Published in final edited form as:

J Clin Lipidol. 2015 ; 9(0): S77–S87. doi:10.1016/j.jacl.2015.06.014.

Temporal Trends in Lipid Screening and Therapy Among Youth from 2002–2012

Justin P. Zachariah, M.D. M.P.H.¹, Catherine J McNeal, M.D. Ph.D.², Laurel A. Copeland, Ph.D.³, Ying Fang-Hollingsworth, M.P.H.³, Eileen M. Stock, Ph.D.³, FangFang Sun, MS³, Joon Jin Song, PhD⁴, Sean T. Gregory, M.B.A. M.S. Ph.D.⁵, Jeffrey O. Tom, M.D. M.S.⁶, Eric A. Wright, Pharm.D.⁷, Jeffrey J. VanWormer, Ph.D.⁸, and Andrea E. Cassidy-Bushrow, Ph.D. M.P.H.⁹

¹Lillie Frank Abercrombie Section of Pediatric Cardiology, Texas Children's Hospital, Baylor College of Medicine, Houston TX

²Departments of Pediatrics and Internal Medicine, Baylor Scott & White Health, Temple TX

³Center for Applied Health Research, Baylor Scott & White Health and Central Texas Veterans Health Care System, Temple TX

⁴Department of Statistical Sciences, Baylor University, Waco TX

⁵Department of Health Policy & Management, College of Public Health, University of South Florida, Tampa, FL

⁶Kaiser Permanente Center for Health Research Hawaii, Honolulu HI

⁷Geisinger Center for Health Research, Danville PA and Department of Pharmacy Practice, Wilkes University, Wilkes-Barre PA

⁸Center for Clinical Epidemiology and Population Health, Marshfield Clinic Research Foundation, Marshfield WI

⁹Department of Public Health Sciences, Henry Ford Hospital, Detroit MI

Abstract

Background—Pediatric lipid management recommendations have evolved from selective screening to universal screening in order to identify and target therapy for genetic dyslipidemias. Data on the success of the selective screening guidelines for lipid testing, dyslipidemia detection and lipid management are conflicting.

Address for correspondence: Justin Zachariah M.D. M.P.H., Pediatric Cardiology, Texas Children's Hospital, 6621 Fannin St., Suite 19345C, Houston, TX 77030, Phone (832) 826-5600, Fax: (832) 825-5921, zachariah@bcm.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

We declare we have no relevant financial conflicts of interest or disclosures.

Some data was presented at American Heart Association Scientific Sessions 2013.

Objective—To determine temporal trends in lipid testing, dyslipidemia categories and pharmacotherapy in a cohort of 653,642 individual youth 2–20 years old from 2002–2012.

Methods—Summary data on lipid test results, lipid-lowering medicine (LLM) dispensings, and ICD-9 diagnoses were compiled from the Virtual Data Warehouses (VDW) of 5 sites in the Cardiovascular Research Network (CVRN). Temporal trends were determined using linear regression.

Results—Among the average 255,160±25,506 children enrolled each year, lipid testing declined from 16% in 2002 to 11% in 2012 ($p < 0.001$ for trend). Among the entire population, the proportion newly detected each year with low density lipoprotein cholesterol (LDL-C) >190mg/dL, a value commonly used to define familial hypercholesterolemia (FH), increased over time from 0.03% to 0.06% ($p = 0.03$ for trend). There was no significant change over time in the proportion of the yearly population initiated on LLM or statins specifically ($0.045 \pm 0.009\%$, $p = 0.59$ (LLM) and $0.028 \pm 0.006\%$, $p = 0.25$, (statin)).

Conclusions—While lipid testing declined during 2002–2012, the detection of FH-level LDL-C increased. Despite this increased detection, pharmacotherapy did not increase over time. These findings highlight the need to enhance lipid screening and management strategies in high-risk youth.

Keywords

dyslipidemia; familial hypercholesterolemia; youth; lipid testing; statin therapy; epidemiology; ASCVD

INTRODUCTION

Higher childhood cholesterol is clearly demonstrated to predict future cardiovascular disease (CVD).¹ More than 20% of adolescents have abnormal LDL-C concentrations and roughly half of those youth are normal weight.² About 0.2% of children inherit very elevated LDL-C as heterozygous familial hypercholesterolemia (FH). Pediatric lipid management guidelines are primarily designed to identify youth with FH, which imparts a 20- to 100-fold greater risk of coronary events, depending on gender, before age 50 compared to the general population.^{1, 3–6} Although there is a paucity of outcomes data in youth with FH, early use of HMG CoA reductase inhibitors (statins) in this population may mitigate the excess risk.^{7–9} In adults, recent data suggest that CVD protection garnered from pharmacologic LDL-C lowering in middle age is inferior to genetically-mediated lifelong lower LDL-C, supporting a focus on life-course risk reduction.¹⁰

