**Lipid Screening in Youth**

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**Abstract**

As improvements in cardiovascular disease (CVD) risk reduction in adults’ plateau and risk factor accumulation in youth accumulates, focus is shifting to children as the future of CVD prevention. Abnormal lipid levels are relatively common in the pediatric population and treatments are available and effective thereby supporting the need to screen children for abnormal lipids. Recent data suggests that lipid screening is occurring in youth but is neither detecting the expected proportion of affected individuals nor translating into higher rates of therapy. Future work should expand on current screening efforts and overcome identified barriers to lipid screening toward the goal of avoiding CVD events and maintaining the ideal CVD health of childhood throughout the life course.

**Introduction**

Salutary trends in adult CVD mortality are documented and appear to stem largely from improvements in atherosclerotic risk factor treatment (1). But key danger signals are also present. First the rate of improvement is waning. Second and perhaps not coincidentally, recent advances focus on reducing thresholds for pharmacological risk factor management and thereby enlarge the proportion of the population eligible for therapy (2, 3). Finally, an alarming trend toward high and increasing obesity, obesity-related dyslipidemia, and type 2 diabetes portend an impending tidal wave of CVD (1).

Recent data has demonstrated the first continuous decline in average life expectancy during peacetime in modern American history wherein some component is due to increasing ASCVD in older age groups (4). Population data from 1999-2016 demonstrates lipid abnormalities in one-fifth of children and one-fourth of teenagers (5). At a point where progress is plateauing and efforts are being made to medicate wider swaths of the adult population, children offer an opportunity in the life course to further intensify CVD risk reduction. Childhood is a key time point for progress because children are already accumulating atherosclerotic phenotypic changes, have a high prevalence of CVD risk factors, are susceptible to deleterious lifestyle influences but are also malleable to lifestyle habit alterations. Typically, children have not yet suffered from actual CVD events nor are they likely to in youth. As CVD primary prevention is preventing the first CVD event by the treatment of risk factors, and secondary prevention is evading recurrent CVD events in patients with a history of CVD, primordial prevention aims to prevent or delay development of CVD risk factors.

Professional groups including the American Academy of Pediatrics, American Diabetes Association, and governmental entities including the National Heart, Lung, and Blood Institute (NHLBI), and Department of Health and Human Services have promulgated scientific statements and practice preferences identifying primordial and primary CVD prevention generally and dyslipidemia management specifically as a priority area (6-8). The 2011 NHLBI guidelines recommend universal lipid screening for the general population at age 9-11 years. The most recent American Heart Association (AHA) guidelines on CVD risk reduction in high risk pediatric patients including homozygous FH, type 1 and 2 diabetes, end-stage renal disease, Kawasaki disease with persistent aneurysms, solid organ transplant vasculopathy, and childhood cancer survivors recommends non-fasting non-HDL screening yearly (9).

It is clear that population-wide interventions can be successful, as illustrated by cigarette use reduction (1). Tobacco smoking reduction has been achieved through mobilizing public sentiment; placing restrictions on the procurement, advertisement, and use of tobacco products; and use of economic disincentives. Similar efforts to reduce the causes of hyperlipidemia, hypertension, or obesity in adults meet entrenched resistance from the lack of data supporting second-hand harm from these lifestyle behaviors leading to trepidation about restricting an individual’s freedom of personal choice. In contrast, addressing CVD risk factors in children may be more acceptable because their lifestyle choices are appropriately constrained by caregivers. To illustrate, the fact that a child would consistently choose ice cream over cauliflower every day is immaterial to whether daily ice cream consumption in children should be discouraged. Therefore, focusing on children offers an opportunity to leverage an identified CVD risk factor abnormality into a multifaceted cardiometabolic remedy. Moreover, children are a powerful motivating factor for lifestyle change in their parents offering the promise for a multiplicative effect on a pediatric intervention. *But first we must find affected children.*

**Why is pediatric lipid screening appropriate?**

The passionate pediatric provider might be motivated to identify all CVD risk factors in every child with the hopes of improving the health of the population one individual at a time. But from a policy and implementation perspective screening tests entail certain trade-offs that must be addressed. These pitfalls include the occurrence of false testing results that may be rare in any individual case but virtually guaranteed when mandatorily applied to many cases; the downstream effects of a false test results in additional confirmatory testing and patient emotional distress; test-related harms when instantiated widely; ethical conflicts between identifying sick individuals versus testing related physical and emotional harms to unaffected individuals; and lastly cost-effectiveness concerns. Each of these general concerns is amplified when the patient in question is a developing, vulnerable child for whom identifying risk factors has lasting implications but screening related harms can also have lasting implications rippling through the family. To be more specific, whereas adult providers find a patient blood draw to be trivial, violating bodily integrity is not as facile in children or for their parents, and therefore for providers to order. Nonetheless, many diseases are screened for including with blood testing in the extremely vulnerable newborn period (10). This state screening of newborns searches for disorders with prevalences on the order of 0.02% for sickle cell disease to 0.004% for phenylketonuria. Each of the screened disorders has therapies of varying efficacy by disease. Decisions to screen for these diseases are in some part determined by adherence to the World Health Organization Criteria for screening after Wilson and Jungner’s classic formulation ([Table 1](https://www.ncbi.nlm.nih.gov/books/NBK395583/table/lipid_youth-screem.table1wils/?report=objectonly)) (11). These classic criteria offer excellent structure for a discussion of pediatric lipid screening.

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| **TABLE 1. Wilson & Jungner Criteria (11)** |
| 1. The condition sought should be an important health problem. |
| 2. There should be an accepted treatment for patients with recognized disease. |
| 3. Facilities for diagnosis and treatment should be available. |
| 4. There should be a recognizable latent or early symptomatic stage. |
| 5. There should be a suitable test or examination. |
| 6. The test should be acceptable to the population. |
| 7. The natural history of the condition, including development from latent to declared disease, should be adequately understood. |
| 8. There should be an agreed policy on whom to treat as patients. |
| 9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole. |
| 10. Case-finding should be a continuing process and not a “once and for all” project. |

**Natural History, Latency, Importance**

The causal relation between low density lipoprotein cholesterol (LDL-C) and CVD events is well established (12-17). Interventions lowering triglycerides (TG) have not been quite as successful but observational studies using genes in instrumental analysis have determined a prospective unconfounded relation between TG and CVD events (18,19). High density lipoprotein cholesterol (HDL) is associated with incident CVD in observational cohorts but multiple HDL specific interventions have not led to CVD event reduction leading to doubts about the so-called HDL hypothesis (16, 20-22).

