



## Temporal trends in lipid testing among children and adolescents: A population based study

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### ABSTRACT

Unfavorable lipid levels during childhood are associated with subsequent development of atherosclerotic cardiovascular disease. The American Academy of Pediatrics and National Heart, Lung and Blood Institute in 2011 recommended universal lipid screening for children between ages 9–11 years and between ages 17–21 years. The objective of the study was to determine temporal trends in lipid testing among children and young adults in a mid-western population. The Rochester Epidemiology Project database was used to identify lipid testing in ages 2–21 years ( $n = 51,176$ ) in the Olmsted County population from January 1, 2008 through December 31, 2014. Generalized estimating equations with Poisson distribution were used to test for temporal trends in lipid testing across the age groups. There was modest increase in lipid testing in children in the age groups, 9–11 years and 17–21 years (1.5% in 2008 to 2.2% in 2014,  $P < 0.001$  and 4.4% in 2008 to 4.6% in 2014,  $P = 0.02$ , respectively). There was a significant decrease in proportion of 17–21 year olds with elevated total cholesterol (16.2% in 2008 to 11.6% in 2014;  $P = 0.01$ ) and non-high density lipoprotein cholesterol (22.6% in 2008 to 12.6% in 2014;  $P < 0.001$ ). In this population-based study, rates of lipid testing increased minimally only in the last six years. Further longitudinal studies are warranted to improve guideline dissemination and address attitudes, practices and barriers to lipid testing in children and young adults.

### 1. Introduction

Atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of death in North America (Pediatrics, 2011). Risk factors and risk behaviors that accelerate the development of atherosclerosis can begin in childhood, and there is increasing evidence that risk reduction delays progression towards clinical disease (HC et al., 2000; Berenson et al., 1998). Levels of non-high density lipoprotein cholesterol (non-HDL-C) and of low density lipoprotein cholesterol (LDL-C) levels in childhood have been shown to correlate with levels during adulthood and predict severity of atherosclerosis and adult ASCVD (McGill et al., 2000; Berenson et al., 1998; Frontini et al., 2008; Raitakari et al., 2003; Lauer and Clarke, 1990; Webber et al., 1991; Porkka et al., 1994; Juhola et al.,

2011; Nicklas et al., 2002; Bao et al., 1996).

Statin therapy beginning in childhood in those with familial hypercholesterolemia may decrease cardiovascular events (Braamskamp et al., 2016). Earlier treatment with statins in children with heterozygous familial hypercholesterolemia is also associated with reduced burden of subclinical atherosclerosis (Wiegman et al., 2004; Rodenburg et al., 2007; Kusters et al., 2014; de Jongh et al., 2002). Selective lipid screening in at-risk children, defined as those with a family history of premature ASCVD or high blood concentrations of cholesterol, was recommended by the National Cholesterol Education Program (NCEP) of the National Heart, Lung, and Blood Institute (NHLBI) in 1992 and subsequently adopted by the American Academy of Pediatrics (AAP) in 1998 (American Academy of Pediatrics, 1992). Lipid screening was also

**Abbreviations:** ASCVD, atherosclerotic cardiovascular disease; HDL, high density lipoprotein; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; mg/dL, milligrams/deciliters; NCEP, National Cholesterol Education Program; NHANES, National Health and Nutrition Examination Survey; NHLBI, National Heart, Lung, and Blood Institute; non-HDL-C, non high density lipoprotein cholesterol; REP, Rochester Epidemiology Project; TC, total cholesterol

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recommended for pediatric patients in whom the family history is not known or those with other risk factors for ASCVD such as obesity, hypertension, and diabetes mellitus (American Academy of Pediatrics, 1992). In 2011, both the AAP and the Expert Panel of the NHLBI recommended universal lipid screening for children between 9 and 11 years and between 17 and 21 years, (Pediatrics, 2011; Daniels et al., 2011) since using family history of premature ASCVD or cholesterol disorders as the primary factor in determining lipid screening for children misses 30% to 60% of children with dyslipidemias (Ritchie et al., 2010; Klancar et al., 2015). Another impetus for these guidelines was the high prevalence of obesity and associated dyslipidemia secondary to poor eating habits and sedentary lifestyle (Pediatrics, 2011). These lipid testing guidelines were part of “Integrated Guidelines” for cardiovascular health and risk reduction that included recommendations regarding diet, physical activity, and management of hypertension and obesity as well as testing lipid levels. The universal screening guidelines, however, remain controversial (Haney et al., 2007; Force et al., 2016). Concerns raised about universal lipid screening relate to a lack of data on the impact of early detection of dyslipidemia on ASCVD during adulthood, the psychological impact of early diagnosis of dyslipidemia and the low predictive value of childhood lipid screening (Ritchie et al., 2010; Haney et al., 2007; Force et al., 2016; Gillman and Daniels, 2012; Newman et al., 2012; Kimm et al., 1998). The US Preventive Services Task Force (USPSTF) concluded that there was insufficient evidence to recommend for or against pediatric lipid screening (Haney et al., 2007; Force et al., 2016).

The impact of these conflicting recommendations on attitudes and practices of health care providers is unclear. Minimal increase in rates of lipid testing has been reported in national surveys of ambulatory well-child visits from 1995 through 2010 (Vinci et al., 2014). The objective of the study was to examine temporal trends in lipid testing from January 1, 2008 through December 31, 2014 among children and young adults in a large, mid-western population.

