



Routine Cholesterol Tests and Subsequent Change in BMI Among Overweight and Obese Children

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ABSTRACT

INTRODUCTION: In 2011, the National Heart, Lung and Blood Institute and American Academy of Pediatrics concluded that both familial and obesity-associated dyslipidemias increase cardiovascular risk and recommended universal cholesterol testing at ages 9 to 11. It remains unknown whether testing influences body mass index (BMI) trajectory, a key modifiable cardiovascular outcome.

METHODS: This quasi-experimental-matched cohort includes children aged 9 to 11 years completing well visits in a diverse primary care network from 2012 to 2014. Participants had baseline BMI ≥ 85 th% and no prior cholesterol testing. Propensity score matching identified untested children similar to tested children on weight measures, practice site, sex, age, race, ethnicity, insurance, and well visit frequency. Change in BMI z-score was assessed over 18 months. Regression adjusted for residual confounding following matching. Data were analyzed in 2018.

RESULTS: Matching improved balance between tested and untested children for all characteristics. The matched cohort of

1808 children was predominantly non-Latino black (48%) or non-Latino white (33%), and Medicaid insured (39%). Baseline BMI z-score was 1.88 for tested and 1.84 for untested children. Of tested children, 25% had cholesterol levels above the 2011 guideline's "acceptable" range. Two children received cholesterol lowering medications. Adjusted analysis found no difference in change in BMI z-score between tested and untested children (0.02, 95% confidence interval $-0.01, 0.04$).

CONCLUSIONS: Individual risk assessment in the form of cholesterol testing is not associated with change in BMI trajectory among overweight and obese children. Though testing may identify familial hypercholesterolemia, results suggest testing does not change BMI trajectory, a key strategy to reduce cardiovascular risk.

KEYWORDS: primary care; prevention; screening; cholesterol; propensity score matching

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WHAT'S NEW?

In a matched cohort of 1808 overweight and obese 9- to 11-year olds, cholesterol testing was not associated with improved weight trajectory, a desired outcome for this high-risk population. Testing identified 2 individuals who received medication for elevated cholesterol levels.

THE VALUE OF cholesterol testing in childhood has been debated for decades.^{1–3} In 2011, the American Academy of Pediatrics (AAP) and the National Heart, Lung and Blood Institute (NHLBI) published a guideline on cardiovascular risk management that recommended universal cholesterol testing in childhood for the first time.⁴ This guideline generated controversy,^{5,6} and in 2014 only 55% of pediatricians endorsed universal testing for children.⁷ Reports suggest that less than 20% of children are tested

in the absence of incentives or other approaches to increase testing.^{8–10}

The 2011 guideline discussed two potential rationales for testing. The first involved identifying children with familial hypercholesterolemia, who may benefit from cholesterol-lowering medication.^{11,12} The second addressed mitigation of long-term cardiovascular risk in the general population. The 2011 guideline noted that both familial and obesity-associated dyslipidemias "place [children] at increased risk for accelerated early atherosclerosis."⁴ Longitudinal cohorts demonstrate that childhood cardiovascular risks, including cholesterol, track into adulthood and predict atherosclerosis.^{13–15} Behaviors that mitigate cardiovascular risk, such as physical activity and diet, also track from childhood to adulthood.^{16,17}

Cholesterol testing in childhood may therefore help clinicians and families better understand long-term individual risks. Health behavior theories demonstrate that perceived risk is a component of positive behavior

adoption when linked to other strategies to support behavior change.¹⁸ Combining epidemiological data and health behavior theory provides a theoretical mechanism by which early cholesterol testing could contribute to long-term cardiovascular health by promoting increased surveillance, positive behaviors, and early treatment among those at greatest risk.