In general, the relationship between lipid disorders and CVD events is well established. In children it is especially well studied in the Mendelian genetic disorder familial hypercholesterolemia, generally attributed to a dominant negative mutation in the receptor for LDL or apolipoprotein B component of LDL (13). Heterozygous FH occurs in 1 in 500 births while more recent studies suggest it may be as common as 1 in 250. Homozygous FH may be as common as 1 in 160,000 to 1 million (23,24). FH leads to markedly elevated LDL levels. Heterozygous girls suffer coronary events before age 60 in approximately 20% of cases and boys in 50% of cases, while homozygous children have events in the second decade of life (25-27,24). Prior to these events, these children are well documented to have vascular changes predictive of future CVD events (28). Even more common is lifestyle related high TG, low HDL atherogenic dyslipidemia which is present in nearly one in five youth under 17 years old (29,30). Data from young adults in CVD-free general population who have suffered unfortunate mortality from unrelated causes clearly demonstrate arterial atherosclerotic plaques and these plaques are predicted by elevated lipid levels earlier in life (31,11). In more recent data, lipids predict thicker carotid intimal medial thickness, stiffer aortae, and other preclinical atherosclerotic changes in CVD unaffected individuals (28, 34-37). Severe and moderate lipid abnormalities occur in youth; these dyslipidemias and hyperlipidemias have important consequences following a predictable pattern from lipid elevation to atherosclerotic progression and eventually CVD events; and are orders of magnitude more common than already universally screened for metabolic conditions.

**Accurate, Suitable, Facile, Repeatable Testing**

Blood testing is the definitive, rather straightforward mode of lipid abnormality detection with false positive rates of less than one percent. Classic practice is to obtain fasting lipid panels as the ideal, especially for detection of triglyceride elevations (6,27,38). However, obtaining fasting lipids in children can be challenging and so nonfasting lipid panels may be obtained initially with fasting panels obtained to confirm as necessary in an attempt to enhance acceptability (6). In addition, life-course issues are a core concern in lipid assessment of children. While prenatal detection of dyslipidemia is noted, infancy and young childhood is a notoriously difficult period for dyslipidemia assessment due to wildly varied diet habit and food preferences during a child’s introduction and embrace of solid food intake. Toddlers not infrequently habituate to an extremely limited dietary range which they broaden a few years later. Dietary habits and lipid levels tend to stabilize in the early school age until around 10 years of age when pubertal changes with a high degree of variability. Hormonal changes around puberty can be associated with substantial changes in lipid levels (6,25,38). Thus, children could be inappropriately labeled “abnormal” from lipid tests since CVD risk factors fluctuate throughout childhood and adulthood (39). The NHLBI Integrated Guidelines for CVD Risk Reduction in Children and Adolescents recommend taking the average of multiple lipid values to help avoid misclassification and errors from regression to the mean (6). But also similar to adults, single lipid measurements in childhood do predict adult atherosclerotic progression, thereby underscoring the utility of even a single lipid test (31-35).

Physical exam findings can induce lipid testing. For example, the presence of tendinous xanthomata on extensor surfaces in young child should trigger lipid investigation for familial hypercholesterolemia or other lipid disorders (6,39). Similarly, many providers appreciate a higher relative risk of lipid abnormalities in overweight or obese individuals. Overweight youth are known to have roughly double the risk of lipid problems while obese youth have roughly three times the risk (29,30,40). However nearly 10% of normal weight individuals have abnormal lipid levels. So, while it is true that excess weigh individuals are at higher risk of abnormal lipids, the converse is also true, that a substantial proportion of youth with abnormal lipids are normal weight. In fact. since nearly 35-45% of youth with abnormal lipids are normal weight, fixating on excess weight youth misses a substantial proportion of the population’s lipid problem. While the origins of both abnormal lipids and obesity derive from suboptimal diets, activity and inactivity levels, the two are not synonymous. This epidemiological conundrum is a key pillar in favor of the NHLBI guidelines recommending the extension from selective to universal screening of youth depending on age group ([Table 2](https://www.ncbi.nlm.nih.gov/books/NBK395583/table/lipid_youth-screem.birthto2ye/?report=objectonly)).

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|  **TABLE 2: NHLBI Recommendations on Lipid Testing by Age Group (6)** |
| Birth to 2 years | No screening |
| 2 to 8 years | Selective ScreeningFasting Lipid Profiles (Average of two sets) for:1st or 2nd degree relative with history of CVD or history of total cholesterol ≥ 240 mg/dL or child has CVD high or moderate risk factors or conditions  |
| 9 to 11 years | Universal Screening Non-fasting Lipid Profile followed by Fasting Lipid Profile for non-HDL≥145 or HDL≤40 or Fasting Lipid Profile with repeat if LDL≥ 130 mg/dL or non-HDL ≥145 mg/dL or HDL < 40mg/dL or TG ≥100mg/dL for under 10-year olds; LDL ≥130 mg/dL for at or over 10 year olds |
| 12 to 16 years | Selective ScreeningFasting Lipid Profiles (Average of two sets) for:1st or 2nd degree relative with history of CVD or history of total cholesterol ≥ 240 mg/dL or child has CVD high or moderate risk factors or conditions |
| 17 to 19 years | Universal ScreeningNon-Fasting Lipid Profile followed by Fasting Lipid Profile (average two sets) if non–HDL>145 mg/dL or HDL cholesterol< 40 mg/dL or Fasting Lipid Profile and If LDL> 130 mg/dL or non–HDL> 145 mg/dL or HDL< 40 mg/dL or TG> 130 mg/dL. Repeat FLP and average results  |
| 20 to 21 years | Universal ScreeningNon-Fasting Lipid ProfileNon–HDL> 190 mg/dL or HDL< 40 mg/dLMeasure FLP twice, average results or Fasting Lipid ProfileIf LDL> 160 mg/dL or non–HDL> 190 mg/dL or HDL< 40 mg/dL or TG> 150 mg/dLRepeat and average results |
| **CVD:** MI, angina, stroke, coronary bypass surgery, coronary stent, coronary angioplasty at or under 55 y in males, 65 y in females **High risk factors:** Hypertension that requires drug therapy (BP> 99th percentile 5 mm Hg), Current cigarette smoker, Body Mass Index at the 97th age-sex specific percentile**High risk conditions:** Diabetes mellitus Type 1 or Type 2, Chronic kidney disease, end-stage renal disease, post–renal transplant, post–orthotopic heart transplant, Kawasaki disease with current aneurysms**Moderate risk factors:** Hypertension that does not require drug therapy, Body Mass Index between 95th percentile and 97th percentile, HDL< 40 mg/dL**Moderate risk conditions:** Kawasaki disease with regressed coronary aneurysms, chronic inflammatory disease (systemic lupus erythematosus, juvenile rheumatoid arthritis), HIV infection, nephrotic syndrome |

