elevations in musculoskeletal laboratory values were also rare. Abnormal creatine kinase levels of 10 times or more the upper limit of normal ranged from 0% to 4.5% among participants in the statin group and from 0% to 1.7% among participants in the control group; 10-year observational follow-up in 1 trial reported no instances of elevated creatine kinase levels. There were no significant differences in Tanner staging or hormonal adverse events between statin and placebo groups in these trials or with longer observational follow-up. A fair-quality observational study (n = 9393) evaluating the association of statins and new-onset diabetes showed no difference in new diabetes diagnoses over up to 9 years of follow-up in individuals taking statins compared with control groups.[1,17]

Studies reporting adverse events in nonstatin trials were small and short term and showed similar harms between the control and intervention groups. The diet and physical activity counseling intervention trial did not mention harms, and the 3 supplement trials for FH reported that there were no adverse events.[1,17]

Multifactorial Dyslipidemia

The 2 behavioral counseling trials discussed above reported no harms associated with this intervention. One small flaxseed study (n = 32) noted a worsening in HDL-C and triglyceride levels[1]; however, the small study size and fluctuation of lipid laboratory values over time and in different age groups makes the clinical significance of this finding unknown. A small fish oil study (n = 42) noted that gastrointestinal symptoms, fishy taste, and frequent nosebleeds were more common in the intervention group than in the control group.[1]

Familial Hypercholesterolemia or Multifactorial Dyslipidemia

In studies including individuals with FH or multifactorial dyslipidemia, gastrointestinal adverse effects were observed with fiber supplements. However, these studies were limited and had short trial durations of 5 to 16 weeks.[1,17]

How Does Evidence Fit With Biological Understanding?

The association between elevated adult lipid levels and adult cardiovascular events is well established. Evidence linking abnormal lipid levels in childhood to adult cardiovascular disease requires studies with decades-long follow-up. Three robust analyses suggest that cumulative exposure to elevated lipid levels in childhood and young adulthood is associated with adult cardiovascular disease; however, the evidence has limitations. The i3C Consortium published a pooled analysis of 7 prospective cohort studies (n = 38 589) that followed up participants who had cardiovascular risk factors measured in childhood over a mean of 35 years and evaluated subsequent cardiovascular events in adulthood. Hazard ratios for a fatal cardiovascular event in adulthood were 1.30 (95% CI, 1.14-1.47) per unit increase in the *z* score for total cholesterol level (which describes standard deviations from the mean) and 1.50 (95% CI, 1.33-1.70) per unit increase in the *z* score for triglyceride level. This increased risk, however, dissipated and became statistically nonsignificant when a combined risk factor score for adults was considered, suggesting that the effect occurs largely because childhood risk factors track to adult risk factors. Additionally, the analysis used combined risk factors, so individual cardiovascular risk factors, such as lipid levels exclusively, were not examined independently.[8]

A pooled analysis of 36 030 participants from 6 US-based cohort studies with a median follow-up period of 17 years examined the independent association between exposure to high lipid levels in young adulthood (ages 18 to 39 years) and later cardiovascular events. Results showed that exposure to LDL-C levels of 100 mg/dL or greater in young adulthood was associated with an adjusted HR of 1.64 (95% CI, 1.27-2.11) for coronary heart disease compared with LDL-C levels of less than 100 mg/dL in young adulthood.[19] Another study selected genes associated with lower LDL-C levels and through a meta-analysis quantified the association between long-term lower LDL-C levels and the risk of coronary heart disease. Results suggested that lower LDL-C levels throughout the life span were associated with substantially lower risk of coronary heart disease in adulthood compared with initiating lipid-lowering treatment later in life.[20] Limitations for applicability of these data include risk factors that were combined and not independently evaluated, generalizability to younger ages in studies in which participants were young adults, and measurement of health outcome in the third or fourth decade of life, which may be too early to detect a cardiovascular event.