Motivated by the probable benefits of long-term therapy and the presumed deficiencies of targeted screening based on high-risk family or personal history, pediatric guidelines have now expanded to include universal screening between ages 9 and 11 years and again between ages 17 and 21 along with targeted screening any time after 2 years of age.^{1, 11} The primary detection or cascade detection of serious dyslipidemias in youth could be affected based on recent adult American Heart Association/American College of Cardiology guidelines or European atherosclerosis Society Consensus panel guidelines.^{12, 13} Therefore data on prior practice patterns in youth is of high importance in determining both unmet

needs and as a baseline for future guideline related effects. Treatment recommendations focus on lifestyle modification for any LDL-C elevation including genetic dyslipidemias. Statin use is generally reserved for youth over 10 years of age with severe LDL-C elevations, generally over 190 mg/dL as a critical threshold associated with FH, or for those with slightly lower LDL-C levels in combination with additional guideline-defined CVD risk factors or conditions who are unresponsive to lifestyle modification.^{14–16}

The change to include universal lipid screening in youth has engendered much controversy.^{1, 14, 15, 17} Critics of universal screening highlight the high cost of non-targeted screening, lack of established clinical effectiveness with respect to CVD event reduction, as well as the possibility of creating diet or CVD-related neuroses and anxiety and family conflict.^{18–20} Additional concern is the potential harm that may be incurred if screening leads to the injudicious use of lipid-lowering medicines (LLM), including the pitfalls of using these medications as a facile response to unhealthy lifestyles and the lack of long-term safety and efficacy data.^{18–20} In juxtaposition to these arguments is that universal screening may be the best approach to identify both children and parents with heterozygous FH (i.e., reverse cascade screening) and in this context may be cost-effective.^{21–23} The detection and treatment of youth with FH appears to be the least controversial and most widely accepted management element in pediatric lipid management. However, comprehensive data to illuminate the state of youth lipid management and especially the detection of FH and institution of LLM are limited and conflicting.^{24–27} To address the data gap, in a large cohort of children and adolescents from 2002–2012, we examine aggregate temporal trends in population lipid testing, dyslipidemia detection, and LLM use. We also attempt to infer clinician-driven testing indications by the temporal trends in observed dyslipidemias in those youth selected for testing.

METHODS

We conducted a retrospective cohort descriptive analysis of patterns of lipid testing, lipid concentrations and LLM among patients aged 2–20 years from 5 health systems in the United States from 2002–2012.

Data extraction

Data were extracted from harmonized virtual data warehouses (VDW) of 5 integrated payer-provider sites of the Cardiovascular Research Network (CVRN): Scott & White Healthcare, Temple TX; Henry Ford Health System, Detroit MI; Kaiser Permanente Hawaii, Honolulu HI; Marshfield Clinic, Marshfield WI; Geisinger Health System, Danville PA. In brief, the CVRN is one of the multiple clinically-focused networks within the Health Maintenance Organization Research Network (HMORN), a federated network of public-domain research centers based in not-for-profit health care systems.^{28, 29} The HMORN VDW is a distributed data-sharing network with standardized procedures to extract and pool claims data and electronic health records including inpatient, outpatient and subspecialty services, testing data including but not limited to laboratory results, and pharmacy claims.^{28, 29} Each site's VDW was interrogated for 2–20 year olds from January 2002 until December 2012. Youth were included if they were enrolled in the respective health plans for at least 12 months

during the observation period irrespective of whether there were any clinical encounters. Summary data was collected on lipid testing, lipid concentrations, and pharmacy claims for LLM. LLM were defined as prescriptions for generic or brand name statins, fibric acid derivatives, ezetimibe, niacin and combination therapies. On the basis of an internal validation study, bile acid sequestrants were excluded due to primarily being used for non-lipid indications, specifically diarrhea. Diagnoses were collected based on International Classification of Diseases, Ninth Revision (ICD-9) codes submitted for all patient encounters without regard to primary versus secondary diagnoses. ICD-9 codes included in this analysis were: obesity (278.0x), and family history of CVD diseases (V17.3 and V17.49). Population mean lipid levels for HDL-C and LDL-C were determined by calculating the arithmetic mean of all values for a respective test in a given year. Data was validated by a chart review at the primary site. To protect patient confidentiality, data was aggregated at the site level. On this basis, the protocol was approved or exempted by the respective Institutional Review Boards. Thus individual-level factors including vital signs, additional risk factors, and/or risk conditions associated with a specific lipid level were not available.