## 2. Patients and methods

### 2.1. Study population

We used the Rochester Epidemiology Project (REP) to identify all children and young adults aged 2–21 years residing in Olmsted County, Minnesota from January 1, 2008 through December 31, 2014. The REP is a medical record linkage system, which enables research by linking together medical records from multiple providers in Olmsted County to unique individuals. Linking medical records was accomplished by REP linkage procedures that have been described previously (St Sauver et al., 2011). Briefly, patient records were matched electronically via multiple rounds of matching, where the first 3 rounds of matching were based on a complete match between the records on at least 4 of the following data points: patient first and last name, date of birth, sex, and Social Security Number. Successive rounds of matching used less stringent criteria, including fuzzy matching of name substrings, use of middle initial, and Soundex (Roesch, 2012). Most of the health care in Olmsted County during this time frame was provided by three health care institutions, Mayo Clinic, Olmsted Medical Center and the Rochester Family Medicine Clinic, which share their medical record information for Institutional Review Board-approved research studies (St Sauver et al., 2011; St Sauver et al., 2012a). The REP captures virtually the entire population residing in Olmsted County, as compared to United States Census estimates, with a slight over-counting of women aged 19–29 years (St Sauver et al., 2012b). In addition, this population is stable, and 70–80% of children in the studied age ranges have complete 10 year follow-up (St Sauver et al., 2012b). Only those who had given permission for their medical records to be used for research (97%) were included in this study. Under Minnesota law, parents must provide permission for their children's records to be used for research, and children are asked to provide permission following their 18th

birthday.

### 2.2. Identification of lipid testing

The diagnostic indices of the REP were searched electronically to identify and obtain results for all lipid testing of children ages 2–21 years in the Olmsted County population from 2008 through 2014 using lipid testing laboratory codes for each institution.

The cut offs for abnormal lipid levels in the study were those recommended by NHLBI for children and youth < 20 years of age, though our study did include young adults 20 and 21 years of age (Pediatrics, 2011). Abnormal lipid levels were defined as total cholesterol (TC) at or above 200 mg/dL, non-HDL-C (calculated as TC minus high density lipoprotein cholesterol [HDL-C]) at or above 145 mg/dL, and HDL-C lower than 40 mg/dL (Pediatrics, 2011). Triglycerides were not included in the overall analysis as we could not determine time between ingestion of last meal and blood draw in this population based study. Similarly LDL levels were not included in the analysis as the equation for LDL levels includes triglycerides.

### 2.3. Demographics

Demographic information was obtained electronically from the patient registration information. Age and insurance status were determined at the initial lipid test for those who had lipid testing and at the initial out-patient visit for those who did not have lipid testing.

### 2.4. Analyses

Demographic characteristics of children who had lipid testing were compared to those that did not have lipid testing using chi-square tests for categorical data. Any testing was defined as having at least one lipid measurement during the study time frame. Logistic regression was used to determine the association of demographic factors and insurance status with having a lipid test from 2008 through 2014; results are reported, in Table 1, as odd ratios and 95% confidence intervals. Multivariable models were used to adjust for age group, gender, race/ethnicity and insurance (categories for each variable shown in Table 1) at the initial test.

The proportion of children undergoing lipid testing was estimated by dividing the number of lipid tests in a given calendar year by the REP census population estimate for the corresponding year. Confidence intervals were estimated assuming the counts (number of lipid tests) followed a Poisson distribution. The REP census creates a timeline for each person assessing utilization from multiple health care providers and assuming residency for a period before and after each visit based on age of the patient to indicate confirmed dates of residency in and outside of Olmsted County. REP census estimates are comparable to US census estimates (St Sauver et al., 2011). Children with multiple lipid tests were counted once in each year they had lipid testing. Children were eligible to be tested each year they were included in the census. The proportion of children having a lipid test was explored graphically by age- and year-patterns. Generalized estimating equations with a Poisson distribution were used to test for temporal trends in lipid testing and abnormal lipid level results, using counts for each calendar year, age group and sex. A two-way interaction term was included to compare temporal trends across age groups. All analyses were performed using SAS, Version 9.4 (SAS Institute, Cary, NC). Two-sided *P* values < 0.05 were considered significant.

## 3. Results

Health records of 51,176 children/young adults between the ages of 2–21 years were obtained, of which 4943 (9.7%) had at least one lipid test during the study period. There were 3829 (7.5%) children who had only one lipid test, 728 (1.4%) who had only two and 386 (0.8%) who

**Table 1**  
Characteristics of Olmsted County study population<sup>a</sup> in 2008–2014.

	Tested N, (%) N = 4943	Not tested <sup>b</sup> N, (%) N = 46,233	Unadjusted odds of lipid testing OR (95% CI) <sup>d</sup>	Adjusted <sup>c</sup> odds of lipid testing OR (95% CI) <sup>c</sup>
<b>Age at 1st lipid test (years)</b>				
2–8	489 (9.9)	17,813 (38.5)	Ref	Ref
9–11	585 (11.8)	5753 (12.4)	3.70(3.27,4.19)	3.75(3.31,4.24)
12–16	1667 (33.7)	9590 (20.7)	6.33(5.71,7.03)	6.31(5.68,7.01)
17–21	2202 (44.6)	13,077 (28.3)	6.13(5.55,6.78)	6.32(5.71,7.00)
<b>Gender, N (%)</b>				
Male	2333 (47.2)	22,891 (49.5)	Ref	Ref
Female	2610 (52.8)	23,342 (50.5)	1.10(1.04,1.16)	1.06(1.00,1.12)
<b>Race/ethnicity</b>				
White	3494 (70.7)	32,214 (69.7)	Ref	Ref
Black	529 (10.8)	4386 (9.5)	1.11(1.01,1.23)	1.61(1.45,1.79)
Asian	206 (4.2)	2763 (6.0)	0.69(0.59,0.80)	0.84(0.72,0.97)
Other/ mixed	233 (4.7)	2117 (4.6)	1.02(0.88,1.17)	1.37(1.18,1.58)
Hispanic	450 (9.1)	3535 (7.7)	1.17(1.06,1.3)	1.53(1.37,1.70)
Refused/ unknown	31 (0.6)	1218 (2.6)		
<b>Insurance at 1st lipid test</b>				
Private	3173 (64.2)	23,670 (51.2)	Ref	Ref
Government	357 (7.2)	5219 (11.3)	0.51(0.46,0.57)	0.47(0.41,0.53)
No insurance	30 (0.6)	1214 (2.6)	0.18(0.13,0.27)	0.14(0.10,0.21)
Missing	1383 (28.0)	16,130 (34.9)	0.64(0.60,0.68)	0.58(0.54,0.62)

<sup>a</sup> All study subjects seen in Olmsted County from 2008 to 2014. Age and insurance based on their initial visit in this time frame. Testing was defined as at least one lipid measurement from 2008 to 2014.

