

Citation:

Salmerón J, Hu FB, Manson JE, Stampfer MJ, Colditz GA, Rimm EB, Willett WC. Dietary fat intake and risk of type 2 diabetes in women. *Am J Clin Nutr*. 2001 Jun; 73 (6): 1,019-1,026.

PubMed ID: [11382654](#)

Study Design:

Prospective Cohort Study

Class:

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

Research Design and Implementation Rating:



POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the association between dietary fat intakes and risk of type 2 diabetes (T2D).

Inclusion Criteria:

- The Nurses' Health Study (NHS) is a longitudinal study of diet and lifestyle factors including 121,700 US female registered nurses (RNs) aged 30-55 years at enrollment
- The cohort was assembled in 1976. In 1980, dietary intake of specific fats and other nutrients was assessed by using a 61-item semi-quantitative food-frequency questionnaire (FFQ). [The FFQ was expanded to 116 food items in 1984]
- For the present study, the authors used information from respondents (98,462 women aged 34-59 years) who answered the 1980 FFQ.

Exclusion Criteria:

- Women were excluded if they did not satisfy *a priori* criteria of energy intake between 500-3,500kcal per day or left >10 questions (out of 61) blank
- Women with a prior diagnosis of diabetes or cancer or incidence of myocardial infarction (MI), angina, stroke or coronary artery surgery were excluded
- After exclusion, the remaining 84,204 women were followed for T2D incidence for the next 14 years (1980-1994).

Description of Study Protocol:

Recruitment

- The Nurses' Health Study cohort was assembled in 1976 when participants returned a mailed questionnaire about known and suspected risk factors for cancer and cardiovascular disease

- The recruitment was described in more detail in an early publication on the Nurses' Health Study, as listed below:
 - Colditz GA, Stampfer MJ, Willett WC, Rosner B, Speizer FE, Hennekens CH. A prospective study of parental history of myocardial infarction and coronary heart disease in women. *Am J Epidemiol* 1986; 123: 48-58.

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

- Validated semi-quantitative FFQ was used to assess the subjects' diets
- The initial FFQ included 61 food items and this was expanded to 116-134 items from 1984 onward
- A common unit or portion size for each food was specified and participants were asked how often on average during the previous year they had consumed that amount
 - The nine responses ranged from less than one time per month to more than six times per day
- Detailed information about types of fat or oil used for cooking and at the table, including type of margarine, was collected
 - Stick or tub choices were provided in 1980 and 1984 and brands in 1986 and 1990
- Composition values for dietary fats and other nutrients were from the Harvard University Food Composition Database, derived from USDA sources and supplemented with manufacturer's information
 - Food composition data were continuously updated to account for changes in food processing and improved analytic methods
- Food intake was assessed at baseline and updated in 1984, 1986 and 1990
 - Polyunsaturated fatty acid (PUFA) intakes reported in this study included only linoleic acid, which accounted for 81% of the total PUFA intake in this cohort
- Nutrient intake was computed by multiplying the frequency of consumption of each food by the nutrient content of the specified portions, taking into account the type of fat used in preparation, including the brand, type and year of margarine use.

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- For each subject, person-time of follow-up was counted from the date of return of the 1980 FFQ to the date of T2D diagnosis, to the time of return of the most recent follow-up questionnaire, or to June 1, 1994, whichever came first
- Women were divided into quintiles by percentage of energy from each type of fatty acid; incidence rates were calculated by dividing the number of events by person-time of follow-up in each quintile
- Pooled logistic regression was used to model the cumulative average of fat intake from all available dietary questionnaires up to the start of each two year follow-up interval in relation to diabetes incidence

- Multivariate nutrient-density models were used that simultaneously included energy intake, percentages of energy from protein and specific fatty acids, and other potential confounding variables
 - Non-dietary covariates included seven two-year time periods, age in five-year categories, BMI, smoking, alcohol consumption, physical activity and history of diabetes in a first-degree relative
- Significant monotonic trends were tested across quintiles of fat intake by assigning each participant the median value for the category and modeling this value as a continuous variable
- All P-values were two-sided
- The effects of specific fatty acids were evaluated by expressing them as percent total energy and including them in models as continuous variables
 - When all types of fats, protein and alcohol are included simultaneously, the coefficients from these nutrient-density models can be interpreted as the effect of exchanging energy from a specific fatty acid for the same amount of energy from carbohydrates
 - The effect of substituting one type of fatty acid for another, using the differences between coefficients from the same model, can also be determined.