Statistical analysis

Outcome domains included a) the occurrence of lipid testing, b) the categorical value of the lipid level defined below, and c) the occurrence of a LLM with a subanalysis of statins specifically. Lipid testing could have occurred as fasting, nonfasting, or in youth on LLM and was reported for each year as a proportion of the entire enrolled cohort per year. Lipid categories included LDL-C above 190mg/dL as an index of likely FH, and both LDL-C between 130–190mg/dL and HDL-C below 40 mg/dL as indices of lifestyle or obesity-related dyslipidemia.^{1, 16, 30, 31} Lipid categories are reported per year as: a) all persons in that category as a proportion of the entire yearly population, termed yearly prevalence; b) the new occurrence of that category in persons who had never previously had lipid test results in that category up to that point in the observation period as a proportion of the yearly cohort, termed yearly incidence; c) all persons in the category as a proportion of only those receiving a lipid test in that year; d) new occurrence of the category only in those tested in that year, as an indirect indicator of provider selection of patients to be tested; and e) the cumulative total of new occurrences of LDL-C over 190mg/dL divided by the cumulative total of unique individuals in the cohort, termed the cumulative incidence of LDL-C over 190mg/dL. For pharmacotherapy, LLM and specifically statins were reported per year as a) total claims per yearly cohort, i.e. prevalent use and b) new claims in the treatment-naïve yearly cohort, i.e. incident use.^{1, 14} By the above described methods, incidence and prevalence values in a particular analytic stratum are equal for the 1st year of data 2002 as we do not have prior data. Temporal trends were assessed by using linear regression with calendar year as the independent predictor of interest with a Type I error of 0.05. SAS 9.2 (SAS Institute INC, Cary, NC) was used for data assembling and analysis.

RESULTS

Demographic characteristics are presented in Table 1, by contributing site. We captured data on a cumulative cohort of 653,642 unique individuals with the yearly cohort declining from

297,070 in 2002 to 213,040 in 2012 (Table 2), consistent with national trends of declining private health insurance coverage.³² The proportion of youth tested for lipids in the yearly cohort declined from 16% in 2002 to 11% in 2012 ($p < 0.001$ for trend). The proportion of the yearly cohort with new physician diagnosis of obesity and the new detection of family history of CVD increased ($p=0.03$ and $p<0.001$, respectively).

Lipid category trends

Temporal trends in lipid categories are given in Table 3. For LDL-C >190 mg/dL, the incident cases detected as a proportion of the total yearly cohort increased from 0.03% to 0.06% ($p=0.03$ for trend, Figure 1a) and as a proportion of those tested from 0.21% to 0.51% ($p=0.008$, Figure 1b). Prevalent cases of LDL-C >190 mg/dL increased from 0.03% to 0.08% ($p=0.001$) of the total cohort and from 0.21% to 0.71% ($p<0.001$) among those who were tested. The cumulative incidence of LDL-C >190 mg/dL was 0.12% over all 10 years.

For more moderate dyslipidemias, incident case detection of LDL-C between 130 and 190mg/dL as a proportion of the total cohort more than tripled from 0.31% to 0.99% ($p=0.001$, Figure 2a) while as a proportion of those tested markedly increased from 1.89% to 9.01% ($p=0.001$, Figure 2b). The yearly prevalence of moderate LDL-C elevation increased in the whole cohort from 0.31% to 1.38% ($p<0.001$, figure 2) and in those tested from 1.89% to 12.58% ($p=0.001$). New detection of HDL-C <40 mg/dL more than tripled from 0.54% to 1.78% ($p<0.001$) as a fraction of the whole cohort, and from 2.87% to 14.67% ($p<0.001$) of those tested. Prevalent cases of HDL-C <40 mg/dL rose from 0.54% to 2.9% ($p<0.001$) of the total group and from 2.87% to 23.93% ($p<0.001$) of the tested group.

Population mean levels of LDL-C declined from 100mg/dL to 87mg/dL ($p=0.001$) and for HDL-C declined modestly from 48 to 46mg/dL ($p=0.03$) among those tested over the observation period (Figure 3).

LLM trends

The rate of LLM or statin initiation did not increase over time, while the prevalence of LLM and statin use significantly rose, but to a clinically modest extent (Table 2, Figure 4). Among the total treatment-naïve yearly population, after 2009 the proportions of new cases of LDL-C >190 mg/dL increased while statin initiation did not increase (Figure 5).

DISCUSSION

Despite multiple expert panel recommendations since 1992 establishing the importance of identifying and treating youth with high-risk dyslipidemias including FH, our data show lipid testing and treatment rates from 2002 – 2012 did not increase in youth and actually appear to have decreased.^{1, 15, 30} As a fraction of the annual commercially-insured population of children and adolescents, the detection of severe LDL-C elevation did increase over time, but the yearly rate and cumulative incidence were far below the expected proportion of the cohort with FH.¹ Focusing on those youth actually tested each year, the proportion detected with moderate LDL-C elevation and low HDL-C increased 5- to 9-fold. Although general pediatric population data from the National Health and Nutrition Examination Study (NHANES) indicate HDL-C levels have generally risen over the

observed period, our data showing increasing detection of low HDL-C and declining cohort mean HDL-C level suggest that providers are selectively testing youth with higher risk of having lifestyle/obesity-associated dyslipidemia.³³ Moreover the proportion with severe LDL-C elevation among those tested was more than double the purported prevalence of FH, suggesting that providers who deign to test lipids may also be selectively screening youth with high risk of genetic dyslipidemia as well. However this focus on high-risk dyslipidemia is not translating to pharmacotherapy, as the yearly rate of new LDL-C>190mg/dL detection far outpaces the rate of LLM initiation in the most recent years. Our data are both consistent and inconsistent with recent reports documenting divergent trends in lipid testing of youth.^{26, 27} Both previous studies and our data consistently demonstrate a substantial lack of screening in youth. This study extends previous work by including dyslipidemia categories and pharmacotherapy rates to highlight a persistent, growing, and remediable gap between the proportion of youth detected with FH-level LDL-C and the proportion of youth being treated with LLM at all.