<sup>b</sup> Age at initial outpatient visit was used for those who did not have lipid test.  
<sup>c</sup> Adjusted for categorical age, gender, race/ethnicity and insurance at 1st lipid test.  
<sup>d</sup> Chi-square *P* value: all *P* < 0.001.  
<sup>e</sup> Chi-square *P* value: age group *P* < 0.0001, sex *P* = 0.0717, race *P* < 0.0001, insurance *P* < 0.0001.

had 2 or more lipid tests during the study period. There were 6745 lipid tests with at least one lipid measured from 2008 through 2014. Demographic characteristics of subjects that had lipid testing and those who did not have testing are shown in Table 1.

There was modest increase in the proportion of children undergoing lipid testing in age group 9–11 years and children/young adults in age group 17–21 years of age (1.5% in 2008 to 2.2% in 2014, *P* < 0.001 for ages 9–11 years and 4.4% in 2008 to 4.6% in 2014, *P* = 0.02 for ages 17–21 years; Table 2 and Fig. 1).

The proportion of children and young adults tested increased markedly with increasing age (Table 2 and Fig. 1). In 2014, those who were 17–21 years of age were two times more likely to have undergone lipid tests during that year compared to those who were 9–11 years of age (Table 2 and Fig. 1). As compared to whites, black and Hispanic patients were more likely to have lipid testing and Asian patients were

**Table 2**  
Percent of children with lipid testing by age and year.

Age	Year of lipid testing						
	2008 (95% CI) <sup>a</sup>	2009 (95% CI) <sup>a</sup>	2010 (95% CI)	2011 (95% CI) <sup>a</sup>	2012 (95% CI) <sup>a</sup>	2013 (95% CI) <sup>a</sup>	2014 (95% CI) <sup>a</sup>
2–8	0.6 (0.4,0.7)	0.5 (0.4,0.6)	0.6 (0.5,0.7)	0.7 (0.5,0.8)	0.7 (0.5,0.8)	0.5 (0.4,0.7)	0.5 (0.4,0.6)
9–11	1.5 (1.1,1.8)	1.3 (1.0,1.6)	1.6 (1.3,1.9)	1.9 (1.5,2.3)	2.3 (1.9,2.6)	2.3 (1.8,2.6)	2.2 (1.8,2.6)
12–16	2.8 (2.4,3.0)	3.3 (2.9,3.6)	3.0 (2.7,3.4)	3.2 (2.9,3.6)	4.0 (3.6,4.4)	4.3 (3.8,4.7)	4.1 (3.6,4.5)
17–21	4.4 (3.9,4.7)	4.2 (3.7,4.5)	4.2 (3.7,4.5)	4.3 (3.8,4.7)	4.5 (4.1,4.9)	5.1 (4.5,5.4)	4.6 (4.1,4.9)
Total	2.2 (2.0,2.3)	2.2 (2.0,2.3)	2.2 (2.0,2.3)	2.3 (2.2,2.4)	2.6 (2.4,2.7)	2.7 (2.5,2.8)	2.5 (2.3,2.6)

<sup>a</sup> Percent of children, 95% confidence interval (CI) assumes the counts follow a Poisson distribution.

**Lipid Test Rate by Year for Age Groups**

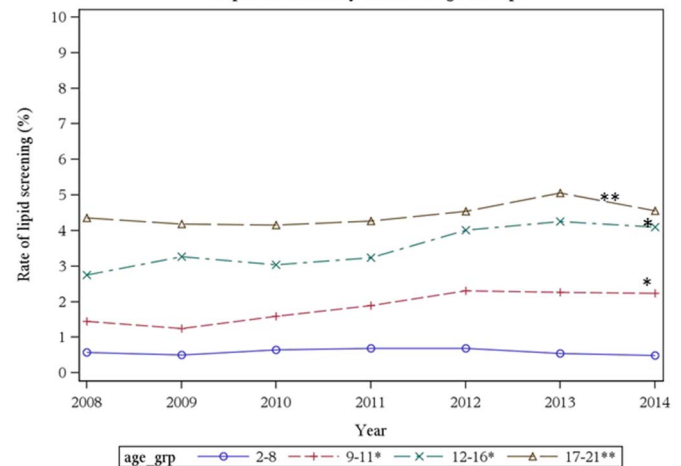


Fig. 1. Prevalence of lipid testing from 2008 to 2014 by age. Lipid test rate by 2–8 years (○), 9–11 years (+), 12–16 years (x), and 17–21 years (Δ). \*Significant *P* < 0.0001 for trend over time of age group 9–11 years and 12–16 years. \*\*Significant *P* = 0.0198 for trend over time of 17–21 years.

less likely to have lipid testing (Table 1). Additionally, children and young adults with private insurance were more likely to have lipid testing. The proportion of children undergoing lipid testing did not differ between males and females (Table 1). We also repeated the analyses after excluding those that previously undergone lipid testing from the numerator and denominator. Overall, only a small number of children (1114; 2%) of the total population had more than one test during the time period. For this reason, excluding children that had previously undergone lipid testing during the study did not alter our results.

