Short-term Change in Body Mass Index in Overweight Adolescents Following Cholesterol Screening

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Objective: To determine the relationship between routine screening for cholesterol level and subsequent change in body mass index (BMI; calculated as weight in kilograms divided by height in meters squared).

Design: Retrospective cohort.

Setting: General pediatrics clinics at 2 academic centers.

Participants: Adolescents with BMIs in the 85th percentile or higher aged 10 to 18 years whose cholesterol levels were screened between June 2003 and June 2005 and controls matched for age, sex, ethnicity, and BMI.

Main Exposure: Cholesterol screening.

Outcome Measures: The primary outcome was the “best” individual BMI change following screening. The secondary outcome was the trend of BMI change during follow-up.

Results: Sixty-four matched pairs met the inclusion criteria (N=128). Subjects were followed up for 3 to 30 months after identification (mean [SD], 18 [8] months). The mean BMI changes for screened subjects did not differ from those of unscreened subjects (−0.33 vs −0.34; P=.97). However, age at time of enrollment significantly modified the results (P=.02). After cholesterol screening, younger subjects initially increased in BMI, while older subjects initially decreased. The overall trend of individual BMI change increased during the follow-up period and was not significantly different between the 2 groups (likelihood ratio test, 0.9; P=.64).

Conclusions: Cholesterol screening of overweight and obese adolescents is not associated with short-term BMI change, though age at time of screening modified subsequent BMI change. Clinicians should not assume that screening will help motivate weight loss, though the effect of age at the time of screening deserves further research.

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Obesity in children has increased throughout the world, and in the United States 33% of adolescents are now considered either overweight (body mass index [BMI; calculated as weight in kilograms divided by height in meters squared] ≥85th percentile and <95th percentile for age and sex) or obese (BMI ≥95th percentile).1 The association of childhood overweight with many risk factors for adult cardiovascular disease including hypertension, hyperlipidemia, and diabetes mellitus type II prompts particular concern.2 Several major prospective epidemiologic studies, including the Muscatine,3,4 Bogalusa,5 Coronary Artery Risk Development in Young Adults,6,7 and Special Turku Coronary Risk Factor Intervention Project8 studies have also demonstrated that obesity and high levels of low-density lipoprotein C in children and adolescents help predict physiologic arterial changes such as increased carotid intimal thickness, which may be precursors to early cardiac clinical events.

Owing in part to the association between elevated cholesterol in childhood and early cardiovascular changes, the National Cholesterol Education Program and the American Heart Association endorse cholesterol screening in children with a family history of premature cardiovascular disease or hyperlipidemia.9,10 Additionally, the recently published American Academy of Pediatrics Clinical Report reinforced the recommendation to screen all overweight children (BMI ≥85th percentile) older than 2 years for elevated cholesterol.10,11 However, other individuals and expert panels have disagreed with this recommendation. They argue that severe cholesterol abnormalities are very rare in adolescents and generally independent of weight status, recommendations for treat-
ment of mild to moderate lipid abnormalities are the same as those for the treatment of overweight itself, or that screening should not start until adulthood. \textsuperscript{11-16}

These disagreements about screening and early indication of specific cardiovascular risk factors do not account for potential secondary effects of screening. For example, some proponents of cholesterol screening highlight the possibility that cholesterol screening itself may help motivate lifestyle or behavioral changes. \textsuperscript{17,18} The recommendation to have blood tests might reinforce physicians’ concern about children’s weight status and the associated health risks. Thus, cholesterol screening could motivate change regardless of whether the results are normal or abnormal. Additionally, an elevated cholesterol result on screening could further motivate families and adolescents to institute therapeutic lifestyle changes and achieve weight loss.

The value and effect of screening on a range of health outcomes has been explored, with contradictory results.\textsuperscript{1,7-22} However, previous studies have not directly evaluated subsequent weight or BMI change in the overweight adolescent population following cholesterol screening.

We performed a retrospective cohort study with matched controls to explore the relationship between cholesterol screening and subsequent BMI change in overweight adolescents. We hypothesized that cholesterol screening in overweight children would be associated with a subsequent short-term decrease in BMI compared with unscreened controls, expecting to observe a difference in both the “best” individual BMI change following screening and the trend of BMI during follow-up.