Our rates of lipid testing were similar to those reported in a separate study based on 3 other HMO populations.²⁷ In pooled data from 2007 – 2010, roughly 10% of youth aged 3 – 19 years of age were tested for lipids. Accounting for their cohort exclusions, the screening rates reported here are in reasonable agreement with the previous report. In contrast, a study from the National Ambulatory Medical Care Survey (NAMCS) database shows an increasing trend in lipid testing, but with rates substantially lower than rates identified herein.²⁶ This discrepancy may be related to differences in the data acquisition process. NAMCS is comprised of a national probability sample of physicians self-reporting visit content data on a sample of outpatient encounters over a one week period. Using this approach, previous data show NAMCS data underrepresent lipid test ordering by roughly 50% in adult patients.³⁴ Moreover the pediatric report only included cholesterol screening performed at well-child visits and not subspecialty practices where high-risk youth may be more likely to be tested and treated.^{26, 35} In contrast, CVRN data are gleaned from billing and electronic medical record processes and thereby have better capture of management actions.^{28, 29}

Our results may imply different screening triggers are being applied. While the overall proportion of youth tested has declined, the proportion with abnormal lipids detected among those tested increased. Our observations of small but increasing proportions with a coded family history of CVD and higher than expected prevalence of FH-level LDL-C elevations in those tested for dyslipidemias may also support the hypothesis that family history is, in part, driving lipid test ordering, or the emphasis on FH is discouraging routine screening, or least likely that families themselves are more aware of their FH history and are seeking testing. However, the cumulative proportion detected with FH level LDL-C concentrations is well below the expected population prevalence, indicating more families deserve investigation for this very high risk condition for children and their parents. Similarly the proportion detected with low HDL-C concentrations increased over time, likely attributable to increased testing in overweight/obese youth. Because our data were aggregated at the site level, we cannot establish a direct link between a youth's BMI and lipid testing. The previous HMORN study reported testing rates of roughly 6% among youth with a BMI < 85 percentile and 27% among those with a BMI ≥ 95 percentile.²⁷ Within the NAMCS cohort,

roughly 5% of those with lipid testing had a diagnosis of obesity based on ICD-9 codes.²⁶ However, such codes are a poor index for the actual presence of obesity. To wit, in our sample we found the rate of new physician diagnosed obesity (based on ICD-9 coding) was between 1 – 1.5%, which is orders of magnitude lower than the population prevalence of pediatric obesity and markedly discordant with the prevalence of low HDL-C and mean HDL-C level trend in our own data.^{33, 36} Overall, a reasonable inference may be that screening triggers have changed over time, but the lack of broad adoption of appropriate screening triggers is leading to a gap in detection of high-risk dyslipidemic youth, notably those with FH-level LDL-C.

Our reported actual LLM rates are consistent with previously reported statin and LLM use rates which predate the most recent guideline recommendations.^{14, 24, 25} In a report looking at prevalence use in 2004, 0.025% of commercially insured and 0.017% of Medicaid-insured youth under 18 years old received a statin prescription.²⁴ In another study of commercially insured youth 5 to 19 years old between 2002 and 2005, the baseline LLM rate was 0.027% with a 15% increase over time, and statins accounted for 68% of LLM prescriptions in 2005.²⁵ The roughly 2-fold higher LLM and statin use in our cohort compared to previous data may reflect the concentrated, regional nature of our data sources or changes in lipid management paradigms over time.^{22, 23} With respect to specific LLM, pediatric guidelines published in 1992 identified bile acid sequestrants as 1st line therapy with statins supplanting this recommendation after 2006.^{1, 14, 15, 30} Our data show that even as early as 2002, statins were nearly 3 times more commonly used than other LLM. Indeed, bile acid sequestrants were excluded in our analyses since a single site chart review indicated they were not used to treat hyperlipidemia throughout the observation period, suggesting that the guidelines did not have much effect on the type of LLM chosen by providers.³⁰ Since incident LLM and statin rates did not change over time, the increasing prevalent use of LLM and statins may imply chronic use of pharmacotherapy. As an upper bound for LLM use, investigators have estimated the proportion of the population theoretically eligible for LLM under earlier guideline recommendations to range from 0.5–1%.^{30, 37} More recent work transposing the 2011 NHLBI pediatric guidelines to the nationally representative population-based NHANES data estimates that 0.85% of children would have indications for statin use.³⁸ All three of these estimates are several-fold higher than the proportion actually treated in 2012. Critics in medical and popular press met pediatric CVD risk reduction guidelines with opprobrium, including concerns about the lack of long-term efficacy, safety, and cost-effectiveness data for lipid screening and treatment in youth; the psychological effects on vulnerable children; predictions of inappropriate statin use “epidemics”; and highlighting potential conflicts of interest.^{18–20} Fortunately, our data show the feared “epidemic” of youth statin use has yet to materialize. Unfortunately, while adult CVD guidelines have engendered rigorous quality improvement initiatives focused on steadily improved guideline adherence, pediatric CVD risk reduction guidelines have not garnered similar systemic implementation initiatives nor cohesive investigation agendas, despite the high CVD event rates in young adults with FH.³⁹ Our data imply that high-risk youth likely to have FH are not being treated, underscoring the need for new quality improvement initiatives.