Throughout the time period included in the study, low HDL-C was the most common lipid abnormality followed by elevated non-HDL-C (Table 3). Low HDL-C was noted in 23.8% of subjects undergoing lipid testing in 2008 and in 21.8% of subjects undergoing testing in 2014. Elevated non-HDL-C was noted in 18.8% of subjects in 2008 and in 10.8% of subjects in 2014 (Table 3). There was a significant decrease in proportion of 17–21 year olds with elevated total cholesterol during the study period (16.2% in 2008 to 11.6% in 2014; *P* = 0.01) and non-HDL-C (22.6% in 2008 to 12.6% in 2014; *P* < 0.001, Table 3, Fig. 2A,B and C).

#### 4. Discussion

In this population-based study, the proportion of children and youth having a lipid test increased minimally from 2008 to 2014. To our knowledge, this is the first population based study to examine trends in rates of lipid testing following the release of the NHLBI and AAP guidelines recommending universal lipid screening (Pediatrics, 2011).

The continued low rates of lipid testing in our study are similar to several other studies that have examined lipid testing via phone surveys

**Table 3**  
Prevalence of abnormal lipid levels out of those tested by year and age group.

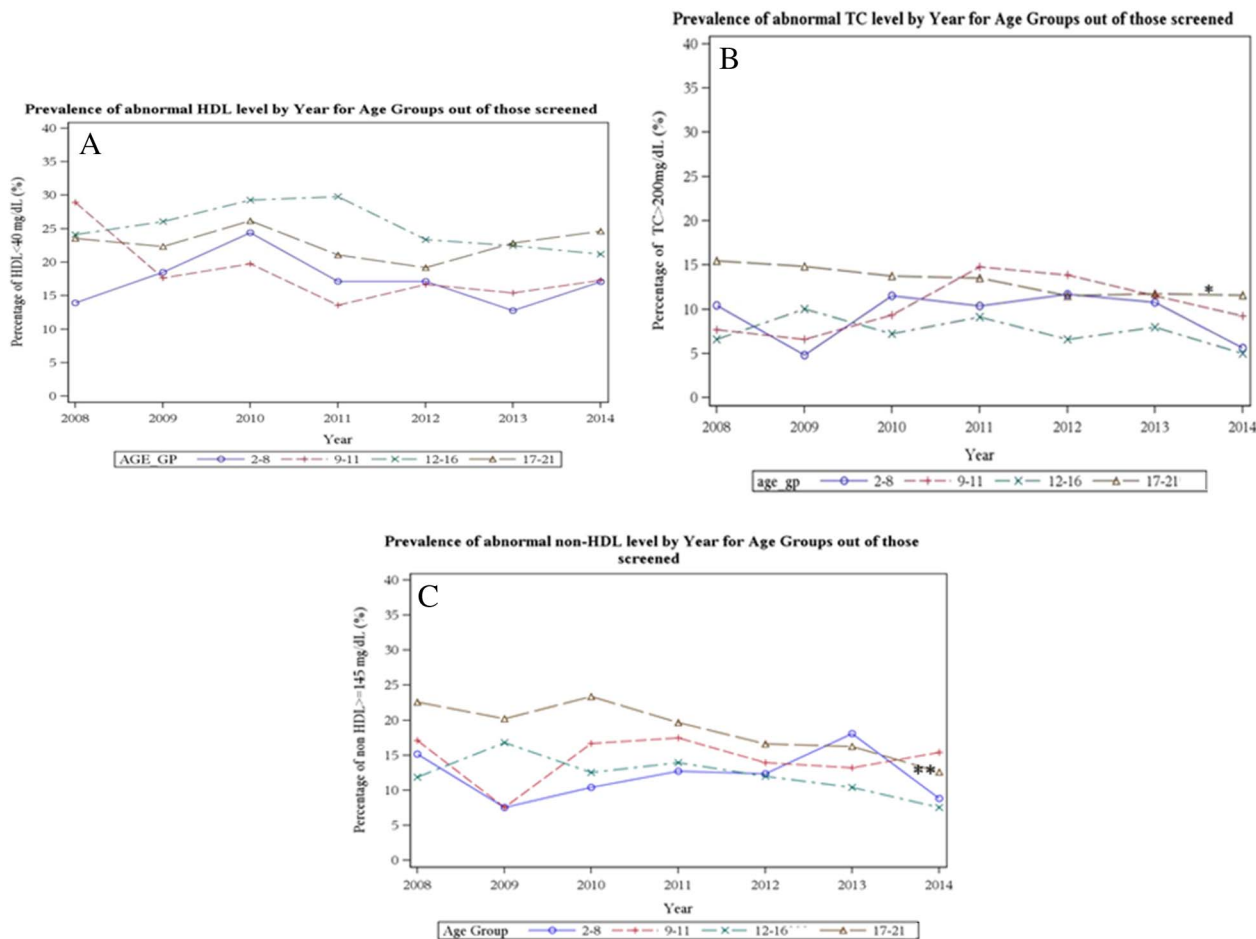
	2008 (95% CI) <sup>a</sup>	2009 (95% CI) <sup>a</sup>	2010 (95% CI) <sup>a</sup>	2011 (95% CI) <sup>a</sup>	2012 (95% CI) <sup>a</sup>	2013 (95% CI) <sup>a</sup>	2014 (95% CI) <sup>a</sup>
<b>TC, ≥ 200 mg/dL</b>							
Overall	12.5 (10.5,14.7)	12.8 (10.8,15.0)	11.4 (9.6,13.5)	12.9 (10.2,14.3)	10.5 (8.8,12.4)	10.7 (9.0,12.6)	8.5 (6.8,10.3)
2–8	10.5 (5.0,19.4)	6.1 (2.0,14.2)	11.9 (6.4,20.4)	9.9 (5.1,17.3)	12.5 (7.1,20.3)	12.1 (6.3,21.2)	5.6 (1.9,13.4)
9–11	8.8 (3.8,17.3)	6.6 (2.1,15.4)	10.4 (5.0,19.2)	14.8 (8.6,23.7)	14.1 (8.6,21.8)	11.7 (6.7,19.0)	9.4 (5.0,16.0)
12–16	6.7 (4.1,10.2)	10.9 (8.0,14.6)	7.3 (4.9,10.5)	9.2 (6.3,12.8)	6.6 (4.5,9.4)	8.2 (5.8,11.3)	5.0 (3.1,7.6)
17–21	16.2 (13.2,19.6)	15.7 (12.7,19.2)	14.2 (11.3,17.5)	13.9 (11.1,17.3)	12.3 (9.6,15.7)	12.2 (9.5,15.3)	11.6 (8.8,15.1)
<b>Non-HDL-C ≥ 145 mg/dL</b>							
Overall	18.8 (16.2,21.6)	17.5 (15.0,20.3)	18.3 (15.6,21.4)	16.9 (6.8,21.8)	14.3 (12.1,16.7)	13.9 (11.8,16.2)	10.8 (8.9,12.9)
2–8	15.2 (7.8,26.5)	7.6 (2.1,19.3)	10.4 (4.5,20.5)	12.8 (6.8,21.8)	12.4 (6.6,21.2)	18.1 (10.1,29.8)	8.9 (3.6,18.3)
9–11	17.1 (9.1,29.3)	7.6 (2.5,17.7)	16.7 (9.1,28.0)	17.5 (10.4,27.6)	14.0 (8.4,21.8)	13.2 (7.6,21.5)	15.4 (9.4,23.8)
12–16	11.9 (8.1,16.9)	16.8 (12.7,21.8)	12.6 (8.7,17.5)	14.0 (10.1,18.9)	12.0 (8.8,16.0)	10.4 (7.6,14.0)	7.6 (5.1,10.8)
17–21	22.6 (18.9,26.8)	20.2 (16.5,24.4)	23.4 (19.2,28.3)	19.7 (15.8,24.3)	16.6 (13.2,20.7)	16.2 (12.9,20.2)	12.6 (9.6,16.3)
<b>HDL-C &lt; 40 mg/dL</b>							
Overall	23.4 (20.5,26.6)	23.1 (20.2,26.3)	26.2 (23.0,29.8)	22.6 (19.7,25.9)	20.1 (17.6,22.9)	21.0 (18.4,23.9)	21.8 (19.1,24.7)
2–8	13.9 (7.0,24.9)	17 (7.8,32.2)	24.4 (14.7,38.0)	16.7 (9.7,26.7)	17.1 (10.2,27.1)	13.3 (6.6,23.7)	15.2 (7.8,26.5)
9–11	29 (18.1,43.8)	17.7 (9.1,30.8)	19.8 (11.5,31.6)	13.6 (7.4,22.8)	16.9 (10.7,25.4)	14.9 (8.8,23.5)	16.8 (10.5,25.4)
12–16	24.1 (18.5,30.9)	26.3 (21.1,32.3)	29.0 (23.0,36.2)	29.9 (24.0,36.8)	23.3 (18.7,28.6)	22.5 (18.2,27.5)	21.3 (17.0,26.3)
17–21	23.6 (19.8,27.9)	22.4 (18.5,26.8)	26.0 (21.6,31.2)	21.2 (17.2,25.9)	19.1 (15.4,23.4)	22.6 (18.6,27.1)	24.7 (20.4,29.6)