### METHODS

#### SAMPLE

We identified overweight (BMI \(85\text{th to }94\text{th percentile}) or obese (BMI \(95\text{th percentile}) adolescents aged 10 to 18 years who had cholesterol screening performed as part of a routine visit between June 2003 and June 2005. This was achieved using computerized search mechanisms in the laboratory order system of the Child and Adolescent General Clinic of the North Carolina Children’s Hospital (University of North Carolina) and the electronic medical record system of the Pediatric Outpatient Center of Brody School of Medicine at East Carolina University. Exclusion criteria included a BMI lower than the 85th percentile, age younger than 10 years at the time of cholesterol screening, known secondary causes of obesity (eg, hypothyroidism), subspecialist-ordered screening, lack of documented height and weight measurement within 1 month of baseline screening, lack of follow-up height and weight measurement at least 3 months after baseline BMI assessment, and lack of identification of an appropriately matched subject (see below for matching criteria). In addition, any subject who was at any time previously screened for cholesterol at University of North Carolina or East Carolina University or noted to be screened at an outside hospital was excluded from the analysis.

Each screened subject was matched with an overweight or obese adolescent subject who was not exposed to cholesterol screening. Unscreened subjects were identified by a manual search of all patients seen in the same time frame at the same clinic site and matched to screened subjects based on baseline age (within 1 year), sex, self-identified race/ethnicity, and BMI (within 3 units). If more than 1 match was found for a particular screened subject, we then chose the “best matched subject with adequate follow-up” based on baseline age, BMI closest to the subject, and number of follow-up height and weight measurements.

#### STUDY DESIGN

The baseline BMI for each subject was recorded from their medical records or calculated from documented height and weight. The date of the baseline BMI at the time of the cholesterol screening was designated \(t0\) for the screened group. The BMI was chosen as the tracking measure based on recent data suggesting that BMI is more accurate than BMI \(z\) score or weight for evaluating change in adiposity over a relatively short study period.\textsuperscript{19} The BMI at the first follow-up visit (designated \(t1\) and all subsequent follow-up visits (\(t2, t3, \text{ et cetera}) were recorded for both the screened and unscreened controls. When only a weight was recorded in isolation at a particular clinic visit, a BMI was calculated from a height documented within a month of that clinic visit. When no height measurement was performed within a month of the clinic visit, the weight and follow-up visit were excluded from the analysis. If unscreened subjects were later screened during follow-up, their information thereafter was censored, and they were not crossed over into the screened group.

Initial laboratory values were documented using both fasting and nonfasting lipid panels, including total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol, when available. The reason for lipid screening was also extracted from the clinic note. The results of cholesterol screening were characterized as normal or abnormal based on total and/or low-density lipoprotein cholesterol levels per the most recent American Academy of Pediatrics Clinical Report,\textsuperscript{10} and follow-up lipid values were recorded if performed for the screened subjects. Finally, if referral to a specialist whose care was likely to include addressing weight loss (eg, nutrition, cardiology, endocrine, sleep apnea, or pulmonary) occurred at some point after screening, the dates of treatment by the specialist(s) were recorded.

#### STATISTICAL ANALYSIS

The \(x^2\) tests of association (Fisher exact test when necessary) and independent \(t\) tests were used to assess differences in baseline characteristics and demographic information between subjects from the 2 centers. The primary outcome was best individual BMI change, defined as either the smallest increase or the largest decrease in BMI after enrollment. Multivariable linear models were used to assess group differences in this outcome. Models were adjusted for center, duration of follow-up, and the 4 matching variables (to control for residual confounding and ensure valid variance estimates).\textsuperscript{23} Effect modification was individually explored for group (screened and unscreened) with center, age at enrollment, ethnicity, sex, and baseline BMI.

A secondary outcome was the trend of BMI change over time. Linear mixed models were used to assess significant differences in BMI change over time between the screened and unscreened groups. Both a random intercept and slope were included in these models. The likelihood ratio test was used to determine whether there was a significant group \(\times t\) interaction (ie, whether the trend over time was different for the 2 groups). Time-dependent covariates were used to assess whether visits to any subspecialty clinic for weight-related issues affected the trends in BMI over time. Data were compiled into...
Table. Demographic Characteristics of the Sample

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Abbreviations: ECU, Brody School of Medicine at East Carolina University; UNC, University of North Carolina.

Excel (Microsoft Corporation, Redmond, Washington) and inferential statistics and modeling were done using SAS Version 9.1 (SAS Institute Inc, Cary, North Carolina). This study was reviewed and approved by the Health Sciences Institutional Review Board at the University of North Carolina (study 070260).

RESULTS

POPULATION CHARACTERISTICS

A total of 64 matched pairs were identified (N=128), with 25 pairs identified at University of North Carolina and 39 at East Carolina University. The mean (SD) age of the subjects was 13.7 (2.2) years. The Table displays patient demographics and baseline characteristics at the 2 clinics. The length of follow-up between sites was not different, but race/ethnicity, age at enrollment, insurance status, and baseline BMI were different between the 2 clinics.

