

Citation:

Lauer RM, Obarzanek E, Kwiterovich PO, Kimm SYS, Hunsberger SA, Barton BA, Van Horn L, Stevens VJ, Lasser NL, Robson AM, Franklin FA, Simonson-Morton DG. Efficacy and safety of lowering dietary intake of fat and cholesterol in children with elevated low-density lipoprotein cholesterol. *JAMA*. 1995; 273: 1,429-1,435.

PubMed ID: [7723156](#)

Study Design:

Randomized Controlled Trial

Class:

A - [Click here](#) for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To assess the efficacy and safety of lowering dietary intake of total fat, saturated fat and cholesterol to decrease low-density lipoprotein cholesterol (LDL-C) levels in children.

Inclusion Criteria:

- Girls ages seven years
- 10 months to 10 years, one month
- Boys ages eight years
- Seven months to 10 years
- 10 months with average LDL-C values greater than or equal to the 80th and less than the 98th percentiles for age and sex.

Exclusion Criteria:

- Medical condition or medication that might affect growth or blood cholesterol
- Behavior problems in the child or family likely to reduce adherence
- Onset of puberty
- Plans to move within the three study years.

Description of Study Protocol:**Recruitment**

Children were recruited from public and private elementary schools, by mass mailings to members of an HMO and from pediatric practices.

Design

Six-center randomized controlled clinical trial

Dietary Intake/Dietary Assessment Methodology

- Dietary assessment was conducted by Registered Dietitians (RD)
- Within two weeks of the clinic visit, three non-consecutive 24-hour dietary recalls were collected using the DISC dietary assessment method (validated)
- Nutrient analyses were then performed (database version 20) and mean nutrient intakes for the three recalls were calculated.

Blinding Used

Data collectors were blinded to group assignment and duplicate blood samples and dietary recalls were also blinded.

Intervention

- Children in this group were to adhere to a diet of 28% energy from total fat, less than 8% from saturated fat, up to 9% from polyunsaturated fat and less than 75mg per 4,200kJ (1,000kcal) per day of cholesterol (not to exceed 150mg per day), also including the age- and sex-specific RDAs for energy, protein and micronutrients
- The program was family-oriented and its strategies were based on social learning theory and social action theory
- Assessment of current eating pattern and development of a personalized program for each participant were conducted at the first intervention with subsequent regular sessions in both group and individual (children and their family members) settings throughout the first year
- Years two and three interventions included less frequent group and individual maintenance sessions supplemented by telephone contacts between sessions
- Group sessions were led by nutritionists, behaviorists and health educators
- At individual sessions staff obtained periodic capillary blood cholesterol measures, provided feedback and answered questions regarding the child's progress toward the dietary goals, nutritional adequacy and growth.

Statistical Analysis

- Analysis of covariance (ANCOVA) models were used for analysis of primary outcome values to test each of the primary hypotheses
- For analyses of secondary outcomes, ANCOVA models were used for continuous outcomes and Wilcoxon tests for ordered categorical outcomes.

Data Collection Summary:

Timing of Measurements

The following measurements were taken at baseline, one year and three years:

- LDL-C
- Total serum cholesterol
- Triglycerides
- HDL-C

- Dietary assessment
- Skinfold thicknesses
- Body circumferences
- Blood pressure. Blood micronutrients, blood albumin and psychological assessments were measured at baseline and three years.

Annual measurements were taken for height, weight and Tanner staging.

Dependent Variables

- Variable 1: (primary efficacy measure) Mean LDL-C level at three years (average of two measurements one month apart)
- Variable 2: (primary safety measure) Mean height at three years (average of closest of three measurements used)
- Variable 3: (primary safety measure) serum ferritin levels at three years
- Variable 4: (secondary efficacy outcome) Mean LDL-C levels at one year (based on a single measurement)
- Variable 5: (secondary efficacy outcome) Mean total cholesterol levels at one and three years
- Variable 6: (secondary safety outcome) RBC folate values
- Variable 7: (secondary safety outcome) Serum zinc levels
- Variable 8: (secondary safety outcome) Serum retinol levels
- Variable 9: (secondary safety outcome) Serum albumin levels
- Variable 10: (secondary safety outcome) Serum HDL-C values
- Variable 11: (secondary safety outcome) LDL-C:HDL-C ratio
- Variable 12: (secondary safety outcome) Total triglyceride levels
- Variable 13: (secondary safety outcome) Sexual maturation (Tanner staging of pubic hair for boys and girls, breast development for girls and genitalia development for boys)
- Variable 14: (secondary safety outcome) Psychosocial health (Achenbach's Child Behavior Checklist, Kovac's Child Depression Inventory, Spielberger's State-Trait Anxiety Inventory for Children, reading and mathematics sub-tests of the Woodcock-Johnson Psycho-Educational Battery, Moos' Family Environment Scale, Eyberg's Child Behavior Inventory and Sarason's Life Experience Survey).

Independent Variables

Intervention therapy (analyzed as a whole), including dietary modification, as well as group and individual sessions encompassing assessment, counseling and education.

Control Variables

- Baseline level
- Sex.