A new 20-year follow-up study (n = 214) from a randomized clinical trial of children and their parents identified with FH demonstrated that early initiation of statins in adolescence was associated with improved cumulative cardiovascular disease–free survival at age 39 years compared with their parents' delayed treatment in adulthood. Children with confirmed FH who started statins in youth (mean statin initiation age, 14.0 [SD, 3.1] years) had higher rates of cardiovascular disease–free survival compared with their parents, for whom statins were not available until adulthood (99% vs 74% cardiovascular disease–free survival; HR, 11.8 [95% CI, 3.0-107.0], adjusted for sex and smoking status).[21] Although these data hold promise, several study characteristics may make results hard to translate to a general screen-detected pediatric population, including small sample size; generalizability to a primary care pediatric population, because all participants were recruited from a lipid clinic and ultimately confirmed to have an FH genetic mutation; and applicability to the US population in which genetic testing for FH may not be widely available or easily accessible.

Response to Public Comment

A draft version of this recommendation statement was posted for public comment on the USPSTF website from January 24, 2023, to February 21, 2023. In response to comments, the USPSTF clarified descriptions of FH prevalence, polygenic variants, and health outcomes in the Importance, Practice Considerations, and Supporting Evidence sections. The USPSTF corrected a reference value in the Practice Considerations section and clarified in the Supporting

Evidence section that the review focused on heterozygous FH because it is the most common monogenic cause of dyslipidemia.

Research Needs and Gaps

Studies are needed that provide the following information.

- Long-term data on the effectiveness of screening for and treatment of lipid disorders in children and adolescents to prevent premature cardiovascular events or death in adulthood.
- Measurement of the diagnostic yield of lipid screening tests through confirmatory lipid and genetic testing to identify children and adolescents with FH and multifactorial dyslipidemia.
- Comparative effectiveness data assessing the optimal age at which to start lipid-lowering interventions for maximal benefit in children and adolescents diagnosed with FH or multifactorial dyslipidemia, including benefits and harms of starting pharmacologic treatment as a child (eg, ages 8 to 10 years) vs as a young adult (early 20s).
- Long-term data on the harms of screening and treatment.

Recommendations of Others

The National Heart, Lung, and Blood Institute's Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents, the American Academy of Pediatrics' Bright Futures program, and the multisociety Guideline on the Management of Blood Cholesterol recommend selectively screening children with a family history of cardiovascular disease or dyslipidemia or other risk factors as early as age 2 years. They also recommend universally screening children aged 9 to 11 years and again at ages 17 to 21 years.[9,10,22] The American Academy of Family Physicians references the USPSTF's 2016 conclusion that there is insufficient evidence to recommend for or against routine screening for lipid disorders in children and adolescents.[23] International guidelines for lipid screening in children and adolescents vary.

ARTICLE INFORMATION

Accepted for Publication: June 7, 2023.

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Author Contributions: Dr Barry had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. The USPSTF members contributed equally to the recommendation statement.

Conflict of Interest Disclosures: Authors followed the policy regarding conflicts of interest described at https://uspreventiveservicestaskforce.org/uspstf/about-uspstf/conflict-interest-disclosures. All members of the USPSTF receive travel reimbursement and an honorarium for participating in USPSTF meetings. Dr Barry reported receiving grants from Healthwise, a nonprofit, outside the submitted work. No other disclosures were reported.

Funding/Support: The USPSTF is an independent, voluntary body. The US Congress mandates that the Agency for Healthcare Research and Quality (AHRQ) support the operations of the USPSTF.

Role of the Funder/Sponsor: AHRQ staff assisted in the following: development and review of the research plan, commission of the systematic evidence review from an Evidence-based Practice Center, coordination of expert review and public comment of the draft evidence report and draft recommendation statement, and the writing and preparation of the final recommendation statement and its submission for publication. AHRQ staff had no role in the approval of the final recommendation statement or the decision to submit for publication.

Disclaimer: Recommendations made by the USPSTF are independent of the US government. They should not be construed as an official position of AHRQ or the US Department of Health and Human Services.

Additional Contributions: We thank Brandy Peaker, MD, MPH (AHRQ), who contributed to the writing of the manuscript, and Lisa Nicolella, MA (AHRQ), who assisted with coordination and editing.

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