The Guidelines recommend using relatively high thresholds to designate abnormal levels in conjunction with taking the average of multiple lipid values to help avoid misclassification and errors from regression to the mean. The NHLBI guidelines reflect the age-specific distribution of lipid levels while at the same time mirroring the acceptable lipid values category groupings of the Adult Treatment Panel III/National Cholesterol Education Program ([Table 3](https://www.ncbi.nlm.nih.gov/books/NBK395583/table/lipid_youth-screem.table3lipi/?report=objectonly)). The key CARDIAC study assessed selective versus universal lipid screening in a general population of more than 20,000 5th graders in West Virginia. Of these more than 70% met NCEP guidelines for selective lipid screening (41). Of those with mildly elevated LDL over 130mg/dL, NCEP guideline-based testing did not capture 30% of cases. Of those with LDL at or over 160 mg/dL, NCEP guidelines missed 37% of affected children. Therefore, universal lipid screening identifies children with either a modest or more marked elevations in LDL-C than selective screening. Universal screening becomes an attractive method to detect both genetic and lifestyle related dyslipidemias when considering parental lack of understanding about lipid levels, the ability of lipid lowering medications to prevent CVD events and treat lipid levels in affected parents, or a parent’s refusal to examine their own cholesterol levels hindering screening programs contingent on other exigencies (42-45). The NHLBI guidelines refine the universal screening to apply in age strata around age 10 primarily to detect genetic dyslipidemias and around age 18 when patient-driven lifestyle habits have been established and modifications can still occur just prior to the transition to full adult independence. On balance, lipid disorders appear to be accurately assessed through a simple investigation that can be repeated on multiple occasions.

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| **TABLE 3. NHLBI Guideline Lipid Thresholds by Age (mg/dl)** |
|  | **Acceptable** | **Borderline** | **Abnormal** |
| Total CholesterolChildren/AdolescentsYoung Adults |  <170<190 |  170-199190-224 |  ≥200≥225 |
| LDL CholesterolChildren/AdolescentsYoung Adults |  <110<120 |  110-129120-159 |  ≥130≥160 |
| Non-HDL Cholesterol Children/AdolescentsYoung Adults |  <120<150 |  120-144150-189 |  ≥145≥190 |
| Triglycerides0-9 years10-19 yearsYoung Adults |  <75<90<115 |  75-9990-129115-149 |  ≥100≥130≥150 |
| HDL CholesterolChildren/AdolescentsYoung Adults |  >45>45 |  40-4540-45 |  <40<40 |

**Treatability**

Lipid disorders also appear to be a treatable phenomenon. Compelling data from Braamskamp et al compared FH offspring who have been treated with stains from an early age followed to age 40 years with their parents until age 40. A dramatic separation in freedom from coronary event curves were seen with cumulative coronary event incidence of 25% in parents while only 1 offspring had an event. The presumed difference between these two genetically comparable groups is the youth age use of 3-hydroxy-3-methyl-glutaryl-CoA reductase (statins). Indeed, the one event in offspring occurred in a youth who self-discontinued therapy. These results suggest long-term LDL-C reduction is beneficial in delaying events (46). The effect of statins in treating LDL-C levels has been examined in randomized, placebo-controlled, clinical trials of FH children and found to be safe and efficacious. RCTs in children with FH age 8 to 17 years show that those in the statin group had regression of carotid IMT thickness (cIMT) while placebo was stable or worsened. In young FH adults’ statins use has led to a substantial reduction in coronary mortality (27,28,36,37,47). In the CHARON study children age 6-9, 10-13 and 14-17 treated with rosuvastatin showed LDL level reduction of 43%, 45%, and 35% respectively. There were no serious adverse events related to treatment and no deleterious effects on growth or sexual maturation (48). An elegant combined meta-analysis of randomized control trials trial-duration statin therapy was compared to metaanalyzed LDL-lowering genetic mutations on CVD events (49). CVD prevention per unit LDL decrease was several fold more effective by genetic polymorphism than by pharmacologic intervention. The implication was that the degree of LDL lowering was synergistically enhanced by the amount of time spent at a reduced LDL concentration (15,50). Another recent study comparing cholesterol at various ages in adulthood found lowering had better outcomes when occurring earlier in life (51). On balance observational data abounds on the safety and efficacy of pharmacologic LDL lowering in hyperlipidemia.

With respect to dietary modification in LDL-C patients, a key study in pediatric practice was the Dietary Intervention Study in Children which delivered a low total fat, saturated fat, and cholesterol message to 7-10-year-olds with elevated LDL. The trial successfully lowered LDL roughly 10% from baseline (52). The STRIP trial provided similar messaging into the infant age group with similar long-term results and no safety concerns throughout younger childhood (53). While it is true that meta-analytic data from adults suggests that dietary quality alterations are not associated with elevated CVD event risk, broad-based adult cohort studied are inappropriately applied to subpopulations presenting early in life with markedly abnormal lipid values (12). In addition, the NHLBI guidelines pursue primordial prevention by recommending for all children a widely accepted sensible diet approach which moderates simple carbohydrates, processed foods, and saturated fat as well as encourages vegetables and lean proteins.