However, recent reviews have noted that the potential causal pathway between cholesterol testing and improved outcomes remains untested.^{19,20} When the US Preventive Services Task Force (USPSTF) reviewed pediatric cholesterol testing in 2016, members of the task force declined to recommend universal testing because they found no evidence linking testing to health outcomes. Instead, they recommended further research on the risks and benefits of routine testing.⁶

We undertook this study to examine whether cholesterol testing in the context of routine well care is associated with one particular benefit, namely subsequent change in body mass index (BMI) among overweight and obese children. We focused on children with elevated BMI, for whom cholesterol testing is less controversial and who may particularly benefit from increased attention to cardiovascular risk and from interventions such as the nutritional counseling recommended in the 2011 guideline. Despite the theoretical plausibility outlined above, we hypothesized that cholesterol testing, as carried out in routine well child care, would not be associated with a change in BMI trajectory.

METHODS

POPULATION

This quasi-experimental matched cohort study used data from the electronic health record (EHR) of a large urban/suburban primary care network owned by Children's Hospital of Philadelphia.²¹ Practices vary in terms of patient demographics, payer mix, and involvement of trainees. The network completed implementation of a single EHR with full electronic reporting for laboratory results in 2008. This study was approved by the Institutional Review Board at the Children's Hospital of Philadelphia.

Children aged 9 to 11 years who completed a well visit between January 1, 2012, and June 30, 2014, with a BMI ≥ 85 th% were eligible for inclusion. Children with cholesterol testing at a well visit represented the tested population and children who had no cholesterol testing at any time from 9 to 11 years were eligible to serve as controls. After identifying eligible children, there were several visit-level exclusions. First, to allow matching on BMI trend, well visits were dropped if there was no BMI within 3 years prior to a potential index visit. Second, because we were interested in the role of cholesterol testing as a general screening tool, we excluded well visits that occurred within 3 years of prior cholesterol testing. Third, to assess our outcome, we dropped visits for which no follow-up was available within a 9- to 18-month follow-up window.

CHOLESTEROL TESTING

Cholesterol testing was defined as any completed test or panel that included a total cholesterol or LDL ordered on the same day as the well visit.

MATCHING VARIABLES

Propensity score matching aimed to match tested and untested children on characteristics associated with testing. Ideally, this method generates a sample that approximates the results of randomization, where tested and untested groups are balanced on relevant confounders. We selected variables for matching based on prior literature and initial work identifying factors in our EHR that were predictive of testing.^{9,22}

Demographic factors used in matching included sex, race/ethnicity (collected by self-report and constructed as Latino, non-Latino White, non-Latino Black, and other), and insurance payer (Medicaid vs other).

Health care factors included practice site, time since prior well visit (months) and, to account for secular trends, visit year.

Cardiovascular risk factors included BMI at the time of testing and BMI at the prior visit. BMI values are calculated from height and weight measurements. Data were cleaned using a validated algorithm that excludes invalid inliers and retains valid outliers.²³ We included prior BMI to adjust for possible impact of a rapid change in BMI. We did not match on blood pressure because this was not associated with testing in preliminary modeling. We did not match on family history because this is not consistently recorded in our EHR.

Finally, clinician factors (eg, MD vs nurse practitioner) were not associated with testing in our dataset, and thus were not included in matching. We matched on practice site, rather than individual clinician, because we theorized that unmeasured site level considerations related to workflow, laboratory availability, and within team learning may be more important than unmeasured individual level considerations. However, we did conduct sensitivity analysis in which we matched on individual clinician instead of practice site.

PRIMARY OUTCOME

The primary outcome was change in BMI z-score between the matched visit and a follow-up visit completed any time during the subsequent 9 to 18 months' follow-up window. When multiple potential visits were available for follow-up, we selected the first one.

Prior attempts to establish a clinically meaningful weight change for pediatrics suggest a difference of 0.5 z-score units or greater represents meaningful change.^{24,25} However, regular BMI z-scores provide poor differentiation between extreme BMIs. Because of this, pediatric obesity experts have suggested either modified z-scores or percent of 95th% as more appropriate outcome measures when including children with extreme BMI values in a sample.^{26,27} Modified z-scores are calculated as the difference between the observed BMI and the median BMI for

age and sex, divided by half the difference between the mean BMI and 2 standard deviations above the mean for age and sex.²⁸ We used modified BMI z-scores in our matching algorithm because they provided the best balance and, in sensitivity analysis, examined modified BMI z-scores as an outcome to ensure that our findings were not sensitive to the limitations of traditional BMI z-scores.

