LIPID SCREENING IN YOUTH

Justin P. Zachariah MD, MPH, Section of Pediatric Cardiology, Texas Children's Hospital, Department of Pediatrics, Baylor College of Medicine, Houston, TX. justin.zachariah@bcm.edu

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ABSTRACT

As improvements in cardiovascular disease (CVD) risk reduction in adults' plateau and risk factors accumulate in youth, 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 towards 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), 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 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, KD 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 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 false test results in terms of 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 implication 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 prevalence's 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) (11). These classic criteria offer excellent structure for a discussion of pediatric lipid screening.

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) and CVD events is well established (12-17). Interventions of 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 (FH), generally attributed to a dominant negative mutation in the receptor for LDL receptor 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 (31-33). Lipids predict thicker carotid intimal medial thickness, stiffer aorta, and other preclinical atherosclerotic changes in CVD unaffected individuals (28, 34-37). More recent data combining

multiple youth cohorts into a single meta-cohort followed through adulthood clearly demonstrates lipids in childhood directly predict clinically definitive "hard" adult CVD events. Intriguing data also suggests childhood lipoprotein (a) concentrations predict adult "hard" CVD events, including in combination with other CVD risk factors like lipids. Thus, 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 non-fasting 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 habits 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 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).

TABLE 2. NHLBI Recommendations on Lipid Testing by Age Group (6)	
Birth to 2 years	No screening
2 to 8 years	Selective Screening Fasting 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 Screening Fasting 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 Screening Non-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 Screening Non-Fasting Lipid Profile Non–HDL> 190 mg/dL or HDL< 40 mg/dL Measure FLP twice, average results or Fasting Lipid Profile If LDL> 160 mg/dL or non–HDL> 190 mg/dL or HDL< 40 mg/dL or TG> 150 mg/dL Repeat 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). 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.

TABLE 3. NHLBI Guideline Lipid Thresholds by Age (mg/dL)

	Acceptable	Borderline	Abnormal
Total Cholesterol			
Children/Adolescents	<170	170-199	≥200
Young Adults	<190	190-224	≥225
LDL Cholesterol			
Children/Adolescents	<110	110-129	≥130
Young Adults	<120	120-159	≥160
Non-HDL Cholesterol			
Children/Adolescents	<120	120-144	≥145
Young Adults	<150	150-189	≥190
Triglycerides			
0-9 years	<75	75-99	≥100
10-19 years	<90	90-129	≥130
Young Adults	<115	115-149	≥150
HDL Cholesterol			
Children/Adolescents	>45	40-45	<40
Young Adults	>45	40-45	<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 statins from an early age followed to age 30 years with their parents until age 30. 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). That data has recently been extended to show protection through age 40. 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 those in the statin group had regression of carotid IMT thickness (cIMT) while the placebo group was stable or worsened. In young FH adults, statin 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 by 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 meta-analyzed 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 life course 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 general population 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 that 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 et 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 testing site or other locations where relevant children and families are gathered. Lipid results can also be integrated into broader health screening report that includes not only other assessment results but also broadly applicable treatment recommendations. Integrated 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 from 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.

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