Data on pharmacological or lifestyle modification in youth leading to CVD event reduction in adulthood are not yet available and are unlikely to be forthcoming given the logistical complexity and cost of clinical trials assessing CVD events in large numbers of children over several decades. In the absence of decades long trial data, the data previously quote on lifecourse cholesterol levels are relevant. In addition, anthropological epidemiology demonstrates lower rates of CVD in cultures with habitually low cholesterol on a population basis (15). Additional supportive data comes from cost-effectiveness modeling. Identifying and treating patients with FH yields costs of about $7000/quality-adjusted life year, which generally falls into a willing-to-pay threshold of virtually every high per capita income and many middle per capita income nations (54). Although the additional costs of universal screening are not known, the benefits of earlier CVD prevention in high-risk individuals would be considerable as will cost savings (55). The inferences from lifestyle and pharmacotherapy data stands against a common criticism that youth are not the appropriate population for lipid management. Indeed data, however limited, suggests youth are indeed worthy of respect as persons and health conditions they accrue are also worthy of inspection and intervention.

For the highly prevalent, high TG-low HDL so-called atherogenic dyslipidemia, the primary treatment of lifestyle modification has been towards weight management (56-60). These studies have noted consistent relations between weight loss and improved TG and HDL that may persist for up to 5 years. Other data suggests that changes in dietary quality toward a lower carbohydrate intake may be effective in a trend towards TG reduction and HDL improvement. Some publications detail the dominant role of dietary quality recommendations without weight loss documenting a roughly one-third reduction in TG (61). Therefore, specific dietary quality modification can modify abnormal lipids without affecting weight immediately. These dyslipidemia-specific dietary modifications are effective but onerous for families and so should not be applied to the entire population. When motivated to avoid medication, youth and families may become more engaged.

**Acceptability**

Focusing on kids ratifies their status as individuals worthy of care independent of their parents. Focusing on kids may also boost identification of dyslipidemic family members in a reverse cascade. Pediatric lipid screening and especially universal screening are controversial despite demonstrated failures of selective screening and examination-based screening (62-64). First, it is highly likely that a very small number will be inappropriately labeled as abnormal lipids due to fluctuating levels during childhood. Second, since obesity increases the risk of abnormal lipid values, objections arise about classifying a multitude of children already psychologically vulnerable from an “abnormal” weight label, with an “abnormal” cholesterol label. Adding to the problems of these already disadvantaged youth makes the child even more demoralized. All providers are concerned about pediatric lipid patients being loosely prescribed statins. The NHLBI panel mandates lifestyle alterations as the primary response, but there is skepticism (64). A survey of US pediatricians in 2013-2014 showed that only 26% were well informed about the 2011 NHLBI guidelines and 68% never or rarely screen healthy 9 to 11-year olds. Instead most providers screened based on family history of CVD or obesity. Most surprisingly, 62% and 89% believe that statins are appropriate for children and adolescents with LDL levels refractory to lifestyle modification but only 8% and 21% initiated statins (65).

Barriers to screening include health insurance availability and having a health care provider. Neither child’s age, family financial status, gender, obesity status, nor other health outcomes seemed to affect the likelihood of participating in lipid screening (41). Parents appeared to find lipid screening acceptable (66). However, in previous cascade screening programs of life-threatening FH where an index case leads to screening of 1st degree relatives, the prevalence of FH detected did not increase perhaps due to over 90% parents wanting possibly affected children to be screened but over 90% also wanting child testing to be done in the home (27,54,67,68). This preference has implications for lipid management logistics as well as inferences for parent preferences regarding minor children. Parental survey results in the general population of African-American families found most mothers of older children were in favor of cholesterol screening, but the majority of children with abnormal lipid levels did not return for follow-up due to doubts about test accuracy and the child’s anxiety or discomfort (69). Exacerbating the complicated parental attitudes are conflicted provider attitudes. Roughly three out of four providers believed future CVD risk could be prevented through pediatric lipid screening and treatment. But large majorities expressed lack of familiarity with pediatric lipid management while at the same time less than one-quarter would refer children to pediatric lipid specialists (70,71). So, lipid testing appears to be widely acceptable to families and providers, but with complex barriers to implementation.

**Effectiveness and Effects of Selective Screening**

Since lipid screening in children appears to satisfy all WHO criteria for screening, it would be useful to know the benefits of screening. Following on the results of the CARDIAC study, recent data details the era of selective screening up to the NHLBI guidelines of late 2011 (72-74). The first such study in the modern era showed lipid testing rates in a geographically dispersed managed health care system network from 2002 to 2012 actually appear to have decreased (72). The proportion detected with severe FH-level LDL elevation did increase over time, but the yearly detection rate and cumulative incidence of those identified were far below the expected proportion of the cohort with FH. Within those tested each year, the proportion detected with moderately high LDL elevation or low HDL increased 5- to 9-fold at a time when nationally representative general pediatric population data indicated HDL levels had generally risen and LDL levels declined. Increased detection of low HDL-C and declining cohort mean HDL-C level led to an inference providers were selectively testing youth with higher risk of having lifestyle dyslipidemia. Among those tested, the proportion with FH-level LDL was more than double the classic prevalence of FH suggesting that providers may also have been selectively screening youth with high risk of genetic dyslipidemia. A separate study based on 3 other managed care populations showed roughly similar screening proportions over a 3-year frame from 2007 to 2010, when accounting for cohort exclusions (74). In contrast, a study from the National Ambulatory Medical Care Survey (NAMCS) database showed an increasing trend in lipid testing, but with rates substantially lower than rates overall (73). The discrepancy may be related to NAMCS being composed of a national probability sample of physician self-reported data of outpatient encounters over a 1-week period. Using this approach, NAMCS data under-reports lipid testing by roughly 50% in adult patients (75). Moreover, the pediatric report included testing at well-child visits only and not subspecialty visits where high-risk youth may be more likely to be tested and treated (76).