ANALYSIS: MATCHING

Matching used the R package MatchIt in RStudio. We used optimal matching and selected 1 match for each tested individual.^{29–31} Optimal matching is a form of propensity score matching that identifies potential matches to minimize differences across multiple characteristics in the tested and untested populations.²⁹ Matching was stratified based on BMI category (85th–95th% or >95th%) and age (in years). Within strata, tested children were matched to untested children based on sex, race/ethnicity, insurance payer, practice site, time since prior well visit, visit year, modified BMI z-score at the time of testing, and modified BMI z-score at prior well visit. After a visit was selected as a matched control, any other visits by the same child were excluded (ie, a child could only be a control once). We used modified BMI z-scores for matching because they allowed us to achieve the best balance between groups on weight-related measures (eg, BMI, BMI z-score). To examine balance between groups following the match, characteristics of tested and untested children were compared using chi-squared and *t* tests, and by examining standardized differences.

ANALYSIS: POSTMATCH

Postmatch analysis was performed in Stata, version 15.³² We compared change in BMI z-score between tested and untested children using paired *t* tests. We also compared change between tested and untested children in linear regression adjusting for variables used in matching to account for residual confounding.³³

We then examined subsequent primary care visits, blood tests, referrals, and medication prescriptions that occurred in the follow-up period, not including the same day as testing. We included primary care visits associated with ICD codes for obesity, dyslipidemia, dietary counseling, or hypertension. We included blood tests related to cardiovascular risk (AST, ALT, glucose, hemoglobin A1c). We included cholesterol-lowering medications mentioned in the 2011 guideline, including statins, bile acid sequestrants, cholesterol absorption inhibitors, fibric acid derivatives, or nicotinic acid.⁴ Finally, we included referrals to gastroenterology, endocrinology, cardiology, and an interdisciplinary obesity clinic. Because many children in the sample had no subsequent utilization, we dichotomized these variables as any versus none.

As noted above, children were specifically excluded from the control cohort if they had any cholesterol testing in the 9- to 11-year window. In our system, blood tests related to cardiovascular risk tend to be ordered together.

We therefore expected blood tests to be more frequent in the tested group, and this examination of utilization in the follow-up period was not intended to make causal claims.

As a subgroup analysis, we examined results of completed cholesterol tests. Thresholds for abnormally high LDL, total cholesterol, and triglycerides were taken from the 2011 guideline (LDL ≥ 130 mg/dL; total cholesterol ≥ 200 mg/dL; triglycerides ≥ 100 mg/dL for 9-year olds and ≥ 130 mg/dL for older children).⁴ We compared outcomes between those with high results and tested children with results in the guidelines “acceptable” range or below.

RESULTS

RESULTS OF MATCHING

We identified 28,403 children with 9- to 11-year well visits, of whom 7765 (27%) had a BMI ≥ 85 th% and met other inclusion criteria. Of children with elevated BMIs at 9- to 11-year well visits, 904 (12%) completed cholesterol testing at the time of the visit. The remaining 6861 children were available as potential untested matches.

Prior to matching, children who were tested differed from untested children. Children who were tested were more likely to report Black race (49% tested, 27% untested) or Latino ethnicity (8% tested, 6% untested). They were more likely to be Medicaid insured (40% tested, 21% untested) and have a BMI ≥ 95 th% (71% tested, 35% untested). In addition, care sites differed in rates of testing. Tested children represented as few as 2% to as many as 35% of children completing 9- to 11-year well visits at various sites.

All 904 tested children were matched to untested children. As intended, matching improved balance on all characteristics (Table 1). The matched cohort was predominantly non-Latino Black (48%) and non-Latino White (33%). Almost half of the cohort was covered by Medicaid insurance (39%). Mean time since prior well visit was 17 months. Included children completed well visits with 340 individual clinicians at 27 office sites.

