



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

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### ARTICLE INFO

#### Keywords:

Lipids  
Screening  
Children  
Dyslipidemia  
Hypercholesterolemia

### 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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<https://doi.org/10.1016/j.pmedr.2017.11.001>

Received 6 July 2017; Received in revised form 19 October 2017; Accepted 3 November 2017

Available online 08 November 2017

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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

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