Several studies have looked at screening after the promulgation of the 2011 NHLBI guidelines. Overall screening rates remain low but one study of patients in an ambulatory pediatric clinic demonstrated an increase in screening rates after 2011 from 17.1% to 20.1% (77). Other similar studies demonstrate no difference in screening patterns (78). Another study reviewed records from two pediatric clinics demonstrating only 27% adherence to the universal screening guidelines (79). With dismal screening rates many centers have implemented quality improvement efforts to increase screening rates. Peterson el al retrospectively reviewed charts of a general pediatric practice before and after guideline implementation, education initiatives, and EHR alerts demonstrating an increase in screening prevalence from 8.9% to 50% at the end of the study period (80). In a similar retrospective chart review an EHR prompt was created which required physicians to choose which lipid screening test was ordered or document why lipid screening was not performed. Lipid testing was also built into the 9, 10 and 11 year well child check order sets. With these efforts along with monthly data presentations by the QI team, authors showed a 64% increase in screening (81). In an alternate approach, a feasibility study on child-parent screening suggests testing at a well-child visit, particularly one where immunizations will be administered, as parents are primed for disease prevention (82).

Lipid screening does not necessarily lead to optimal outcomes. As noted, previous European data suggests a cascade screening approach did not substantively increase the prevalence of detected FH. In the CARDIAC universal screening study, parent telephone interviews were conducted between four and six weeks after screening. Only 40% of 342 respondents with at-risk children had made changes to their children’s diets in the immediate follow-up period and only 34% had modified physical activity (66). Data from the managed care network study showed that despite increased detection of severe dyslipidemia pharmacotherapy had not increased at all (72). The yearly rate of newly detected FH level LDL dwarfed the rate of pharmacotherapy initiation, signaling that screening for lipid abnormalities is not a panacea for improved lipid management. Finally, the International Childhood Cardiovascular Cohort Consortium found that incorporating lipid screening and clinical risk factor assessment provided a statistically significant improvement in prediction of cIMT in adulthood (83).

**Conclusions and Future Directions**

Pediatric lipid testing appears to satisfy multiple criteria to make it worthy of wide screening. It is acceptable, accurate, repeatable, and testing is widely available. The natural history is well understood and childhood is a clear period of mounting severity but still latent and modifiable through acceptable therapies including lifestyle modification and simple pharmacotherapy. Accumulated data suggests selective screening is ineffective at detecting relevant cases and in translation to robust therapies lending support for universal screening programs. But several aspects are worthy of attention and future study in pursuing lipid testing of youth. Several aspects bolstering the success of universal screening efforts have been enumerated by the CARDIAC study investigators. Informational materials managing expectations about what happens on screening day, the risk factors assessed in the program, and follow up after the screening is useful. Another paramount task is effectively processing screening results and facilitating referral to treatment facilities, which requires cooperation between local hospitals, laboratories, and testing site. Testing programs can be leveraged to discuss primordial prevention and primary prevention in the testing site or other locations where relevant children and families are gathered. Lipid results can also be integrated into broader health screening reports that includes not only other assessment results but also broadly applicable treatment recommendations. Integrating these previously documented features into ongoing or future programs would be of great utility. Moving forward additional data needs to be gathered on the broader effects of universal screening. These effects may include dyslipidemia cases detected, the referral to lifestyle modification practitioners, pharmacotherapy initiation and effects of therapy on improving lipid levels. Longer term studies are needed to document the CVD event risk modification stemming of early life CVD risk factor modification. Determinants of lipid testing, dyslipidemia identification, and lipid therapy need to be determined including at the patient, family, provider, practice, and geographic levels. While it appears to be a worthwhile endeavor, more study is urgently needed on improving the implementation of pediatric lipid screening.

**References**

1. Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. N Engl J Med. 2007;356(23):2388-98.

2. Group SR, Wright JT, Jr., Williamson JD, Whelton PK, Snyder JK, Sink KM, et al. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2015 Nov 26;373(22):2103-16. PubMed PMID: 26551272. Pubmed Central PMCID: 4689591.

3. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto AM, Jr., Kastelein JJ, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008 Nov 20;359(21):2195-207. PubMed PMID: 18997196.

4. Woolf SH, Schoomaker H. Life Expectancy and Mortality Rates in the United States, 1959-2017. JAMA.2019;322(20):1996–2016.

5. Perak AM, Ning H, Kit BK, de Ferranti SD, Van Horn LV, Wilkins JT, & Lloyd-Jones DM (2019). Trends in Levels of Lipids and Apolipoprotein B in US Youths Aged 6 to 19 Years, 1999-2016. Jama, 321(19), 1895–1905.

6. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics. 2011;128 Suppl 5:S213-S56.

7. American Academy of Pediatrics. National Cholesterol Education Program: Report of the Expert Panel on Blood Cholesterol Levels in Children and Adolescents. Pediatrics. 1992 Mar;89(3 Pt 2):525-84. PubMed PMID: 1538956. Epub 1992/03/01. eng.

8. Services DoHaH. Patient Protection and Affordable Care Act. 2010 [cited 2015 January 2015]. Available from: <http://www.gpo.gov/fdsys/pkg/BILLS-111hr3590enr/pdf/BILLS-111hr3590enr.pdf>.

9. de Ferranti SD, Steinberger J, Ameduri R, Baker A, Gooding H, Kelly AS, et al. (2019). Cardiovascular Risk Reduction in High-Risk Pediatric Patients: A Scientific Statement From the American Heart Association. Circulation, 139(13), 487–32.

10. Newborn screening expands: recommendations for pediatricians and medical homes--implications for the system. Pediatrics. 2008;121(1):192-217.

11. Wilson JMG, Jungner G. PRINCIPLES AND PRACTICE OF SCREENING FOR DISEASE. In: Organization WH, editor. Geneva: World Health Organization; 1968.

12. Astrup A, Dyerberg J, Elwood P, Hermansen K, Hu FB, Jakobsen MU, et al. The role of reducing intakes of saturated fat in the prevention of cardiovascular disease: where does the evidence stand in 2010? Am J Clin Nutr. 2011 Apr;93(4):684-8. PubMed PMID: 21270379. Pubmed Central PMCID: 3138219. Epub 2011/01/29. eng

13. Brown MS, Goldstein JL. Familial hypercholesterolemia: A genetic defect in the low-density lipoprotein receptor. N Engl J Med. 1976;294(25):1386-90.

14. Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. BMJ. 2003;326(7404):1423.

15. O'Keefe JH, Jr., Cordain L, Harris WH, Moe RM, Vogel R. Optimal low-density lipoprotein is 50 to 70 mg/dl: lower is better and physiologically normal. J Am Coll Cardiol. 2004 Jun 2;43(11):2142-6. PubMed PMID: 15172426. Epub 2004/06/03. eng.