<sup>a</sup> Percent of children, 95% confidence interval (CI) assumes the counts follow a Poisson distribution.

and record reviews of well-child visits (Kimm et al., 1998; Vinci et al., 2014; Kimm et al., 1990; Valle et al., 2015; Wilson et al., 2015). Data from the National Ambulatory Medical Care Survey involving health maintenance visits among patients aged 2–19 years revealed lipid test orders in only 3% of visits and negligible increase in testing rates (2.5% in 1995 to 3.2% in 2010) (Vinci et al., 2014). Only 10% of pediatric patients enrolled in managed care organizations (n = 301,080)

between 2007 and 2010 had lipid testing (Margolis et al., 2014). Decline in lipid testing from 2002 to 2012 was reported in children and young adults aged 2–20 years from five integrated payer-provider sites of the Cardiovascular Research Network (Zachariah et al., 2015). All previous studies were, however, conducted before or shortly after the release of the 2011 NHLBI guidelines.

The low rates of lipid testing in our opinion to a large extent arise



**Fig. 2.** Plot of abnormal lipid levels from 2008 to 2014 by age out of those that had lipid tests. Age groups: 2–8 years (O); 9–11 years (+); 12–16 years (x); 17–21 years (Δ). Abnormal (A) total cholesterol, (B) non-HDL, (C) HDL levels. \*Significant  $P < 0.05$  for trend/time. \*\*Significant  $P < 0.001$  for trend/time.