The dissonant trends between lipid screening versus abnormal lipid levels identified, and between very elevated FH lipid concentrations versus the number treated, may be the result

of secular or other unmeasured features that changed in the cohort over time, including clinical provider beliefs and attitudes or patient/family beliefs and attitudes. Pediatric provider survey results suggest that clinician knowledge and behaviors are likely to be a key driver.^{40, 41} While 74% of providers believed that pediatric lipid screening and treatment would reduce future CVD event risk, only 23% referred children to pediatric lipid specialists, and large majorities expressed discomfort with lipid management, lack of familiarity with lipid value thresholds, and opposition to the use of LLM.⁴¹ Parental surveys found most mothers of older children were in favor of screening and lowering of cholesterol levels.⁴² However the majority of children with abnormal lipid levels did not return for follow-up due to doubts about test accuracy and anxiety or discomfort of the child.⁴² Parental and patient attitudes toward current pediatric lipid guideline recommendations are not yet measured. Integrated data infrastructure is needed to evaluate lipid testing, treatment rates, and attitudes over time. Utilizing such infrastructure to glean real-world, longitudinal practice data is of critical importance to assessing long-term effectiveness and cost-benefit, since previous reports have noted that the costs of screening across alternative approaches (universal, selective or population interventions) have little impact on the cost-effectiveness of different screening approaches.²¹ Rather, it is the cost of treatment (including LLM) which ultimately determines the cost-effectiveness and long-term value of CVD event reduction. Our data suggest implementing proper treatment to reduce CVD events in identified high risk youth will require new provider and parent engagement initiatives.

Limitations

The cohort data presented are observational and do not permit causal attribution. Other variables were not accounted for in these analyses, including variable length of follow-up, demographics and other confounders. For example, exact indications for lipid testing or LLM use were not assessed on an individual basis at every site. However these summary data are robust on general lipid testing and treatment trends, which is one process metric of population lipid management. It is possible that some persons obtained and paid for lipid testing or pharmacotherapy outside of the health plan system or that prescribed medications were not claimed by affected patients. Insured populations may not reflect disadvantaged populations. Harmonization of state-by-state Medicaid data could help characterize similar data in America's most vulnerable children.

CONCLUSIONS

From 2002–2012, lipid screening rates in children and adolescents declined while the proportion detected with abnormal lipid levels increased, implying a change in lipid screening triggers. LLM and statin use rates did not increase over this time period, despite the higher rates of very high LDL-C concentrations detected. Further work may identify ways to improve lipid management in youth.

Acknowledgments

This work was supported by National Heart, Lung, and Blood Institute K23 HL111335 (JPZ) and RC2LH10666-01 (Cardiovascular Research Network), Wilhelm Family Foundation (CJM), and the Baylor Scott & White Center for Applied Health Research (LAC).

No funding source had any role in the design and conduct of the study, in the collection, analysis, and interpretation of the data, and in the preparation, review, or approval of the manuscript