16. Sachdeva A, Cannon CP, Deedwania PC, Labresh KA, Smith SC, Jr., Dai D, et al. Lipid levels in patients hospitalized with coronary artery disease: an analysis of 136,905 hospitalizations in Get With The Guidelines. Am Heart J. 2009 Jan;157(1):111-7 e2. PubMed PMID: 19081406. Epub 2008/12/17. eng.

17. Taylor F, Ward K, Moore TH, Burke M, Davey SG, Casas JP, et al. Statins for the primary prevention of cardiovascular disease. Cochrane Database SystRev. 2011 (1):CD004816.

18. Keech A, Simes RJ, Barter P, Best J, Scott R, Taskinen MR, et al. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. Lancet. 2005 Nov 26;366(9500):1849-61. PubMed PMID: 16310551.

19. Pare G, Anand SS. Mendelian randomisation, triglycerides, and CHD. Lancet. 2010 May 8;375(9726):1584-6. PubMed PMID: 20452504.

20. Holmes MV, Asselbergs FW, Palmer TM, Drenos F, Lanktree MB, Nelson CP, et al. Mendelian randomization of blood lipids for coronary heart disease. European heart journal. 2015 Mar 1;36(9):539-50. PubMed PMID: 24474739. Pubmed Central PMCID: PMC4344957.

21. Rader DJ, Hobbs HH. Disorders of Lipoprotein Metabolism. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 18. New York: McGraw-Hill; 2012.

22. Barter PJ, Caulfield M, Eriksson M, Grundy SM, Kastelein JJ, Komajda M, et al. Effects of torcetrapib in patients at high risk for coronary events. N Engl J Med. 2007 Nov 22;357(21):2109-22. PubMed PMID: 17984165.

23. Cuchel M, Bruckert E, Ginsberg HN, Raal FJ, Santos RD, Hegele RA, et al. (2014). Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. European Heart Journal, 35(32), 2146–2157.

24. Wiegman A, Gidding SS, Watts GF, Chapman MJ, Ginsberg HN, Cuchel M, et al. Familial hypercholesterolaemia in children and adolescents: gaining decades of life by optimizing detection and treatment. European heart journal. 2015 Sep 21;36(36):2425-37. PubMed PMID: 26009596. Pubmed Central PMCID: 4576143.

25. Daniels SR, Gidding SS, de Ferranti SD. Pediatric aspects of familial hypercholesterolemias: recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Clin Lipidol. 2011 Jun;5(3 Suppl):S30-7. PubMed PMID: 21600527. Epub 2011/05/27. eng.

26. Hopkins PN, Toth PP, Ballantyne CM, Rader DJ. Familial hypercholesterolemias: prevalence, genetics, diagnosis and screening recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Clin Lipidol. 2011 Jun;5(3 Suppl):S9-17. PubMed PMID: 21600530. Epub 2011/05/27. eng.

27. Williams RR, Hasstedt SJ, Wilson DE, Ash KO, Yanowitz FF, Reiber GE, et al. Evidence that men with familial hypercholesterolemia can avoid early coronary death. An analysis of 77 gene carriers in four Utah pedigrees. JAMA. 1986;255(2):219-24.

28. Kusters DM, Avis HJ, de Groot E, Wijburg FA, Kastelein JJ, Wiegman A, et al. Ten-year follow-up after initiation of statin therapy in children with familial hypercholesterolemia. JAMA. 2014 Sep 10;312(10):1055-7. PubMed PMID: 25203086. Epub 2014/09/10. eng.

29. Kit BK, Carroll MD, Lacher DA, Sorlie PD, J.M. D, C.L. O. Trends in serum lipids among US youths aged 6 to 19 years,1988-2010. JAMA. 2012;307(3):591-600.

30. Kit BK, Kuklina E, Carroll MD, Ostchega Y, Freedman DS, Ogden CL. Prevalence of and Trends in Dyslipidemia and Blood Pressure Among US Children and Adolescents, 1999-2012. JAMA Pediatr. 2015 Jan 19. PubMed PMID: 25599372. Epub 2015/01/20. Eng.

31. Berenson GS, Srinivasan SR, Bao W, Newman WP, 3rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N Engl J Med. 1998 Jun 4;338(23):1650-6. PubMed PMID: 9614255.

32. Newman WP, 3rd, Freedman DS, Voors AW, Gard PD, Srinivasan SR, Cresanta JL, et al. Relation of serum lipoprotein levels and systolic blood pressure to early atherosclerosis. The Bogalusa Heart Study. N Engl J Med. 1986 Jan 16;314(3):138-44. PubMed PMID: 3455748.

33. Relationship of atherosclerosis in young men to serum lipoprotein cholesterol concentrations and smoking. A preliminary report from the Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. JAMA. 1990 Dec 19;264(23):3018-24. PubMed PMID: 2243430.

34. Juhola J, Magnussen CG, Viikari JS, Kahonen M, Hutri-Kahonen N, Jula A, et al. Tracking of serum lipid levels, blood pressure, and body mass index from childhood to adulthood: the Cardiovascular Risk in Young Finns Study. J Pediatr. 2011 Oct;159(4):584-90. PubMed PMID: 21514597.

35. Raitakari OT, Juonala M, Kahonen M, Taittonen L, Laitinen T, Maki-Torkko N, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. JAMA. 2003 Nov 5;290(17):2277-83. PubMed PMID: 14600186. Epub 2003/11/06.

36. Avis HJ, Vissers MN, Stein EA, Wijburg FA, Trip MD, Kastelein JJ, et al. A systematic review and meta-analysis of statin therapy in children with familial hypercholesterolemia. ArteriosclerThrombVasc Biol. 2007;27(8):1803-10.

37. Versmissen J, Oosterveer DM, Yazdanpanah M, Defesche JC, Basart DC, Liem AH, et al. Efficacy of statins in familial hypercholesterolaemia: a long term cohort study. BMJ. 2008;337:a2423.

38. Daniels SR, Greer FR. Lipid screening and cardiovascular health in childhood. Pediatrics. 2008;122(1):198-208.

39. Risk of fatal coronary heart disease in familial hypercholesterolaemia. Scientific Steering Committee on behalf of the Simon Broome Register Group. BMJ. 1991 Oct 12;303(6807):893-6. PubMed PMID: 1933004. Pubmed Central PMCID: 1671226. Epub 1991/10/12. eng.

