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J Am Coll Cardiol. Author manuscript; available in PMC 2017 November 08.

Published in final edited form as:

J Am Coll Cardiol. 2016 November 08; 68(19): 2122–2123. doi:10.1016/j.jacc.2016.08.041.

Adolescent Dyslipidemia and Standardized Lifestyle Modification: Benchmarking Real-World Practice

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In order to combat atherosclerotic disease at its root, the 2011 National Heart, Lung, and Blood Institute Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents recommend lifestyle modifications specific to the dyslipidemia type as the primary response for the nearly 20% of 8-17 year-olds in the United States with abnormal cholesterol, reserving pharmacotherapy reserved for those with persistently highest risk[1,2]. But the translation of well-resourced, lifestyle intervention trial efficacy to real-world clinical effectiveness is not clear. We examined the effects of lifestyle modification goal-setting on dyslipidemia change in actual pediatric subspecialty practice.

Youth managed for dyslipidemia in Boston Children's Hospital's preventive cardiology clinics from September 2010 through March 2014 with a baseline and at least one follow-up visit were eligible for this analysis. A lipid Standardized Clinical Assessment and Management Plan (SCAMP®) formed the basis for data collection. The SCAMP encourages the clinician to identify three or more lifestyle modifications relevant to the patient's lipid profile, like saturated fat intake reduction for youth with elevated low-density lipoprotein cholesterol (LDL-C). In a separate encounter on the same day, the registered dietician along with the patient and family identified specific actions within the clinician prescription to be implemented tailored to the child's lipid profile and lifestyle pattern, such as reducing the child's full-fat cheese intake. After six months of monitoring, if NHLBI guideline-defined thresholds are not met, pharmacotherapy may be recommended. The current analysis includes patients never started or prior to starting lipid medications. Secondary analysis of

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quality improvement data was approved by the Boston Children's Hospital Committee on Clinical Investigation.

Total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were measured from fasting blood samples obtained at local laboratories. Low density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation. Data analyses were conducted separately for four non-exclusive subgroups: baseline LDL-C ≥ 190mg/dL, LDL-C between 130 and 189 mg/dL, HDL-C <40mg/dL, or TG>150mg/dL. Body mass index (BMI) was calculated as weight(kilograms) divided by the squared height(meters), referenced to age-sex normative values, and obesity defined as ≥ 95th percentile. Linear mixed models were used to estimate mean lipid level change from initial to last visit during the lifestyle modification period, adjusted for age, sex, baseline lipid level. We also assessed effect modification by BMI improvement versus not. Analyses were conducted in SAS version 9.3 (Cary,NC) and two-sided $p < 0.05$ was deemed significant.

The cohort included 501 dyslipidemic youth with median follow-up of 231 days [25%-75% range 13,1260]. Of these, 20% had LDL-C ≥190mg/dL, 45% had LDL-C 130-189mg/dL, 32% had diminished HDLC, and 39% had elevated TG [Table]. LDL-C ≥190mg/dL patients tended to be younger, less obese, and have lower blood pressure than the other groups. The most common dietary recommendations were to decrease trans-fat and saturated fat intake (63%), to increase fruit and vegetable intake (62%), to decrease the glycemic index (30%), to decrease portion size (15%), or to decrease sugar sweetened beverage consumption (14%). A recommendation to increase exercise was given to 55% and to continue current exercise to 35%.

The mean value of each abnormal lipid fraction improved and a proportion within each category normalized while BMI decreased very modestly: (BMI Z-score −0.05 [IQR −0.22, 0.05], $p<0.0001$; proportion obese 39% vs 36%, $p=0.03$). BMI decline appeared to modify the slope of change in moderate LDL-C elevation (No BMI decline −2.6±1.8, $p=0.14$; BMI decline −9.6±2.3, $p<0.0001$) and TG elevation (No BMI decline −18.3±11.5, p=0.11l BMI decline −54.69±13.9 $p=0.0001$) while HDL-C and LDL 190mg/dL were not modified by BMI decline.

The presented data represent a feasible, short term, clinical practice benchmark for pediatric lipid management. Previous studies offering dietary advice successfully lowered LDL-C by roughly 10% and sustained improvement for 3 years with no growth or safety concerns.[3] Our data suggests comparable improvements may be achieved in less-resourced, real world practice. High TG and low HDL-C dyslipidemia studies note relations between weight loss and modest lipid improvements that may persist for nearly 5 years.[4] Other studies suggest lowering carbohydrate intake alone may improve TG and HDL-C.[5] Our results suggest lifestyle modification to improve moderate LDL-C elevation or TG may depend on weight loss. Generalizability of the current findings may be limited by the tertiary care structure, inadequate power for subset analyses, limited comparison of specific lifestyle recommendations since providers coalesced around only a few, unmeasured medical history confounders, and local laboratory variation. Although we accounted for baseline lipid level, residual regression to the mean cannot be excluded. Overall, our data suggest real world

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clinical practice can approximate trial data in addressing the 1 in 5 youth with abnormal lipids.

Acknowledgments

Supported by the Boston Children's Hospital Institute for Relevant Clinical Data Analytics (IRCDA) and National Heart, Lung, and Blood Institute HL111335(JPZ).

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PRIMARY DATA TABLE

	LDL-C ≥190mg/dL	130mg/dL≤LDL-C<190	HDL-C <40mg/dL	TG≥150mg/dL
N	100	228	159	196
Age (y)	11±5	13±4	14±4	14±4
Female	51%	41%	35%	47%
Median BMI percentile (25%, 75% IQR)	75 (49, 95)	87 (64, 97)	97 (91,99)	96 (88,99)
Obese (%)	24%	35%	62%	54%
Systolic BP (mmHg)	109±14	118±43	118±13	122±46
Diastolic BP (mmHg)	63±9	64±10	65±11	66±10
LDL-C baseline (mg/dL)	239±45	155±16	134±57	132±54
LDL-C change (%)	−15 (−31, −1)	−8 (−19, 1)	−3 (−20,10)	−4 (−19,12)
HDL-C baseline (mg/dL)	50±11	50±14	33±6	40±11
HDL-C change (%)	−2 (−13, 16)	3 (−8, 14)	9 (−4,25)	4 (−5,18)
TG baseline (mg/dL)	106±82	142± 112	251±190	287±164
TG change (%)	−2 (−27, 24)	−8 (−29, 22)	−17 (−42,9)	−27 (−47,−4)
Proportion Normalized	8%	31%	36%	36%

BMI percentile referenced to Centers for Disease Control age -sex specific normative values and obese defined as above the 95^{th} percentile

Lipid change given as unadjusted median and IQR.

Abbreviations: IQR- interquartile range, mg/dL- milligrams per deciliter, BMI- body mass index, mmHg- millimeters mercury, LDL-C- low density lipoprotein cholesterol, HDL-C- high density lipoprotein cholesterol, TG- triglycerides