References

1. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: Summary report. *Pediatrics*. 2011; 128(Suppl 5):S213–S256. [PubMed: 22084329]
2. May AL, Kuklina EV, Yoon PW. Prevalence of cardiovascular disease risk factors among us adolescents, 1999–2008. *Pediatrics*. 2012; 129:1035–1041.
3. Mortality in treated heterozygous familial hypercholesterolaemia: Implications for clinical management. Scientific steering committee on behalf of the simon broome register group. *Atherosclerosis*. 1999; 142:105–112. [PubMed: 9920511]
4. Risk of fatal coronary heart disease in familial hypercholesterolaemia. Scientific steering committee on behalf of the simon broome register group. *BMJ*. 1991; 303:893–896. [PubMed: 1933004]
5. Brown MS, Goldstein JL. Familial hypercholesterolemia: A genetic defect in the low-density lipoprotein receptor. *N Engl J Med*. 1976; 294:1386–1390. [PubMed: 177875]
6. Williams RR, Hasstedt SJ, Wilson DE, Ash KO, Yanowitz FF, Reiber GE, Kuida H. Evidence that men with familial hypercholesterolemia can avoid early coronary death. An analysis of 77 gene carriers in four utah pedigrees. *JAMA*. 1986; 255:219–224. [PubMed: 3941501]
7. Avis HJ, Vissers MN, Stein EA, Wijburg FA, Trip MD, Kastelein JJ, Hutten BA. A systematic review and meta-analysis of statin therapy in children with familial hypercholesterolemia. *Arterioscler.Thromb.Vasc Biol*. 2007; 27:1803–1810. [PubMed: 17569881]
8. Versmissen J, Oosterveer DM, Yazdanpanah M, Defesche JC, Basart DC, Liem AH, Heeringa J, Witteman JC, Lansberg PJ, Kastelein JJ, Sijbrands EJ. Efficacy of statins in familial hypercholesterolaemia: A long term cohort study. *BMJ*. 2008; 337:a2423. [PubMed: 19001495]
9. Vuorio A, Kuoppala J, Kovanen PT, Humphries SE, Strandberg T, Tonstad S, Gylling H. Statins for children with familial hypercholesterolemia. *Cochrane.Database Syst.Rev*. 2010;CD006401. [PubMed: 20614444]
10. Ference BA, Yoo W, Alesh I, Mahajan N, Mirowska KK, Mewada A, Kahn J, Afonso L, Williams KA Sr, Flack JM. 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; 60:2631–2639. [PubMed: 23083789]
11. Wierzbicki A, Ratcliffe C. The 2007 heart-uk survey of lipid clinics and clinical practice in the uk. *Atherosclerosis*. 2008; 199:234.
12. Kusters DM, Avis HJ, de Groot E, Wijburg FA, Kastelein JJ, Wiegman A, Hutten BA. Ten-year follow-up after initiation of statin therapy in children with familial hypercholesterolemia. *JAMA*. 2014; 312:1055–1057. [PubMed: 25203086]
13. Stone NJ, Robinson J, Lichtenstein AH, Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC Jr, Watson K, Wilson PW. 2013 acc/aha guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: A report of the american college of cardiology/american heart association task force on practice guidelines. *Circulation*. 2013
14. Daniels SR, Greer FR. Lipid screening and cardiovascular health in childhood. *Pediatrics*. 2008; 122:198–208. [PubMed: 18596007]
15. Kavey RE, Allada V, Daniels SR, Hayman LL, McCrindle BW, Newburger JW, Parekh RS, Steinberger J. Cardiovascular risk reduction in high-risk pediatric patients: A scientific statement from the american heart association expert panel on population and prevention science; the councils on cardiovascular disease in the young, epidemiology and prevention, nutrition, physical activity and metabolism, high blood pressure research, cardiovascular nursing, and the kidney in heart disease; and the interdisciplinary working group on quality of care and outcomes research: Endorsed by the american academy of pediatrics. *Circulation*. 2006; 114:2710–2738. [PubMed: 17130340]
16. 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; 5:S9–S17. [PubMed: 21600530]

17. America's children: Key national indicators of well-being, 2011. 2011
18. Newman TB, Pletcher MJ, Hulley SB. Overly aggressive new guidelines for lipid screening in children: Evidence of a broken process. *Pediatrics*. 2012; 130:349–352. [PubMed: 22826571]
19. Gillman MW, Daniels SR. Is universal pediatric lipid screening justified? *JAMA*. 2012; 307:259–260. [PubMed: 22253390]
20. Psaty BM, Rivara FP. Universal screening and drug treatment of dyslipidemia in children and adolescents. *JAMA*. 2012; 307:257–258. [PubMed: 22174386]
21. Berwick DM, Cretin S, Keeler E. Cholesterol, children, and heart disease: An analysis of alternatives. *Pediatrics*. 1981; 68:721–730. [PubMed: 6796932]
22. Morris JK, Wald DS, Wald NJ. The evaluation of cascade testing for familial hypercholesterolemia. *Am J Med Genet A*. 2012; 158A:78–84. [PubMed: 22139944]
23. Wald DS, Bestwick JP, Wald NJ. Child-parent screening for familial hypercholesterolaemia: Screening strategy based on a meta-analysis. *BMJ*. 2007; 335:599. [PubMed: 17855284]
24. Lasky T. Statin use in children in the united states. *Pediatrics*. 2008; 122:1406–1408. [PubMed: 19047265]
25. Cox ER, Halloran DR, Homan SM, Welliver S, Mager DE. Trends in the prevalence of chronic medication use in children: 2002–2005. *Pediatrics*. 2008; 122:e1053–e1061. [PubMed: 18977954]
26. 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; 311:1804–1807. [PubMed: 24794376]
27. Margolis KL, Greenspan LC, Trower NK, Daley MF, Daniels SR, Lo JC, Kharbanda EO, Sinaiko AR, Magid DJ, Parker ED, Chandra M, Tavel HM, O'Connor PJ. Lipid screening in children and adolescents in community practice: 2007 to 2010. *Circulation. Cardiovascular quality and outcomes*. 2014; 7:718–726. [PubMed: 25160839]
28. Go AS, Magid DJ, Wells B, Sung SH, Cassidy-Bushrow AE, Greenlee RT, Langer RD, Lieu TA, Margolis KL, Masoudi FA, McNeal CJ, Murata GH, Newton KM, Novotny R, Reynolds K, Roblin DW, Smith DH, Vupputuri S, White RE, Olson J, Rumsfeld JS, Gurwitz JH. The cardiovascular research network: A new paradigm for cardiovascular quality and outcomes research. *Circ Cardiovasc Qual Outcomes*. 2008; 1:138–147. [PubMed: 20031802]
29. Ross TR, Ng D, Brown JS, Pardee R, Hornbrook MC, Hart G, Steiner JF. The hmo research network virtual data warehouse: A public data model to support collaboration. *eGEMs (Generating Evidence & Methods to improve patient outcomes)*. 2014; 2
30. American academy of pediatrics. National cholesterol education program: Report of the expert panel on blood cholesterol levels in children and adolescents. *Pediatrics*. 1992; 89:525–584. [PubMed: 1538956]
31. 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; 5:S30–S37. [PubMed: 21600527]
32. Cohen RA, Martinez ME. Health insurance coverage: Early release of estimates from the national health interview survey, 2011. 2012
33. 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; 307:591–600. [PubMed: 22871871]
34. 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; 42:276–280. [PubMed: 15076827]
35. Gregory ST, McNeal CJ, Copeland LA. Rates of cholesterol screening of youth. *JAMA*. 2014; 312:1353–1354. [PubMed: 25268451]
36. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the united states, 2011–2012. *JAMA*. 2014; 311:806–814. [PubMed: 24570244]
37. Ford ES, Li C, Zhao G, Mokdad AH. Concentrations of low-density lipoprotein cholesterol and total cholesterol among children and adolescents in the united states. *Circulation*. 2009; 119:1108–1115. [PubMed: 19221218]
38. McCrindle BW, Tyrrell PN, Kavey RE. Will obesity increase the proportion of children and adolescents recommended for a statin? *Circulation*. 2013; 128:2162–2165. [PubMed: 24190936]