40. May AL, Kuklina EV, Yoon PW. Prevalence of cardiovascular disease risk factors among US adolescents, 1999-2008. Pediatrics. 2012 Jun;129(6):1035-41. PubMed PMID: 22614778. Epub 2012/05/23. eng.

41. Ritchie SK, Murphy EC, Ice C, Cottrell LA, Minor V, Elliott E, et al. Universal versus targeted blood cholesterol screening among youth: The CARDIAC project. Pediatrics. 2010 Aug;126(2):260-5. PubMed PMID: 20624798.

42. Hollman G, Olsson AG, Ek AC. Disease knowledge and adherence to treatment in patients with familial hypercholesterolemia. The Journal of cardiovascular nursing. 2006 Mar-Apr;21(2):103-8. PubMed PMID: 16601526.

43. Kools S, Kennedy C, Engler M, Engler M. Pediatric hyperlipidemia: child and adolescent disease understandings and perceptions about dietary adherence. Journal for specialists in pediatric nursing: JSPN. 2008 Jul;13(3):168-79. PubMed PMID: 18638047.

44. Mackie TI, Tse LL, de Ferranti SD, Ryan HR, Leslie LK. Treatment decision making for adolescents with familial hypercholesterolemia: Role of family history and past experiences. J Clin Lipidol. 2015 Jul-Aug;9(4):583-93 e1-3. PubMed PMID: 26228677.

45. Wierzbicki A, Ratcliffe C. The 2007 Heart-UK Survey of Lipid Clinics and Clinical Practice in the UK. Atherosclerosis. 2008;199:234.

46. Braamskamp, MJAM, Kastelein JJP, Kusters DM, Hutten BA, Wiegman A (2016). Statin Initiation During Childhood in Patients With Familial Hypercholesterolemia. Journal of the American College of Cardiology, 67(4), 455–456.

47. Vuorio A, Kuoppala J, Kovanen PT, Humphries SE, Strandberg T, Tonstad S, et al. Statins for children with familial hypercholesterolemia. Cochrane Database SystRev. 2010 (7):CD006401.

48. Braamskamp MJAM, Langslet G, McCrindle BW, Cassiman D, Francis GA, Gagné C, Gaudet D, Morrison KM, Wiegman A, Turner T, Kusters DM, Miller E, Raichlen JS, Wissmar J, Martin PD, Stein EA, Kastelein JJP (2015). Efficacy and safety of rosuvastatin therapy in children and adolescents with familial hypercholesterolemia: Results from the CHARON study. Journal of Clinical Lipidology, 9(6), 741–750.

49. Ference BA, Yoo W, Alesh I, Mahajan N, Mirowska KK, Mewada A, et al. Effect of long-term exposure to lower low-density lipoprotein cholesterol beginning early in life on the risk of coronary heart disease: a Mendelian randomization analysis. J Am Coll Cardiol. 2012 Dec 25;60(25):2631-9. PubMed PMID: 23083789. Epub 2012/10/23. eng.

50. Keys A, Menotti A, Aravanis C, Blackburn H, Djordevic BS, Buzina R, et al. The seven countries study: 2,289 deaths in 15 years. Prev Med. 1984 Mar;13(2):141-54. PubMed PMID: 6739443. Epub 1984/03/01. eng.

51. Brunner FJ, Waldeyer C, Ojeda F, Salomaa V, Kee F, Sans S, et al. (2019). Application of non-HDL cholesterol for population-based cardiovascular risk stratification: results from the Multinational Cardiovascular Risk Consortium. Lancet (London, England), 394(10215), 2173–2183.

52. Efficacy and safety of lowering dietary intake of fat and cholesterol in children with elevated low-density lipoprotein cholesterol. The Dietary Intervention Study in Children (DISC). The Writing Group for the DISC Collaborative Research Group. JAMA. 1995 May 10;273(18):1429-35. PubMed PMID: 7723156.

53. Lapinleimu H, Viikari J, Jokinen E, Salo P, Routi T, Leino A, et al. Prospective randomised trial in 1062 infants of diet low in saturated fat and cholesterol. Lancet. 1995 Feb 25;345(8948):471-6. PubMed PMID: 7861873.

54. Marks D, Thorogood M, Neil SM, Humphries SE, Neil HA. Cascade screening for familial hypercholesterolaemia: implications of a pilot study for national screening programmes. Journal of medical screening. 2006;13(3):156-9. PubMed PMID: 17007658.

55. Berwick DM, Cretin S, Keeler E. Cholesterol, children, and heart disease: an analysis of alternatives. Pediatrics. 1981 Nov;68(5):721-30. PubMed PMID: 6796932. Epub 1981/11/01. eng.

56. Epstein LH, Kuller LH, Wing RR, Valoski A, McCurley J. The effect of weight control on lipid changes in obese children. American journal of diseases of children. 1989 Apr;143(4):454-7. PubMed PMID: 2929526.

57. Jacobson MS, Tomopoulos S, Williams CL, Arden MR, Deckelbaum RJ, Starc TJ. Normal growth in high-risk hyperlipidemic children and adolescents with dietary intervention. Prev Med. 1998 Nov-Dec;27(6):775-80. PubMed PMID: 9922057. Epub 1999/01/28. eng.

58. Kirk S, Brehm B, Saelens BE, Woo JG, Kissel E, D'Alessio D, et al. Role of carbohydrate modification in weight management among obese children: a randomized clinical trial. J Pediatr. 2012 Aug;161(2):320-7 e1. PubMed PMID: 22381024. Pubmed Central PMCID: 3406261.

59. Siegel RM, Rich W, Joseph EC, Linhardt J, Knight J, Khoury J, et al. A 6-month, office-based, low-carbohydrate diet intervention in obese teens. Clinical pediatrics. 2009 Sep;48(7):745-9. PubMed PMID: 19264718.

60. Sondike SB, Copperman N, Jacobson MS. Effects of a low-carbohydrate diet on weight loss and cardiovascular risk factor in overweight adolescents. J Pediatr. 2003 Mar;142(3):253-8. PubMed PMID: 12640371.