Data Collection Summary:

Timing of Measurements

- FFQs were given at baseline and updated in 1984, 1986 and 1990
- Non-dietary factors were assessed in 1980 and updated every two years during follow-up
 - Validity of self-reported weight for this cohort was previously reported ($r=0.96$ between self-reported and measured weight)
 - Physical activity in metabolic equivalents per week was estimated based on self-reported duration per week of various forms of exercise including intensity levels
 - In 1982, participants provided information on the history of diabetes in first-degree relatives.

Dependent Variables

- The primary outcome was diagnosis of T2D
 - A reported diagnosis of diabetes, resulted in an additional supplementary questionnaire to confirm the report and date of diagnosis
 - Diagnoses of T1D or gestational diabetes were excluded
 - T2D was confirmed if one or more of the following criteria were met:
 - One or more classic symptoms plus fasting plasma glucose of $>7.78\text{mmol/L}$ (140mg/dL) or a random plasma concentration of $>11.11\text{mmol/L}$ (200mg/dL)
 - More than two elevated plasma glucose measurements on different occasions
 - Treatment with medication for hypoglycemia (insulin or hypoglycemic agents)
 - These were the same criteria used by the National Diabetes Data Group and the World Health Organization (WHO) at the time the study was conducted
- Deaths were identified from state vital records and the National Death Index or family members.

Independent Variables

Dietary fat intake.

Control Variables

- Age in five-year categories
- BMI
- Smoking
- Alcohol consumption
- Physical activity
- History of diabetes in a first-degree relative.

Description of Actual Data Sample:

- *Initial N*: 84,204 women
- *Attrition (final N)*: 2%
- *Age*: 34-59 years in 1980
- *Ethnicity*: Not specified
- *Other relevant demographics*: Female RNs
- *Anthropometrics*: Not applicable
- *Location*: US.

Summary of Results:

Variables	Lowest Quintile Relative Risk (RR)	Highest Quintile RR (95% CI)	P for trend
Total Fat	28.9% energy	46.1% energy	
Age and BMI adjusted	1.0	1.12 (0.99, 1.27)	0.006
Multivariate	1.0	0.97 (0.85, 1.11)	0.96
SFA	10.7% energy	18.8% energy	
Age and BMI adjusted	1.0	1.27 (1.12, 1.44)	<0.0001
Multivariate	1.0	1.11 (0.97, 1.28)	0.05
MUFA, PUFA and TFA adjusted	1.0	0.99 (0.80, 1.21)	0.98
MUFA	10.9% energy	19.3% energy	
Age and BMI adjusted	1.0	1.29 (1.14, 1.47)	<0.0001
Multivariate	1.0	1.13 (0.99, 1.39)	0.07
MUFA, PUFA and TFA adjusted	1.0	1.06 (0.84, 1.33)	0.51
PUFA	2.9% energy	6.2% energy	
Age and BMI adjusted	1.0	0.87 (0.77, 0.99)	0.02
Multivariate	1.0	0.85 (0.75, 0.97)	0.009
MUFA, PUFA and TFA adjusted	1.0	0.75 (0.65, 0.88)	0.0002

trans FA	1.3% energy	2.95% energy	
Age and BMI adjusted	1.0	1.26 (1.11, 1.43)	0.002
Multivariate	1.0	1.15 (1.01, 1.32)	0.09
MUFA, PUFA and TFA adjusted	1.0	1.31 (1.10, 1.56)	0.02
Cholesterol	131mg per day	273mg per day	
Age and BMI adjusted	1.0	1.32 (1.16, 1.50)	<0.0001
Multivariate	1.0	1.42 (1.23, 1.65)	<0.0001
MUFA, PUFA and TFA adjusted	1.0	1.36 (1.17, 1.59)	<0.0001