PRIMARY OUTCOME

BMI z-score change was -0.04 (95% confidence interval [CI] -0.06 to -0.03) among tested and -0.06 (95% CI -0.08 to -0.05) among untested children (Table 2). The unadjusted difference in BMI z-score change was 0.02 (95% CI -0.01 to 0.05), with tested children having a smaller decrease in BMI z-score compared to those who were not tested. In regression adjusting for the variables used in the match to account for residual differences, we observed a nonsignificant difference in BMI z-score change of 0.02 (95% CI -0.01 , 0.04) between the tested and untested children (Table 3). In other words, we continued to find no significant association between cholesterol testing and difference in BMI z-score change. Z-score to weight conversions vary based on distance from the mean. However, as an example, for a 10-year-old girl of mean height with BMI at the 98th%, our results indicate that testing would be associated with a predicted

Table 1. Characteristics of Matched Cohort

Characteristic, N (%) or Mean (SD)	Tested N = 904	Not Tested N = 904	P Value*	Standardized Difference†
Demographics				
Female	442 (48.9%)	440 (48.7%)	.93	0.004
Race/ethnicity			.68	
Latino	72 (8.0%)	68 (7.5%)		0.019
Non-Latino Black	445 (49.2%)	423 (46.8%)		0.048
Non-Latino White	228 (31.9%)	306 (33.9%)		0.040
Other	99 (11.0%)	107 (11.8%)		0.025
Characteristics at testing				
BMI z-score	1.88 (0.41)	1.84 (0.40)	.06	0.098
BMI category			>.99	
85th–95th%	264 (29.2%)	264 (29.2%)		0
>95th%	640 (70.8%)	640 (70.8%)		0
Medicaid insurance	360 (39.8%)	336 (37.2%)	.25	0.055
Age			>.99	
9	250 (27.7%)	250 (27.7%)		0
10	384 (38.5%)	384 (38.5%)		0
11	306 (33.9%)	306 (33.9%)		0
Year			.46	
2012	331 (36.6%)	312 (34.5%)		0.044
2013	372 (41.2%)	398 (40.0%)		0.057
2014	201 (22.2%)	194 (21.5%)		0.019
Prior well visit				
Time to prior well visit (mon)	16.8 (5.4)	16.6 (5.5)	.41	0.037
Prior BMI z-score	1.77 (0.51)	1.73 (0.51)	.10	0.078
Prior BMI category			.29	
<85th%	73 (8.1%)	91 (10.1%)		0.070
85th–95th%	275 (30.4%)	280 (31.0%)		0.013
>95th%	556 (61.5%)	533 (59.0%)		0.051

*P values represent results of chi-squared tests for categorical variables and *t* tests for continuous variables.

†Standardized differences were calculated as the difference in means between tested and untested children, divided by the overall cohort standard deviation.³³

Table 2. Outcomes Following Cholesterol Testing

N (%) or Mean (SD)	Tested N = 904	Not Tested N = 904	P Value*
Change in BMI z-score	−0.04 (0.25)	−0.06 (0.25)	.10
Primary care follow-up†	595 (65.8%)	482 (53.3%)	<.001
Referrals‡	138 (15.3%)	59 (6.3%)	<.001
Lab testing§	209 (32.2%)	98 (13.6%)	<.001
Medications	2 (0.2%)	0 (0%)	.16

*P values represent results of chi-squared tests for categorical variables and paired *t* tests for continuous variables.

†Primary care follow-up included any visits in the 18-month follow-up window associated with ICD codes for obesity, hypertension, dyslipidemia, or dietary counseling.

‡Referrals include referrals to gastroenterology, endocrinology, cardiology, or a multidisciplinary healthy weight program.

§Lab testing includes AST, ALT, glucose, or hemoglobin A1c.

||Medications include lipid-lowering medications mentioned in the 2011 guideline.