61. Pratt RE, Kavey RE, Quinzi D. Combined dyslipidemia in obese children: response to a focused lifestyle approach. J Clin Lipidol. 2014 Mar-Apr;8(2):181-6. PubMed PMID: 24636177.

62. Newman TB, Pletcher MJ, Hulley SB. Overly aggressive new guidelines for lipid screening in children: evidence of a broken process. Pediatrics. 2012 Aug;130(2):349-52. PubMed PMID: 22826571. Epub 2012/07/25. eng.

63. Gillman MW, Daniels SR. Is universal pediatric lipid screening justified? JAMA. 2012;307(3):259-60.

64. Psaty BM, Rivara FP. Universal screening and drug treatment of dyslipidemia in children and adolescents. JAMA. 2012;307(3):257-8.

65. de Ferranti SD, Rodday AM, Parsons SK, Cull WL, O'Connor KG, Daniels SR, Leslie LK (2017). Cholesterol Screening and Treatment Practices and Preferences: A Survey of United States Pediatricians. The Journal of Pediatrics, 185, 99–105.e2.

66. Cottrell L, John C, Murphy E, Lilly CL, Ritchie SK, Elliott E, et al. Individual-, family-, community-, and policy-level impact of a school-based cardiovascular risk detection screening program for children in underserved, rural areas: the CARDIAC Project. J Obes. 2013;2013:732579. PubMed PMID: 23840946. Pubmed Central PMCID: PMC3687496.

67. Hardcastle SJ, Legge E, Laundy CS, Egan SJ, French R, Watts GF, et al. Patients' perceptions and experiences of familial hypercholesterolemia, cascade genetic screening and treatment. International journal of behavioral medicine. 2015 Feb;22(1):92-100. PubMed PMID: 24585182.

68. Morris JK, Wald DS, Wald NJ. The evaluation of cascade testing for familial hypercholesterolemia. Am J Med Genet A. 2012 Jan;158A(1):78-84. PubMed PMID: 22139944. Epub 2011/12/06. eng.

69. Price JH, Casler SM. African-American mothers' perceptions of cholesterol and its effects on their children. J Natl Med Assoc. 1996 Mar;88(3):145-50. PubMed PMID: 8839029. Pubmed Central PMCID: 2608033. Epub 1996/03/01. eng.

70. Kimm SY, Payne GH, Stylianou MP, Waclawiw MA, Lichtenstein C. National trends in the management of cardiovascular disease risk factors in children: second NHLBI survey of primary care physicians. Pediatrics. 1998 Nov;102(5):E50. PubMed PMID: 9794980. Epub 1998/10/31. eng.

71. Dixon DB, Kornblum AP, Steffen LM, Zhou X, Steinberger J. Implementation of Lipid Screening Guidelines in Children by Primary Pediatric Providers. J Pediatr. 2013 Nov 16. PubMed PMID: 24252785. Epub 2013/11/21. Eng.

72. Zachariah JP, McNeal CJ, Copeland LA, Fang-Hollingsworth Y, Stock EM, Sun F, et al. Temporal trends in lipid screening and therapy among youth from 2002 to 2012. J Clin Lipidol. 2015 Sep-Oct;9(5 Suppl):S77-87. PubMed PMID: 26343215. Pubmed Central PMCID: 4562073.

73. Vinci SR, Rifas-Shiman SL, Cheng JK, Mannix RC, Gillman MW, de Ferranti SD. Cholesterol testing among children and adolescents during health visits. JAMA. 2014 May 7;311(17):1804-7. PubMed PMID: 24794376. Epub 2014/05/06. eng.

74. Margolis KL, Greenspan LC, Trower NK, Daley MF, Daniels SR, Lo JC, et al. Lipid screening in children and adolescents in community practice: 2007 to 2010. Circulation Cardiovascular quality and outcomes. 2014 Sep;7(5):718-26. PubMed PMID: 25160839. Pubmed Central PMCID: 4167939. Epub 2014/08/28. eng.

75. Gilchrist VJ, Stange KC, Flocke SA, McCord G, Bourguet CC. A comparison of the National Ambulatory Medical Care Survey (NAMCS) measurement approach with direct observation of outpatient visits. Med Care. 2004 Mar;42(3):276-80. PubMed PMID: 15076827. Epub 2004/04/13. eng.

76. Gregory ST, McNeal CJ, Copeland LA. Rates of cholesterol screening of youth. JAMA. 2014 Oct 1;312(13):1353-4. PubMed PMID: 25268451.

77. Wilson DP, Davis S, Matches S, Shah D, Leung-Pineda V, Mou M, Hamilton L, McNeal CJ, Bowman WP(2015). Universal cholesterol screening of children in community-based ambulatory pediatric clinics. Journal of Clinical Lipidology, 9(S), S88–S92.

78. Mihalopoulos NL, Stipelman C, Hemond J, Brown LL, Young PC (2018). Universal Lipid Screening in 9- to 11-Year-Olds Before and After 2011 Guidelines. Academic Pediatrics, 18(2), 196–199.

79. Valle CW, Binns HJ, Quadri-Sheriff M, Benuck I, Patel A (2015). Physicians’ Lack of Adherence to National Heart, Lung, and Blood Institute Guidelines for Pediatric Lipid Screening. Clinical Pediatrics, 54(12), 1200–1205.

80. DeSantes K, Dodge A, Eickhoff J, Peterson AL (2017). Improving Universal Pediatric Lipid Screening. The Journal of Pediatrics, 188, 87–90.

81. Kern L, Crow J, Williams CB, Boies E, Gahagan S, Rhee KE (2017). Increasing Universal Lipid Screening Among 9- to 11-Year-Old Children Through a Quality Improvement Initiative. Clinical Pediatrics, 56(7), 640–647.

82. Wald DS, Bestwick JP, Morris JK, Whyte K, Jenkins L, Wald NJ (2016). Child–Parent Familial Hypercholesterolemia Screening in Primary Care. New England Journal of Medicine, 375(17), 1628–1637.

83. Koskinen J, Juonala M, Dwyer T, Venn A, Thomson R, Bazzano L, et al. (2018). Impact of Lipid Measurements in Youth in Addition to Conventional Clinic-Based Risk Factors on Predicting Preclinical Atherosclerosis in Adulthood. Circulation, 137(12), 1246–1255.