39. Sachdeva A, Cannon CP, Deedwania PC, Labresh KA, Smith SC Jr, Dai D, Hernandez A, Fonarow GC. Lipid levels in patients hospitalized with coronary artery disease: An analysis of 136,905 hospitalizations in get with the guidelines. *Am Heart J*. 2009; 157:111–117. e112. [PubMed: 19081406]
40. Kimm SY, Payne GH, Stylianou MP, Wacławski MA, Lichtenstein C. National trends in the management of cardiovascular disease risk factors in children: Second nhlbi survey of primary care physicians. *Pediatrics*. 1998; 102:E50. [PubMed: 9794980]
41. Dixon DB, Kornblum AP, Steffen LM, Zhou X, Steinberger J. Implementation of lipid screening guidelines in children by primary pediatric providers. *J Pediatr*. 2013
42. Price JH, Casler SM. African-american mothers' perceptions of cholesterol and its effects on their children. *J Natl Med Assoc*. 1996; 88:145–150. [PubMed: 8839029]
43. Wiegman A, Gidding SS, Watts GF, Chapman MJ, Ginsberg HN, Cuchel M, Ose L, Averna M, Boileau C, Boren J, Bruckert E, Catapano AL, Defesche JC, Descamps OS, Hegele RA, Hovingh GK, Humphries SE, Kovanen PT, Kuivenhoven JA, Masana L, Nordestgaard BG, Pajukanta P, Parhofer KG, Raal FJ, Ray KK, Santos RD, Stalenhoef AF, Steinhagen-Thiessen E, Stroes ES, Taskinen MR, Tybjaerg-Hansen A, Wiklund O. European Atherosclerosis Society Consensus P. Familial hypercholesterolaemia in children and adolescents: Gaining decades of life by optimizing detection and treatment. *European heart journal*. 2015

Highlights

- Detection of dyslipidemias and use of lipid lowering medicine was examined in youth
- Lipid testing declined over time
- And yet more severe and moderate dyslipidemias were detected
- But pharmacotherapy did not increase
- The gap between detection and treatment deserves more investigation

Figure 1.

a and 1b: The yearly new detection in dark gray and yearly prevalence in light gray of LDL-C >190mg/dL. (1a) within the total cohort and (1b), among those tested for lipids.

Cumulative new detection of LDL-C >190mg/dL was 0.12% and the expected prevalence of familial hypercholesterolemia is 0.2–0.5% (i.e. between 1 in 200 and 1 in 500).^{1, 43}

Figure 2.

a and 2b: Within the total cohort, the yearly new detection of LDL-C 130–190 mg/dL (red), prevalence of LDL-C 130 to 190 mg/dL (yellow), the yearly new detection of HDL-C <40mg/dL (green) and prevalence of HDL-C <40mg/dL (blue) (2a) within the total cohort and (2b) among those tested for lipids.

Figure 3. Among those tested each year, the population mean LDL-C (dark diamond) and HDL-C (light squares) in milligrams per deciliter(mg/dL).

Figure 4. Within the total cohort each year, new initiation of statins (dark diamond), and prevalent prescriptions for statins (light square).

Figure 5.
Within the total cohort, new detection of LDL-C over 190mg/dL (dark gray) and new initiation of statins (light gray).