Table 3. Adjusted Outcomes*

	Coef (95% CI)	OR (95% CI)	P Value
Change in BMI z-score	0.02 (−0.01, 0.04)		.09
Primary care follow-up†		1.66 (1.36, 2.03)	<.001
Referrals‡		2.50 (1.79, 3.49)	<.001
Lab testing§		3.00 (2.36, 3.81)	<.001

*Results of regression adjusting for demographics, year of visit, time since last well visits, BMI at well visit, and BMI at prior well visit.

†Primary care follow-up included any visits in the 18-month follow-up window associated with ICD codes for obesity, hypertension, dyslipidemia, or dietary counseling.

‡Referrals include referrals to gastroenterology, endocrinology, cardiology, or a multidisciplinary healthy weight program.

§Lab testing includes AST, ALT, glucose, or hemoglobin A1c.

increased weight of 0.58 kg (95% CI -0.28 to 1.82) during follow-up compared to a similar girl who does not undergo testing.

In sensitivity analysis, there was no significant difference between tested and untested children when modified BMI z-score was considered as an outcome (adjusted change in modified BMI z-score 0.03 , 95% CI -0.01 to 0.06). In addition, results did not differ when the matching was conducted on clinician in place of clinic site.

OTHER UTILIZATION

Utilization was examined during the 18 months following testing (excluding day of testing). Among the tested children, 66% were subsequently seen in primary care for cardiovascular or weight-related diagnoses, 15% were referred to specialty care, and 32% completed subsequent blood tests related to cardiovascular risk. Among untested children, 53% were subsequently seen in primary care, 6% were referred to specialty care, and 14% completed subsequent blood tests (Table 2). These differences were significant in regression analysis, with increased odds of the primary care visit (odds ratio [OR] 1.66 ; 95% CI 1.36 , 2.03), referral (OR 2.50 ; 95% CI 1.79 , 3.49), and further testing (OR 3.00 ; 95% CI 2.36 , 3.81) among tested versus untested (Table 3).

Two children of the 904 tested (0.2%) received subsequent cholesterol lowering medications. Both of these children were tested and had the 2 highest total cholesterol results in the cohort (320 and 373 mg/dL).

SUBGROUP ANALYSIS: OUTCOMES AMONG THOSE WITH CHOLESTEROL TESTING

Of the 904 tested children, there were 227 children (25%) with total cholesterol, LDL, or triglycerides above the range designated "acceptable" by the 2011 guideline. Per guideline, all of these children should have received dietary counseling and primary care follow-up at a minimum. There were 34 children (4%) with cholesterol levels for which the guideline recommended referral for possible medication management, assuming levels could be confirmed on repeat testing and were not responsive to dietary changes. Compared to the tested children with the results at or below "acceptable," those with higher cholesterol levels were more likely to be seen in primary care (75% vs 63%) or to receive specialty referrals (20% vs 14%). However, they were no more likely to undergo subsequent lab testing (22% vs 23%). In unadjusted analysis, abnormal results were not associated with a difference in change in BMI z-score (-0.06 vs -0.04 , *t* test *P* value $.24$). Using regression to adjust for baseline BMI and demographic factors, there continued to be no association between elevated results and change in BMI z-score (coefficient -0.01 , 95% CI -0.05 , 0.03).

DISCUSSION

In this quasi-experimental propensity score matching cohort study, we found no difference in BMI change among children with cholesterol testing compared to

those without. We thus found no evidence that routine cholesterol testing, as it occurs in general pediatric practice, plays a role in modifying weight trajectory among overweight children. Moreover, this was observed in a cohort where tested children subsequently had more laboratory testing, primary care visits, and referrals than untested children. Although cholesterol testing is the specific focus of much debate, it seems to be one part of a longitudinal bundle of care related to cardiovascular risk that is received by some children and has uncertain value.

We used BMI z-score as our primary outcome. A BMI z-score change of 0.5 is considered clinically significant.^{24,25} Our cohort did not experience z-score changes of this magnitude. Findings were consistent when examining modified BMI z-scores, which are more sensitive to changes at extreme values.