Description of Actual Data Sample:

- *Initial N*: 663
- *Attrition (final N)*:
 - For the three-year lipid assessment, 95.8% of intervention participants and 92.1% of usual care participants were seen
 - Ferritin values were available for 288 intervention children (86.2%) and 279 usual care children (84.8%)

- Attendance at intervention sessions, including make-up sessions, averaged
 - 96% during the first six months
 - 91% during the second six months and during the second year
 - 89% during the third year
- Age:
 - 9.7 years for boys
 - 9.0 years for girls
- Ethnicity: Unknown
- Other relevant demographics: None
- Anthropometrics: NS differences between the intervention and usual care groups
- Location: Unknown.

Summary of Results:

Dependent Variable	Treatment Group Mean Measures All Confidence Intervals (CIs) 95%	Control Group Mean Measures All CIs 95%	Statistical Significance of Group Difference
Mean LDL-C level at three years (mg/dL)	115.3±18.7	118.6±19.4	P=0.02
Mean height at three years (cm)	156.2±8.1	156.1±8.6	P=0.97
Serum Ferritin levels at three years (mcg/L)	29.6±18.0	33.6±22.9	P=0.08
Mean LDL-C levels at one year (mg/dL)	122.6±18.2	127.2±19.4, 95% CI	P<0.001
Mean total cholesterol levels at one and three years (mg/dL)	Year 1: 191.4±20.9 Year 3: 183.3±21.5	Year 1: 197.4±21.4 Year 3: 186.4±22.3	P<0.001 P=0.04
RBC folate values (nmol/L red blood cells)	Year 1: 740±463 Year 3: 687±263	Year 1: 681±271 Year 3: 651±266	P=0.09 P=0.11
Serum zinc levels (µmol/L)	Year 1: 14.4±2.0 Year 3: 14.1±2.1	Year 1: 14.4±1.6 Year 3: 14.2±2.2	P=0.91 P=0.43

Serum retinol levels (µmol/L)	Year 1: 1.42±0.24 Year 3: 1.50±0.27	Year 1: 1.39±0.24 Year 3: 1.49±0.28	P=0.04 P=0.29
Serum albumin levels (g/L)	Year 1: 45.9±2.3 Year 3: 45.3±2.5	Year 1: 45.8±2.4 Year 3: 45.4±2.4	P=0.37 P=0.79
Serum HDL-C values (mg/dL)	Year 1: 55.1±11.1 Year 3: 52.7±10.0	Year 1: 56.8±11.1 Year 3: 52.6±10.3	P=0.03 P=0.75
LDL-C:HDL-C ratio (mmol/L)	Year 1: 2.30±0.58 Year 3: 2.27±0.56	Year 1: 2.33±0.59 Year 3: 2.34±0.57	P=0.34 P=0.10
Total triglyceride levels (mg/dL)	Year 1: 86.2±38.7 Year 3: 99.5±46.0	Year 1: 87.1±39.4 Year 3: 98.9±44.8	P=0.84 P=0.62
Sexual maturation	Data not shown in study	Data not shown in study	NS differences between groups at year one or year three
Psychosocial health	Data not shown in study Kovach's Child Depression Inventory showed a lower adjusted mean depression score for intervention group at three years	Data not shown in study	P=0.03

- Levels of LDL decreased in both groups, with greater decreases in the intervention group
- Both groups' serum ferritin levels decreased at one year and at three years, but the difference between the groups was NS.

Other Findings

- There were NS differences in mean weight or BMI or sum of skinfolds between the groups
- Waist-to-hip ratio was lower in the intervention group than in the usual care group at one year but was not different at three years
- At both one and three years mean systolic and diastolic blood pressures were not different between the two groups
- There were NS differences between the two groups in micronutrient intake; yet statistical differences were apparent between groups for total fat, saturated fat, dietary cholesterol, and monounsaturated fat at both one and three years with the intervention group consuming less than the usual care group in all respective areas. Polyunsaturated fat intake was statistically

significant between groups at year three.

Author Conclusion:

- The author concludes that the DISC trial results provide evidence of efficacy in achieving modest lowering of LDL-C levels over three years while maintaining adequate growth, iron stores, nutritional adequacy and psychological well-being during the critical growth period of adolescence
- The results indicate that under supervision, children can safely and successfully lower their LDL-C levels through dietary change.

Reviewer Comments:

This study includes strong methodology and successful outcomes for primary and secondary efficacy and safety measures.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

- | | | |
|----|---|-----|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | Yes |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | Yes |

Validity Questions

- | | | |
|------|---|-----|
| 1. | Was the research question clearly stated? | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |
| 1.3. | Were the target population and setting specified? | Yes |
| 2. | Was the selection of study subjects/patients free from bias? | Yes |

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	Were study groups comparable?	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	Was method of handling withdrawals described?	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	Was blinding used to prevent introduction of bias?	Yes

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	Were outcomes clearly defined and the measurements valid and reliable?	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

7.7.	Were the measurements conducted consistently across groups?	Yes
8.	Was the statistical analysis appropriate for the study design and type of outcome indicators?	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	Are conclusions supported by results with biases and limitations taken into consideration?	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	Is bias due to study's funding or sponsorship unlikely?	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes