Citation:

Jakobsen MU, O'Reilly EJ, Heitmann BL, et al. Major types of dietary fat and risk of coronary heart disease: A pooled analysis of 11 cohort studies. *Am J Clin Nutr.* May 2009; 89(5): 1,425-1,432.

PubMed ID: 19211817

Study Design:

Meta-analysis or Systematic Review

Class:

M - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

- To investigate the associations between energy intake from monounsaturated fatty acids (MUFAs), polyunsaturated fatty acids (PUFAs) and carbohydrates and risk of coronary heart disease (CHD) while assessing the potential effect-modifying role of sex and age
- To clarify whether energy from unsaturated fatty acids or carbohydrates should replace energy from saturated fatty acids (SFAs) to prevent CHD.

Inclusion Criteria:

- Published follow-up study with 150 or more incident coronary events
- Availability of usual dietary intake
- A validation or repeatability study of the diet-assessment method used
- More detail on the inclusion criteria for studies in the Pooling Project of Cohort Studies on Diet and Coronary Disease were provided in an earlier publication describing the methodological details of this pooled analysis. The evaluation of quality of the studies for the pooled analysis was conducted during the inclusion/exclusion process and is described in detail in Smith-Warner et al. (2008), cited by the authors.

Exclusion Criteria:

- Age less than 35 years
- History of cardiovascular disease, diabetes or cancer (other than non-melanoma skin cancer)
- Extreme energy intake (i.e., more or less than three SDs from the study-specific log-transformed mean energy intake of the population).

Description of Study Protocol:

Recruitment

Specific for each of the pooled study, but not described in this article.

Design

Analysis of pooled data used proportional hazards models.

Dietary Intake/Dietary Assessment Methodology

- Dietary intake was determined at baseline by using a food-frequency questionnaire (FFQ) or a dietary history interview
- The validation and repeatability of the diet-assessment methods were evaluated and were found reasonable for population studies of the nutrients of interest
- Total energy intake was calculated as the sum of energy intake derived from fat, carbohydrates and protein
- Derived exposure measures were dietary intake of monounsaturated fatty acids (MUFAs; primarily *n*-9 oleic acid), polyunsaturated fatty acids (PUFAs; including n-3 and n-6 fatty acids; primarily *n*-6 linoleic acid) and carbohydrates
- The MUFA and PUFA for which the data are reported in the Israeli Ischemic Heart Disease Study (IIHD) were the *n*-9 MUFA oleic acid and the *n*-6 PUFA linoleic acid.

Statistical Analysis

- Within each study, hazard ratios (HRs) with 95% confidence intervals (CIs) for the incidence of a coronary event and of mortality from CHD were calculated by using Cox proportional hazards regression with time in study (y) as the time metric. The observation time for each participant was defined as the number of months from the date on which information on diet was obtained until CHD occurrence, death of another cause, disappearance or end of follow-up, whichever came first. Studies with follow-up periods more than 10 years were truncated to reduce possible effect modification by time
- Two models were used to investigate whether energy intake from unsaturated fatty acids or carbohydrates should replace the energy intake from SFAs to prevent coronary events
- Model One included intakes of MUFAs, PUFAs, trans fatty acids (TFAs), carbohydrates and protein expressed as percentages of total energy intake (as continuous variables) and total energy intake (kcal per day; as a continuous variable). Age at baseline (y) and the calendar year in which the baseline questionnaire was returned were entered into the model through the strata statement, thus assuming the same effect for the variable of interest but allowing the underlying hazard functions to differ with respect to age and time of collection of dietary information
- Model Two included variables in Model One and CHD risk factors measured at baseline:
    - Smoking (never smokers, former smokers, and current smokers of one to four, five to 14, 15 to 24 or 25 or more cigarettes per day)
    - Body mass index (in kg/m^2; less than 23, 23 to less than 25, 25 to less than 27.5, 27.5 to less than 30 or 30 or more)
    - Physical activity (levels one to five)
    - Highest attained educational level (high school)
    - Alcohol intake (zero, zero to less than five, five to less than 10, 10 to less than 15, 15 to less than 30, 30 to less than 50 or 50g per day or more)
    - History of hypertension (yes or no)
    - Energy-adjusted quintiles of fiber intake (g per day)

- Cholesterol intake (mg per day).
- A missing indicator variable was created for each categorical variable
- The estimated HRs for unsaturated fatty acids and carbohydrates can be interpreted as the estimated differences in risk of a 5% lower energy intake from SFAs and a concomitant higher energy intake from unsaturated fatty acids and carbohydrates, respectively
- The study-specific logs of HRs were weighted by the inverse of their variances, and a pooled (combined) estimate of the HRs was computed by using a random-effects model. Evidence for between-studies heterogeneity among the study-specific HRs was assessed by using the estimated between-studies variance component Q statistic
- To evaluate potential effect modification by age, the study population was divided into two age groups in further analyses (less than 60 years at entry and 60 or more years at entry. Effect modification by sex and age was investigated by including a cross-product interaction term between the exposure variable and sex or age. Pooled P-values for the test of interaction were calculated by using squared Wald statistics by pooling the study-specific interaction log HRs and dividing by the square of the SE of the pooled interaction term. The resulting statistic was referred to a chi-square distribution with one degree of freedom
- The proportional hazards assumption was checked by including a cross-product interaction term between the exposure variable and the stratifying variable age (y). We tested the exposure variables for non-linearity in a spline regression model. The analyses were performed by using SAS statistical software, v9.1 and Stata statistical software, v9.0.