To our knowledge, ours is the first study to attempt to evaluate the influence of the 2011 NHLBI recommendation for routine testing on a health outcome, or to focus on the recommendation for screening among younger children.⁴ Prior evaluations of the 2011 guidelines focused on adherence to the recommendation,^{8,9} as well as on the perspective of clinicians and adolescents on screening.^{7,34} Evaluations focusing on possible health consequences will be critical to informing future recommendations, and to resolving discrepancies between professional recommendations, such as the current discrepancy between the 2011 guideline and the 2016 USPSTF recommendation. Focusing on short-term outcomes among populations with heightened risk for poor cardiovascular outcomes, such as those with obesity, may be a feasible strategy for generating clinically relevant findings.

The prevalence of obesity in the cohort from which we drew our sample was lower than in the United States as a whole (12% in our sample, 18% in national data).³⁵ Our overall cholesterol testing rate of 12% was within the range of other reports.^{9,10} Because we excluded recently tested children and those tested outside of well care, this rate underestimates overall testing in our system. The overrepresentation of Black race and Medicaid insurance that we observed among tested children has been reported previously.²²

Our findings on subsequent laboratory testing should not be interpreted as causal, because our control cohort explicitly excluded children with any cholesterol testing from ages 9 to 11 years. Care differences between children with testing versus without could reflect family or clinician preferences or explicit criterion for specialty referral. In the present study, we attempted to adjust for health care utilization preferences by matching on the time since prior well visit.

Subgroup analysis comparing children with abnormally high versus normal cholesterol results also found no differences in subsequent weight trajectory. Based on the overall study and these results, clinicians should not assume that learning about elevated cholesterol plays an important role in promoting weight stabilization or weight loss. However, cardiovascular disease is complex and it is conceivable that individualized information influenced important outcomes not captured by our study design. For

example, some children may have increased physical activity, which may improve metabolic health even in the absence of improved weight status.

Two individuals out of the 904 children tested in our cohort subsequently received cholesterol-lowering medications. This is roughly what might be expected based on population reports of familial hypercholesterolemia prevalence of 1 in 500.^{11,12}

Our study has several limitations. Even using advanced matching programs, we had difficulty identifying matches for all tested children with regards to BMI. This is consistent with prior assessments showing that elevated BMI is a strong predictor of cholesterol testing in pediatrics.^{9,22} Our findings addressed only 9- to 11-year olds with elevated BMI in a single health system and may not be generalizable to other populations. Though matching is quasi-experimental, this remains an observational study. We cannot account for unmeasured potential confounders, such as family history, patient preferences, individual motivation, or resources to support change.³³

Finally, the most clinically relevant limitation may be our inability to report on lifestyle education or counseling that may have followed testing, or on patient and family response to test results or associated care. These factors are not consistently captured in our EHR, but are important considerations to determining the value of routine testing. One observational study reported cholesterol testing as a component of effective efforts to reduce pediatric cardiovascular risk, when linked to other support for health behavior change.³⁶ Pediatric primary care-based interventions addressing obesity are more common than those addressing cholesterol levels, and successful interventions related to obesity have also required multifactorial behavior change approaches.^{37,38} We are unaware of a successful pediatric obesity intervention that has explicitly included cholesterol testing. Our results suggest that testing alone, as it occurs in current practice, is an insufficient strategy to promote weight loss for high-risk children. However, we cannot exclude the possibility that there may be a role for testing as part of a more comprehensive evidence-based strategy.

In conclusion, we found no association between cholesterol testing and differences in subsequent BMI trajectory. Testing was associated with increased subsequent health care visits. Our findings raise important questions about the consequences of testing, if any, as a strategy for cardiovascular risk reduction in the general overweight population. Cholesterol testing in our cohort identified individuals in need of medical management consistent with rates of familial hypercholesterolemia reported in the general population. Strategies to address and modify cardiovascular risk in pediatric settings should examine the role of testing when embedded in a more comprehensive program of education and behavior change support.

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