from the lack of consensus among expert groups including the US Preventive Services Task Force and health care providers regarding the justification for universal screening (Ritchie et al., 2010; Haney et al., 2007; Force et al., 2016; Gillman and Daniels, 2012; Newman et al., 2012; Uy and Agawu, 2013; Dixon et al., 2014; de Ferranti et al., 2017). Only 58% out of surveyed AAP physicians agreed with universal screening, and 23% felt screening was low priority (de Ferranti et al., 2017). 68% reported they never/rarely/sometimes screened healthy 9- to 11-year-olds and instead, more providers usually/most/all of the time screened based on family cardiovascular history (61%) and obesity (82%). Screening 17- to 21-year-olds was more common in all categories (de Ferranti et al., 2017). In another online survey of primary care providers in Minnesota, three fourths of providers believed that lipid screening and treatment would reduce future cardiovascular risk but only 16% performed universal screening with one third performing no screening and half screening selectively (Dixon et al., 2014). Almost half reported uneasiness addressing lipid disorders and one-third reported unfamiliarity with screening guidelines (Dixon et al., 2014). The majority of providers (83%) were uncomfortable managing lipid disorders, and 57% were opposed to the use of lipid-lowering medications in children (Dixon et al., 2014). Other potential likely reasons for low rates of lipid testing include including lack of insurance reimbursement for testing, considerable lag time between publication of practice guidelines and subsequent uptake leading to change in clinical practice and differences in guidelines among different specialties.

Our findings of higher rates of testing with increasing age are consistent with earlier observations (Vinci et al., 2014; Margolis et al., 2014). Similar to other studies, we noted higher rates of lipid tests among black (Vinci et al., 2014) and Hispanic patients. Higher rates of lipid testing in black and Hispanic subjects, as well as older subjects, may have been a result of higher prevalence of overweight and obesity within these ethnic groups and with increasing age (Ogden et al., 2014; Ogden et al., 2016).

We noted higher prevalence of low HDL and elevated non-HDL-C in our study compared to other studies (Margolis et al., 2014; Kit et al., 2015). The higher prevalence of low HDL-C in our study (23.4% in 2008, 22.6% in 2011 and 20.1% in 2012) compared to NHANES (15.6% in 2007–2008 and 12.8% in 2011–2012) (Kit et al., 2015) is likely to due to higher rates of screening in obese children in our study. Minnesota ranks 35/51 in terms of ranking for prevalence of overweight and obesity among children 10–17 years old. In 2016, combined overweight and obesity rate among children 10–17 years old was 27.7% (<https://stateofobesity.org/states/mn>). The rates of low HDL-C in our study are however closer to those reported by Margolis et al. in patients enrolled in 3 large integrated health care systems in the US between 2007 and 2010 (Margolis et al., 2014). These similarities are likely due to greater rates of testing in obese youth seen in the health care systems (Margolis et al., 2014). The rates of elevated non-HDL-C are higher in our study (18.8% in 2008, 16.9% in 2011 and 14.3% in 2012) in comparison to the NHANES (10% in 2007–2008 and 8.4% in 2011–2012) (Kit et al., 2015). These differences may be secondary to over representation of obese children and those with family history of hypercholesterolemia in our study.

We noted decreasing rates over time of low HDL-C and elevated non-HDL-C in subjects that had undergone lipid testing. The magnitude of improvement in rates of low HDL-C during the study period was similar between our study and NHANES (14% decrease in our study from 2008 to 2012 and 18% decrease in NHANES from 2007–2008 to 2011–2012) (Kit et al., 2015). The rates of elevated non-HDL-C however decreased by a larger magnitude in our study compared to the NHANES (24% decrease in our study from 2008 to 2012 and 16% decrease in NHANES from 2007–2008 to 2011–2012) (Kit et al., 2015). These differences are likely secondary to differences in characteristics of study subjects including risk factors. Dietary improvements such as decrease in caloric intake may be potential contributor to improvement in lipids (Ford and Dietz, 2013). Additionally, greater rates of lipid

testing among youth without a risk factor due to increased awareness about lipids influencing cardiovascular health among health care providers/families may have contributed to decreasing rates of dyslipidemia.

The main strengths of the study are the population-based setting and the large sample size of children in the age categories recommended in universal screening guidelines. Most importantly, we examined trends in lipid testing over a period of several years before and after the release of the guidelines recommending universal lipid screening. Another strength was the measurement of non-HDL cholesterol. Non-HDL cholesterol has been shown to be a better predictor of coronary heart disease than LDL cholesterol (Arsenault et al., 2011). In an analysis from the Bogalusa study, non-HDL-C was at least as good a predictor as other lipid tests (i.e., LDL-C, TC, HDL-C, and the ratio of TC/HDL-C) for predicting increased carotid intima-media thickness (an indirect marker for atherosclerosis) (Frontini et al., 2008). In the Pathobiological Determinants of Atherosclerosis in Youth study (PDAY study), non-HDL-C and HDL-C levels were the best lipid predictors of pathologic atherosclerotic lesions in autopsies of children who had died from noncardiac causes (Rainwater et al., 1999).

There are several limitations in our study. First, the relatively short time span of three years after the 2011 guideline publication may not have been sufficient time to change practices of health care providers. Second, there is a lack of information regarding weight and body mass index (BMI). Fasting lipid screening is recommended in children with obesity as dyslipidemia including elevation in triglycerides is seen in a significant proportion of children with obesity (Pediatrics, 2011). Third, we did not have information on the clinical indication for lipid testing (including family history of hypercholesterolemia or premature ASCVD, endocrinopathy such as hypothyroidism or use of medications that can cause dyslipidemia). Given the absence of BMI and family history data, we were not able to distinguish between lipid screening and lipid tests obtained as part of clinical management such as in children with familial hypercholesterolemia or obesity. Lack of information in changing age distribution in the population was a limitation. Additionally, lack of LDL cholesterol measurements can be considered a limitation, though presence of non-HDL cholesterol was a strength given the better predictive value of non-HDL cholesterol for ASCVD. The use of the REP population as a denominator provides population-based estimates of testing but may underestimate testing rates (St Sauver et al., 2011). Overall, approximately 80% of children in this community visit a health care provider for some reason every year (St Sauver et al., 2012b). If all visits are considered possible opportunities for testing, using only children that visited a provider annually as a denominator would yield slightly higher testing rates. However, trends in testing would remain the same. It is important to point out that this study examines the lipid tests that were completed. Physicians may have recommended and ordered lipid tests but these tests may not have been completed due to fear of phlebotomy, cost concerns and other beliefs on part of the child or their family. Finally, the results from this study (that examined children and young adults from a predominantly white and middle-class community) cannot be generalized to other populations with greater ethnic diversity and those residing in other geographical locations. The presence of a tertiary care hospital in Olmsted County may also lead to higher number of children with chronic disorders including cardiac disorders and therefore may influence results.