- During 14-year follow-up, 2,507 cases of T2D were documented
- Total fat intake, compared to equivalent carbohydrate intake as percent energy, was not associated with risk of T2D
 - 5% increase in energy from total fat resulted in RR=0.98 (95% CI:0.94,1.02)
- SFA or MUFA intakes were not significantly associated with increased risk of T2D
- PUFA intake was associated with decreased risk of T2D
 - 5% increase in energy from PUFA resulted in RR=0.63 (0.53, 0.76: P<0.0001)
- Trans FA (TFA) intake was positively associated with increased risk of T2D
 - 2% increase in energy from TFA resulted in RR=1.39 (1.15, 1.67: P=0.0006)
- Calculated that replacing 2% energy from TFA isocalorically with PUFA would lead to 40% lower risk of T2D.

Other Findings

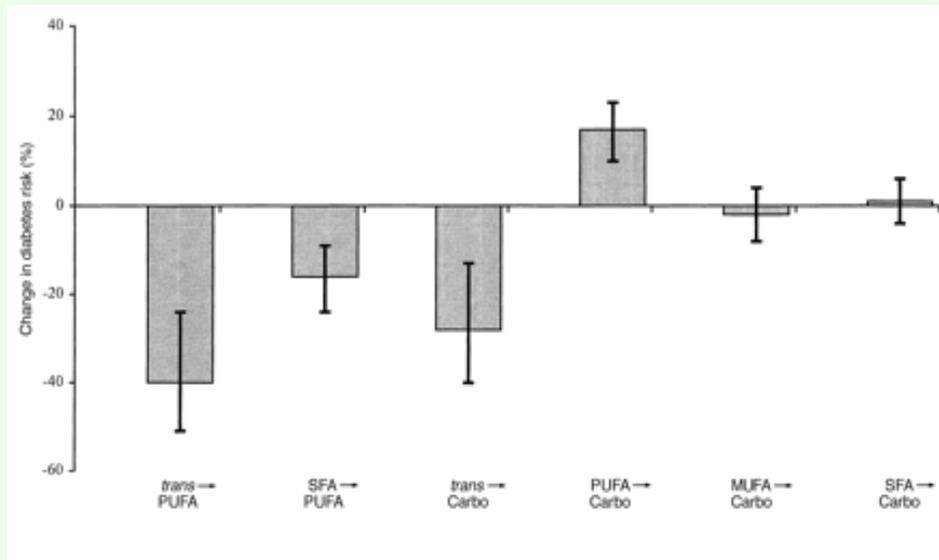


Figure 1. Estimated changes in risk of type 2 diabetes associated with isoenergetic substitutions of 2% of energy. Associations were adjusted for the same covariates as in Table 2. *trans*, *trans* fatty acids; *PUFA*, polyunsaturated fatty acids; *SFA*, saturated fatty acids; *Carbo*, carbohydrates; *MUFA*, monounsaturated fatty acids. The arrows indicate substitution of the second fat listed for the first fat listed. Bars represent 95% CIs. [From Salmeron et al., *Am J Clin Nutr* 2001; 73:1019-26.]

Author Conclusion:

- Total fat, SFA and MUFA intakes are not associated with risk of T2D in women
- Trans FA intake are associated with increased risk of T2D in women

- PUFA intake is associated with decreased risk of T2D in women
- Replacement of PUFA for TFA would likely reduce risk of T2D.

Reviewer Comments:

None.

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?	Yes
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)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
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?	Yes
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?	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
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.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	No
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?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
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)?	N/A
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?	Yes
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