Data Collection Summary:

Study Variables

- Dietary intake
- Energy consumption
- Percentage of energy from carbohydrates, fats and protein
- Fatal CHD (including sudden death)
- Non-fatal MI
- Age
- Gender.

Control Variables

- Smoking habit (never smokers, former smokers, and current smokers of one to four, five to 14, 15 to 24 or 25 or more cigarettes per day)
- Body mass index (in kg/m^2; less than 23, 23 to less than 25, 25 to less than 27.5, 27.5 to less than 30 or 30 or more)
- Physical activity (levels one to five)
- Highest attained educational level (high school)
- Alcohol intake (zero, zero to less than five, five to less than 10, 10 to less than 15, 15 to less than 30, 30 to less than 50 or 50g or more per day)
- History of hypertension (yes or no)
- Energy-adjusted quintiles of fiber intake (g per day)
- Cholesterol intake (mg per day).

Description of Actual Data Sample:

- *Initial N:* 11 studies were included containing a total of 344,696 people
- *Attrition (final N):* The total final population from all studies consisted of 344,696 people (71% women)
- *Age:* 35 years and older
- *Anthropometrics:* Described but not shown
- *Location:* Data collected from different research centers.

Summary of Results:

- During four to 10 years of follow-up, 5,249 coronary events and 2,155 coronary deaths occurred among 344,696 persons (71% women)
- There was an indication of an overall direct association between substitution of MUFAs and risk of coronary events (HR: 1.19; 95% CI: 1.00, 1.42), but not between substitution of MUFAs and risk of coronary deaths
- There was an overall significant inverse association between substitution of PUFAs and risk of coronary events (HR: 0.87; 95% CI: 0.77, 0.97) and between substitution of PUFAs and risk of coronary deaths (HR: 0.74; 95% CI: 0.61, 0.89)
- There was an overall significant direct association between substitution of carbohydrates and risk of coronary events (HR: 1.07; 95% CI: 1.01, 1.14) but not between substitution of carbohydrates and risk of coronary deaths
- There was no effect modification by sex
- Among women aged less than 60 years, there was a slim significant inverse association between substitution of PUFAs and risk of coronary events (HR: 0.73; 95% CI: 0.53, 1.01); but not among women aged 60 years or older
- Among men, there was no significant association between substitution of PUFAs and risk of coronary events
- Among women aged less than 60 years, there was a strong significant inverse association between substitution of PUFAs and coronary deaths (HR: 0.49; 95% CI: 0.29, 0.83); but not among women aged 60 years or older
- Among men, there was no significant association between substitution of PUFAs and risk of coronary deaths
- There was no effect modification by age among women or men. There was no effect modification by sex among persons aged less than 60 years or 60 years and older.

Author Conclusion:

In conclusion, the associations found in this study suggest that replacing SFA intake with PUFA intake rather than MUFA or carbohydrate intake, prevents CHD over a wide range of intakes and among all middle-aged and older women and men.

Reviewer Comments:

- *This was a quantitative pooled analysis of high quality prospective cohort studies, defined as Class M*
- *Although the quality assessment of the studies included was not provided in detail in*

Jakobsen et al, the authors cited an earlier publication that described the methodological detail of the Pooling Project of Prospective Studies of Diet and Cancer (Smith-Warner et al, 2006)

- *Quality assessment of the studies was provided in the inclusion criteria for the pooled analysis project.*

Research Design and Implementation Criteria Checklist: Review Articles

Relevance Questions		
1.	Will the answer if true, have a direct bearing on the health of patients?	Yes
2.	Is the outcome or topic something that patients/clients/population groups would care about?	Yes
3.	Is the problem addressed in the review one that is relevant to nutrition or dietetics practice?	Yes
4.	Will the information, if true, require a change in practice?	Yes

Validity Questions		
1.	Was the question for the review clearly focused and appropriate?	Yes
2.	Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search termsused described?	Yes
3.	Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased?	Yes
4.	Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible?	Yes
5.	Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined?	Yes
6.	Was the outcome of interest clearly indicated? Were other potential harms and benefits considered?	Yes
7.	Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described?	Yes
8.	Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed?	Yes
10.	Was bias due to the review's funding or sponsorship unlikely?	N/A