Table 1

Demographic Characteristics in 2012

Site	Geisinger Health System	Henry Ford Health System	Kaiser Permanente	Marshfield Clinic	Scott&White
State	Pennsylvania	Michigan	Hawaii	Wisconsin	Texas
Female (%)	49%	51%	49%	60%	49%
Age category					
2–8 years (%)	33%	23%	36%	34%	34%
9–11 years (%)	16%	14%	16%	15%	16%
12–17 years (%)	34%	38%	32%	32%	33%
18–21 years (%)	17%	25%	17%	19%	17%
Race/Ethnicity					
Non-Hispanic White	92%	54%	12%	95%	45%
Non-Hispanic Black	3%	42%	1%	1%	5%
Hispanic	3%	1%	8%	1%	6%
Asian, Other, Missing	2%	3%	79%	3%	43%

Table 2

Yearly rates of lipid testing and lipid-lowering medications (LLM) use and statin use from 2002 to 2012

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	p for trend§
N	297,070	284,635	277,728	265,041	259,543	257,873	250,208	240,890	233,086	227,642	213,040	
Lipid Test (%)	16%	16%	16%	16%	16%	15%	15%	14%	13%	12%	11%	<0.001
New Obesity Diagnosis	1.31%	0.99%	1.05%	1.19%	1.14%	1.09%	1.24%	1.24%	1.29%	1.58%	1.35%	0.03
New detection of CVD Family History	0.03%	0.02%	0.03%	0.03%	0.04%	0.07%	0.14%	0.13%	0.14%	0.17%	0.17%	<0.001
Medication Use												
New LLM	0.067%	0.036%	0.039%	0.039%	0.053%	0.049%	0.041%	0.045%	0.040%	0.040%	0.043%	0.3
New Statin	0.046%	0.025%	0.025%	0.024%	0.031%	0.031%	0.026%	0.024%	0.025%	0.026%	0.027%	0.1
LLM Prevalence	0.056%	0.054%	0.060%	0.065%	0.083%	0.085%	0.086%	0.086%	0.083%	0.087%	0.088%	<0.001
Statin Prevalence	0.038%	0.041%	0.043%	0.046%	0.057%	0.057%	0.062%	0.058%	0.058%	0.064%	0.066%	<0.001

Results given as proportion of total cohort per year.

§ P for trend indicates p value from linear regression with calendar year as independent variable.

LLM indicates Lipid lowering medication. CVD indicates cardiovascular disease.

Table 3

Incidence and Prevalence of Lipid Categories in the Total Cohort and Among Those Tested for Lipids Each Year from 2002 to 2012

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	p for trends
Total Cohort												
Incidence												
LDL-C > 190 mg/dL	0.03%	0.01%	0.01%	0.03%	0.03%	0.03%	0.02%	0.02%	0.03%	0.05%	0.06%	0.03
LDL-C 130 to 190 mg/dL	0.31%	0.25%	0.31%	0.33%	0.38%	0.42%	0.39%	0.41%	0.55%	0.90%	0.99%	0.001
HDL-C <40 mg/dL	0.54%	0.39%	0.55%	0.58%	0.63%	0.80%	0.94%	1.19%	1.23%	1.97%	1.78%	<0.001
Prevalence												
LDL-C > 190 mg/dL	0.03%	0.02%	0.02%	0.04%	0.04%	0.05%	0.04%	0.04%	0.05%	0.06%	0.08%	0.001
LDL-C 130 to 190 mg/dL	0.31%	0.28%	0.36%	0.42%	0.48%	0.54%	0.52%	0.56%	0.74%	1.16%	1.38%	<0.001
HDL-C <40 mg/dL	0.54%	0.44%	0.64%	0.71%	0.82%	1.08%	1.29%	1.66%	1.85%	2.88%	2.90%	<0.001
Tested only												
Incidence												
LDL-C > 190 mg/dL	0.21%	0.09%	0.08%	0.17%	0.17%	0.18%	0.16%	0.15%	0.26%	0.38%	0.51%	0.008
LDL-C 130 to 190 mg/dL	1.89%	1.49%	1.91%	2.04%	2.37%	2.74%	2.67%	2.94%	4.22%	7.52%	9.01%	0.001
HDL-C <40 mg/dL	2.87%	2.04%	2.96%	3.11%	3.47%	4.66%	5.70%	7.62%	8.43%	14.83%	14.67%	<0.001
Prevalence												
LDL-C > 190 mg/dL	0.21%	0.13%	0.13%	0.26%	0.26%	0.30%	0.29%	0.28%	0.41%	0.53%	0.71%	<0.001
LDL-C 130 to 190 mg/dL	1.89%	1.71%	2.21%	2.61%	3.03%	3.58%	3.56%	4.03%	5.68%	9.73%	12.58%	0.001
HDL-C <40 mg/dL	2.87%	2.32%	3.46%	3.85%	4.56%	6.30%	7.86%	10.64%	12.69%	21.67%	23.93%	<0.001
Population Mean												
LDL-C (mg/dL)	100	92	97	94	96	96	91	85	85	86	87	0.001
HDL-C (mg/dL)	48	49	40	49	45	47	48	47	46	46	46	0.03

Total cohort indicates the denominator is comprised of all youth enrolled in the given year. Tested only indicates the denominator is derived from those tested for lipids in a given year. Incidence indicates the proportion of new cases detected in each year. Prevalence indicates all cases, new or preexisting, as a proportion of the respective cohort each year. P for trend indicates p value from linear regression with calendar year as independent variable.