Citation:

Sheridan MJ, Cooper JN, Erario M, Cheifetz CE. Pistachio nut consumption and serum lipid levels. *J Am Coll Nutr.* 2007 Apr; 26 (2): 141-148.

PubMed ID: 17536125

Study Design:

Randomized crossover (time series) 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 determine whether consuming pistachio nuts at 15% of calories could have a significant impact on lipid profiles of subjects with moderate hypercholesterolemia.

Inclusion Criteria:

Subjects with moderate hypercholesterolemia (cholesterol higher than 210mg per dL).

Exclusion Criteria:

- Currently being treated for hyperlipidemia, hypertension, diabetes mellitus and kidney or liver disease
- Under age 18 years
- Known food allergies
- Smoker
- Consuming more than three alcoholic drinks per week
- Women on hormone therapy.

Description of Study Protocol:

Recruitment

Community advertisement or by physician referral and screened by a nurse clinical coordinator.

Design

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- Prospective dietary intervention, time-series crossover design, randomized as to order of diet assignment
- Subjects consumed normal diets during a five-day baseline period
- One half randomized to the pistachio diet for four weeks, followed by four weeks to the regular diet
- One half randomized to the regular diet for four weeks, followed by four weeks on the pistachio diet
- There was no lag time between diet crossover.

Dietary Intake/Dietary Assessment Methodology

- Subjects submitted a consecutive three-day food diary before entering the baseline period
- Each week of the pistachio diet, subjects keep one-day food records that were analyzed to ensure the subjects were consuming the assigned quantity of pistachio nuts. There was no definitive compliance measure of pistachio consumption.

Blinding Used

Study personal performing the statistical analyses were blinded to the dietary sequence of the subjects.

Intervention

Pistachio diet involved consuming pistachio nuts for 15% of daily caloric intake (two to three ounces per day):

- Pistachios given to patients in pre-measured storage bags (calorie content calculated for individual subjects)
- Subjects instructed to substitute the nuts for normally consumed high-fat snacks, or as fat calories
- Otherwise, the subjects consumed their normal, regular diets
- Subjects returned pistachio storage bags at each visit.

Statistical Analysis

- Sample size based on 0.80 power and a type 1 error of $\alpha=0.05$ to detect a difference in 15 subjects
- Values of all lipid and nutritional variables were the average measurements at week zero (baseline), week four and week eight
- Results reported as means ± SEMs and mean differences ± 95% CI, unless noted otherwise
- Changes over time evaluated using a repeated measures analysis-of-variance technique
- Significance level set at 0.05
- Analysis conducted using SAS software.

Data Collection Summary:

Timing of Measurements

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Baseline and weeks two and four of each dietary phase.

Dependent Variables

Change scores for the following:

- Weight and height recorded as BMI (measured without heavy clothing or shoes)
- Blood pressure, obtained after a five-minute rest in sitting position
- One-day food diaries, analyzed using "Nutritionist Five" software
- HDL cholesterol was separated from the plasma and measured using the method of Warnick
- Total cholesterol in the remaining plasma and triglycerides were measured by an enzymatic procedure on a Hitachi 747-200 analyzer
- LDL cholesterol was calculated by subtraction using the method of Friedewald
- Apolipoprotiens A-1 and B-100 were measure by immunonephelometry on a BN-II
- Lipid profile was measured after an overnight fast with samples analyzed within one day and all procedures were performed according to the Lipid Standardization Program of the Centers for Disease Control and Prevention and the NHLBI.

Independent Variables

- Pistachio diet
- Regular diet.

Control Variables

Subjects were asked to maintain the same physical activity and other lifestyle habits throughout the study.

Description of Actual Data Sample:

- *Initial N:* 20 (16 male, 4 female)
- *Attrition (final N):* 15 (11 male, 4 female)
- *Age:* 36 to 75 years
- *Anthropometrics:* Averages at baseline for all participants:
  - BMI was 28±0.9kg/m^2
  - Fasting serum cholesterol, 246±6mg per dL
  - Triglyceride, 141±11mg per dL
  - Systolic blood pressure, 129±4mmHg
  - Diastolic blood pressure, 84±3mmHg
  - Pulse, 78±2
- *Location:* Inova Fairfax Hospital, VA.

Summary of Results:

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- No change in blood pressure; BMI; total energy; or percent of total energy from protein, carbohydrate, total fat, or monounsaturated fat
- The pistachio diet had a significant decrease in saturated fat and significant *increase* in polyunsaturated fat and dietary fiber
- Significant differences favoring the pistachio diet observed for HDL, TC/HDL, LDL/HDL and B-100/A-1
- When the pistachio diet is compared with baseline, improvements in TC, LDL, Apo A-a, Apo B-100 additionally are significant.

Variables	Mean (SEM)			Difference (95% CI)		Difference (95% CI)	
	Baseline	Pistachio	Regular	Pistachio vs. Regular	P-value	Pistachio vs. BL	P-value
Lipids (mg per dL)							
Total Chol	246 (5.8)	237 (8.0)	246 (8.7)	-9.2 (-21, 2.4)	0.11	-8.9 (-19, 1.5)	0.09
Triglyceride	141 (11)	131 (11)	130 (14)	0.67 (-25-26)	0.96	-10 (-23, 2.8)	0.11
HDL	55 (3.5)	57 (3.5)	54 (3.4)	2.3 (0.48, 4.0)	0.02	1.5 (-0.22, 3.3)	0.08
TC/HDL	4.7 (0.29)	4.4 (0.26)	4.8 (0.31)	-0.38 (-0.57, -0.19)	0.001	-0.32 (-0.55, -0.08)	0.01
LDL	164 (6.9)	148 (9.9)	163 99.3)	-15 (-31, 0.94)	0.06	-16 (-31, -.0.99)	0.04
LDL/HDL	3.1 (0.25)	2.8 (0.25)	3.2 (0.26)	-0.40 (-0.66, -0.15)	0.004	-0.39 (-0.66, -0.11)	0.009
VLDL	28 (2.2)	26 (2.2)	29 (3..2)	-2.7 (-7.1, 1.7)	0.22	-2.1 (-4,8, 0.71)	0.13

Author Conclusion:

- The addition of pistachio nuts at 15% of daily fat calories (two to three ounces per day) over a consecutive four-week period can favorably modify lipoprotein levels in subjects with moderate hypercholesterolemia
- The metabolic mechanisms by which pistachios and other nuts affect serum lipid levels, the possible role played by other non-fatty acid compounds and whether these decrease the risk of coronary heart disease will require continuing investigation.

Reviewer Comments:

- *The authors acknowledge that four weeks does not allow them to make any inferences about the sustainability of either the improved lipid values or eating pistachios at that level longer term*
- *It is unclear if the funding source (the Califormia Pistachio Commission) presents a conflict of interest for this research.*

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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?**	???
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?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
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.)	N/A

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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?	Yes
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 interveningfactors 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

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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?	N/A
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?	N/A
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)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes

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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?**	N/A
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?**	???
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	???

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