Justification for screening was documented in 57 of 64 subjects. Isolated overweight or obesity was documented as the reason for screening in 86% of the screened subjects, and 14% had obesity in addition to other risk factors such as a family history of hyperlipidemia or family history of early myocardial infarction. Based on documentation at the initial clinic visit, 83.1% of the screened subjects were counseled on diet and/or exercise or referred to a nutritionist for counseling; 61.5% of the unscreened group had lifestyle counseling documented at the matched initial visit (P=.006).

PRIMARY ANALYSIS: BEST INDIVIDUAL BMI CHANGE

The unadjusted mean best individual BMI change was not different between the screened (−0.33 units; 95% confidence interval, −0.93 to 0.26) and unscreened groups (−0.34 units; 95% confidence interval, −0.94 to 0.25; P=.97). After adjustment for clinic, ethnicity, age, sex, baseline BMI, and follow-up time, there was still no significant mean difference between groups' BMI change (difference, 0.02; 95% confidence interval, −0.82 to 0.86).

Exploration of possible effect modification demonstrated that individually, both age of subjects at time of screening and center appeared to individually modify the effect of screening group on best BMI change. For age at screening (P=.03) and center (P=.02 for age at screening and P=.02 for center). However, after controlling for an age × screening group interaction, the center × group effect appeared to no longer be significant (P=.08). The Figure graphically displays the trends associated with the effect that age at time of screening has on the best BMI change for screened children and for unscreened children. Of the younger screened sub-
jests, there was a trend toward increased BMI after screening; of the older screened subjects, there was a trend toward decreased BMI after screening. The resultant BMI change trend for unscreened subjects demonstrated an inverse pattern to the screened subjects. Ethnicity ($P = .83$), sex ($P = .46$), and baseline BMI ($P = .22$) did not modify the effect between screening group and best BMI change.

SECONDARY ANALYSIS: BMI TRENDS OVER TIME

To explore trends in BMI over time for the screened and unscreened groups, a mixed model was run with a random intercept and slope and fixed group, time, age, center, and the group × age and group × time interaction terms. The interaction terms for this model were not significant (likelihood ratio test, 0.9; degree of freedom, 2; $P = .64$), and in the final model there was no significant difference in BMI trend over time between the screened and unscreened groups ($P = .95$). However, there were significant age ($P < .01$) and time ($P = .02$) effects in the final model. The time effect is positive (the average BMI increases 0.45 units per year for a given group and age), and the age effect is also positive (the average BMI increases 1.07 units per year of age for a given point in time and group). Thus, regardless of age or screening group, BMI increased over time.

ANALYSIS OF THE EFFECT OF REFERRAL TO SPECIALTY CARE

We also explored the effect of referral to specialty care on subsequent BMI change. The effect of care in any potentially weight-related specialty on the trend in BMI over time was explored using a time-varying covariate. Of the 31% (n = 40) of patients who were referred to a subspecialty clinic, 30% (n = 12) were referred to a second subspecialty clinic. Referral to either 1 or 2 specialists was not associated with a change in BMI trend over time ($P = .80$ and $P = .48$, respectively).

COMMENT

Screening for cholesterol was not associated with subsequent BMI improvement when measured at a single point in time of follow-up. Additionally, over a longer period of time, the BMI trend for screened and unscreened groups increased without a significant difference between groups.

Previous studies examining the effectiveness of screening tests to motivate cardiovascular risk reduction behavior in adults have yielded conflicting results. For example, O’Malley et al demonstrated that elevated calcium scores determined by electron beam tomography of the coronary arteries in adults did not increase the effectiveness of therapeutic lifestyle change counseling. Meanwhile, Bankhead et al completed a systematic review and meta-analysis that demonstrated improved cholesterol levels and health behavior after cholesterol screening.

There are many reasons why studies of adult therapeutic lifestyle changes have limited generalizability to children or adolescent patients. First, adolescents are still in an active process of development and have wide variation in decision-making skills. Second, regardless of the cardiovascular risk factors present, adolescents have much lower absolute risk of cardiovascular events over the next 10 to 20 years than adults. Third, adolescent health behavior, food consumption, and physical activity are still directly influenced by parental health practices. In support of a possible age- and developmental stage–based difference, we found that after screening, older adolescents had associated positive BMI changes and younger adolescents seemed to have a worse BMI trend. Older adolescents may better understand their health and why they were screened and have increasing independent control over their food and lifestyle choices. Meanwhile, the associated weight increase in younger adolescents may echo the findings of Rosenberg et al in 1997. These found that a new diagnosis of hyperlipidemia in children and adolescents was associated with a negative effect on behaviors. Though this study did not directly assess health behavior, it is reasonable to assume that negative generalized behaviors such as aggression and risk-taking may have a negative effect on health behavior. The potentially complex age-at-screening interaction that was suggested by our findings should not be used as a predictive model, which would need further investigation in prospective randomized trials with larger subject samples.

The obesity epidemic has caused health care providers for children to address issues such as cardiovascular risk stratification and therapeutic lifestyle changes counseling. Pediatricians and their professional societies have mobilized and embraced screening as part of an ethos of prevention and early identification. Other groups, such as the United States Preventive Services Task Force, suggest that cholesterol screening has not yet demonstrated some of the important criteria necessary to justify screening. However, the analytic framework and traditional criteria to justify screening tests do not take into account the possibility that the act of screening itself might have some therapeutic benefit. If this were the case, then use of the laboratory test might be justified without meeting the usual diagnostic test utility criteria.

There are several limitations of our study that deserve note. First, the retrospective cohort design limits the ability to infer a causal relationship between screening and BMI change. It is possible that physicians screened overweight adolescents they perceived as less motivated in an effort to persuade them to make lifestyle changes, potentially confounding our results. Identifying patients at just 2 sites and at academic centers limits the generalizability of the study to other settings. Additionally, we do not know exactly what counseling was provided about therapeutic lifestyle changes or whether patients actually changed dietary or physical activity patterns.

Finally, we do not know exactly how cholesterol results were communicated to patients. This missing information, combined with the fact that few subjects had abnormal cholesterol results, limits our ability to determine whether screened children with abnormal results decreased their BMI more than unscreened children. In our limited sample, those with abnormal results on cho-
lesterol screening had no greater improvement in their subsequent BMI trends than those with normal screening results (results not shown), but our sample was not powered to detect subtle differences. Additionally, we could not explore whether normal cholesterol results in overweight children may somehow communicate false reassurance about overweight status (ie, “He/she’s okay despite being overweight”); if present, this message could decrease motivation for adolescents and/or families to making lifestyle changes that are important, regardless of the cholesterol results. These 2 potential hypotheses could be explored in an adequately powered prospective randomized trial. Our results can only be applied to the primary study question about the general effect of screening itself, irrespective of result, on short-term subsequent BMI pattern.

Prior to the study, we were concerned that if screening were associated with a decrease in BMI, this may be explained by a “good doctor effect” instead of the screening itself. This effect would suggest that physicians who knew and followed current screening guidelines would also be more effective at motivating BMI decrease. A greater percentage of subjects in the screened group had weight loss or exercise counseling documented at the time of enrollment, which supports the idea that physicians who screened would be more likely to provide counseling. However, because there was not a significant difference between groups it is unlikely that this potential effect affected the results.

Despite these limitations, our study has important strengths. The matched cohort design, with subjects from 2 sites, and the carefully adjusted analysis with assessment of BMI as both a best-case scenario and a time-oriented trajectory should have accounted for significant confounders and captured a significant change in BMI status.

In summary, cholesterol screening of overweight and obese adolescents was not associated with subsequent reduction in BMI. The adolescent’s age at the time of screening significantly interacted with these results, suggesting that older and younger adolescents may respond very differently to screening. This interaction of adolescent age and cholesterol screening calls for further exploration to determine if there is an age during childhood when cholesterol screening has a decidedly positive or negative therapeutic result.

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Author Contributions: Drs Doshi, Perrin, and Steiner had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Doshi, Perrin, and Steiner. Acquisition of data: Doshi, Perrin, and Lazorick. Analysis and interpretation of data: Doshi, Perrin, Lazorick, Esserman, and Steiner. Drafting of the manuscript: Doshi, Perrin, Lazorick, Esserman, and Steiner. Critical revision of the manuscript for important intellectual content: Doshi, Perrin, Esserman, and Steiner. Statistical analysis: Esserman and Steiner. Obtained funding: Perrin. Administrative, technical, and material support: Perrin, Lazorick, and Steiner. Study supervision: Perrin and Steiner.

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REFERENCES


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**Announcement**

Submissions. The Editors welcome contributions to Picture of the Month. Submissions should describe common problems presenting uncommonly, rather than total zebras. Cases should be of interest to practicing pediatricians, highlighting problems that they are likely to at least occasionally encounter in the office or hospital setting. High-quality clinical images (in either 35-mm slide or electronic format) along with parent or patient permission to use these images must accompany the submission. The entire discussion should comprise no more than 750 words. Articles and photographs accepted for publication will bear the contributor’s name. There is no charge for reproduction and printing of color illustrations. For details regarding electronic submission, please see: http://archpeds.ama-assn.org.