## 5. Conclusion

In this population-based study, there was only a modest increase in proportion of children and young adults ages 9–11 years and 17–21 years undergoing lipid testing between the years 2008 and 2014, a time period during which guidelines recommending universal lipid screening in these age groups were released. Further longitudinal studies are warranted to improve guideline dissemination and address

attitudes, practices and barriers to implementation of universal lipid screening in children and young adults.

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#### Conflicts of interest

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#### Transparency document

The Transparency document associated with this article can be found, in online version.

#### References

- American Academy of Pediatrics, 1992. National cholesterol education program: report of the expert panel on blood cholesterol levels in children and adolescents. *Pediatrics* 89, 525–584.
- Arsenault, B.J., Boekholdt, S.M., Kastelein, J.J., 2011. Lipid parameters for measuring risk of cardiovascular disease. *Nat. Rev. Cardiol.* 8, 197–206.
- Bao, W., Srinivasan, S.R., Wattigney, W.A., Bao, W., Berenson, G.S., 1996. Usefulness of childhood low-density lipoprotein cholesterol level in predicting adult dyslipidemia and other cardiovascular risks. *The Bogalusa Heart Study. Arch. Intern. Med.* 156, 1315–1320.
- Berenson, G.S., Srinivasan, S.R., Bao, W., Newman 3rd, W.P., Tracy, R.E., Wattigney, W.A., 1998. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. *The Bogalusa Heart Study. N. Engl. J. Med.* 338, 1650–1656.
- Braamskamp, M.J., Kastelein, J.J., Kusters, D.M., Hutten, B.A., Wiegman, A., 2016. Statin initiation during childhood in patients with familial hypercholesterolemia: consequences for cardiovascular risk. *J. Am. Coll. Cardiol.* 67, 455–456.
- Daniels, S.R., Gidding, S.S., de Ferranti, S.D., National Lipid Association Expert Panel on Familial H, 2011. Pediatric aspects of familial hypercholesterolemias: recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. *J. Clin. Lipidol.* 5, S30–37.
- de Ferranti, S.D., Rodday, A.M., Parsons, S.K., et al., 2017. Cholesterol screening and treatment practices and preferences: a survey of United States pediatricians. *J. Pediatr.* 185, 99–105.
- de Jongh, S., Lilién, M.R., op't Roodt, J., Stroes, E.S., Bakker, H.D., Kastelein, J.J., 2002. Early statin therapy restores endothelial function in children with familial hypercholesterolemia. *J. Am. Coll. Cardiol.* 40, 2117–2121.
- Dixon, D.B., Kornblum, A.P., Steffen, L.M., Zhou, X., Steinberger, J., 2014. Implementation of lipid screening guidelines in children by primary pediatric providers. *J. Pediatr.* 164, 572–576.
- Force, U.S.P.S.T., Bibbins-Domingo, K., Grossman, D.C., et al., 2016. Screening for lipid disorders in children and adolescents: US preventive services task force recommendation statement. *JAMA* 316, 625–633.
- Ford, E.S., Dietz, W.H., 2013. Trends in energy intake among adults in the United States: findings from NHANES. *Am. J. Clin. Nutr.* 97, 848–853.
- Frontini, M.G., Srinivasan, S.R., Xu, J., Tang, R., Bond, M.G., Berenson, G.S., 2008. Usefulness of childhood non-high density lipoprotein cholesterol levels versus other lipoprotein measures in predicting adult subclinical atherosclerosis: the Bogalusa Heart Study. *Pediatrics* 121, 924–929.
- Gillman, M.W., Daniels, S.R., 2012. Is universal pediatric lipid screening justified? *JAMA* 307, 259–260.
- Haney, E.M., Huffman, L.H., Bougatsos, C., Freeman, M., Steiner, R.D., Nelson, H.D., 2007. Screening and treatment for lipid disorders in children and adolescents: systematic evidence review for the US Preventive Services Task Force. *Pediatrics* 120, e189–214.
- McGill Jr., H.C., McMahan, C.A., Zieske, A.W., et al., 2000. Associations of coronary heart disease risk factors with the intermediate lesion of atherosclerosis in youth. *The Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. Arterioscler. Thromb. Vasc. Biol.* 20, 1998–2004.
- Juhola, J., Magnussen, C.G., Viikari, J.S., et al., 2011. Tracking of serum lipid levels, blood pressure, and body mass index from childhood to adulthood: the Cardiovascular Risk in Young Finns Study. *J. Pediatr.* 159, 584–590.
- Kimm, S.Y., Payne, G.H., Lakatos, E., Darby, C., Sparrow, A., 1990. Management of cardiovascular disease risk factors in children. A national survey of primary care physicians. *Am. J. Dis. Child.* 144, 967–972.
- Kimm, S.Y., Payne, G.H., Stylianou, M.P., Wacławski, M.A., Lichtenstein, C., 1998. National trends in the management of cardiovascular disease risk factors in children: second NHLBI survey of primary care physicians. *Pediatrics* 102, E50.
- Kit, B.K., Kuklina, E., Carroll, M.D., Ostchega, Y., Freedman, D.S., Ogden, C.L., 2015. Prevalence of and trends in dyslipidemia and blood pressure among US children and adolescents, 1999–2012. *JAMA Pediatr.* 169, 272–279.
- Klancar, G., Grošelj, U., Kovac, J., et al., 2015. Universal screening for familial hypercholesterolemia in children. *J. Am. Coll. Cardiol.* 66, 1250–1257.
- Kusters, D.M., Avis, H.J., de Groot, E., et al., 2014. Ten-year follow-up after initiation of statin therapy in children with familial hypercholesterolemia. *JAMA* 312, 1055–1057.
- Lauer, R.M., Clarke, W.R., 1990. Use of cholesterol measurements in childhood for the prediction of adult hypercholesterolemia. *The Muscatine Study. JAMA* 264, 3034–3038.
- Margolis, K.L., Greenspan, L.C., Trower, N.K., et al., 2014. Lipid screening in children and adolescents in community practice: 2007 to 2010. *Circ. Cardiovasc. Qual. Outcomes* 7, 718–726.
- Newman, T.B., Pletcher, M.J., Hulley, S.B., 2012. Overly aggressive new guidelines for lipid screening in children: evidence of a broken process. *Pediatrics* 130, 349–352.
- Nicklas, T.A., von Duvillard, S.P., Berenson, G.S., 2002. Tracking of serum lipids and lipoproteins from childhood to dyslipidemia in adults: the Bogalusa Heart Study. *Int. J. Sports Med.* 23 (Suppl. 1), S39–43.
- Ogden, C.L., Carroll, M.D., Kit, B.K., Flegal, K.M., 2014. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA* 311, 806–814.
- Ogden, C.L., Carroll, M.D., Lawman, H.G., et al., 2016. Trends in obesity prevalence among children and adolescents in the United States, 1988–1994 through 2013–2014. *JAMA* 315, 2292–2299.
- Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. *Pediatrics* 128 (Suppl. 5), S213–256.
- Porkka, K.V., Viikari, J.S., Taimela, S., Dahl, M., Akerblom, H.K., 1994. Tracking and predictiveness of serum lipid and lipoprotein measurements in childhood: a 12-year follow-up. *The Cardiovascular Risk in Young Finns study. Am. J. Epidemiol.* 140, 1096–1110.
- Rainwater, D.L., McMahan, C.A., Malcom, G.T., et al., 1999. Lipid and apolipoprotein predictors of atherosclerosis in youth: apolipoprotein concentrations do not materially improve prediction of arterial lesions in PDAY subjects. *The PDAY Research Group. Arterioscler. Thromb. Vasc. Biol.* 19, 753–761.
- Raitakari, O.T., Juonala, M., Kahonen, M., et al., 2003. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA* 290, 2277–2283.
- Ritchie, S.K., Murphy, E.C., Ice, C., et al., 2010. Universal versus targeted blood cholesterol screening among youth: the CARDIAC project. *Pediatrics* 126, 260–265.
- Rodenburg, J., Vissers, M.N., Wiegman, A., et al., 2007. Statin treatment in children with familial hypercholesterolemia: the younger, the better. *Circulation* 116, 664–668.
- Roesch, A., 2012. Matching data using sounds-like operators and SAS® compare functions. In: *SAS (Ed.), SAS Global Forum*, pp. 1–11.
- St Sauver, J.L., Grossardt, B.R., Yawn, B.P., Melton 3rd, L.J., Rocca, W.A., 2011. Use of a medical records linkage system to enumerate a dynamic population over time: the Rochester epidemiology project. *Am. J. Epidemiol.* 173, 1059–1068.
- St Sauver, J.L., Grossardt, B.R., Leibson, C.L., Yawn, B.P., Melton 3rd, L.J., Rocca, W.A., 2012a. Generalizability of epidemiological findings and public health decisions: an illustration from the Rochester Epidemiology Project. *Mayo Clin. Proc.* 87, 151–160.
- St Sauver, J.L., Grossardt, B.R., Yawn, B.P., et al., 2012b. Data resource profile: the Rochester Epidemiology Project (REP) medical records-linkage system. *Int. J. Epidemiol.* 41, 1614–1624.
- Uy, J.D., Agawu, A., 2013. Screening is not as simple as it may seem. *Pediatrics* 131, e1384–1385.
- Valle, C.W., Binns, H.J., Quadri-Sheriff, M., Benuck, I., Patel, A., 2015. Physicians' lack of adherence to National Heart, Lung, and Blood Institute guidelines for pediatric lipid screening. *Clin. Pediatr. (Phila.)* 54, 1200–1205.
- Vinci, S.R., Rifas-Shiman, S.L., Cheng, J.K., Mannix, R.C., Gillman, M.W., de Ferranti, S.D., 2014. Cholesterol testing among children and adolescents during health visits. *JAMA* 311, 1804–1807.
- Webber, L.S., Srinivasan, S.R., Wattigney, W.A., Berenson, G.S., 1991. Tracking of serum lipids and lipoproteins from childhood to adulthood. *The Bogalusa Heart Study. Am. J. Epidemiol.* 133, 884–899.
- Wiegman, A., Hutten, B.A., de Groot, E., et al., 2004. Efficacy and safety of statin therapy in children with familial hypercholesterolemia: a randomized controlled trial. *JAMA* 292, 331–337.
- Wilson, D.P., Davis, S., Matches, S., et al., 2015. Universal cholesterol screening of children in community-based ambulatory pediatric clinics. *J. Clin. Lipidol.* 9, 888–892.
- Zachariah, J.P., McNeal, C.J., Copeland, L.A., et al., 2015. Temporal trends in lipid screening and therapy among youth from 2002 to 2012. *J. Clin. Lipidol.* 9, S77–87.