

Citation:

Nöthlings U, Murphy SP, Wilkens LR, Henderson BE, Kolonel LN. Dietary glycemic load, added sugars, and carbohydrates as risk factors for pancreatic cancer: The Multiethnic Cohort Study. *Am J Clin Nutr.* 2007 Nov; 86(5): 1,495-1,501.

PubMed ID: [17991664](#)

Study Design:

Prospective Cohort Study

Class:

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

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To investigate associations between dietary glycemic load, dietary carbohydrates, sucrose, fructose, total sugars and added sugars and pancreatic cancer risk.

Inclusion Criteria:

Participant of the Multiethnic Cohort Study in Hawaii and Los Angeles, which is composed of men and women who were 45 to 75 years old at cohort creation, and enrolled in the study between 1993 and 1996.

Exclusion Criteria:

- Did not belong to one of the five targeted racial-ethnic groups (African Americans, Japanese Americans, Latinos, Native Hawaiians and Whites)
- Implausible diets
- Body mass index (BMI) information was missing or implausible
- Missing information on smoking status or intensity or duration of smoking
- Self-reported prevalent diabetes mellitus
- Prevalent pancreatic cancer at cohort entry.

Description of Study Protocol:**Recruitment**

Previous publications describe details of the original cohort study.

Design

Prospective cohort with eight years of follow-up.

Dietary Intake/Dietary Assessment Methodology

Food-frequency questionnaire (FFQ) validated for use in the study's multiethnic population.

Statistical Analysis

- Differences across quartiles of glycemic load were tested with the Cochran-Armitage test for trend for categorical variables and the T-test for slope in linear regression models of mean values
- Cox proportional hazards models using age as the time metric were calculated to derive relative risks
- Person-times were determined by beginning with the date of cohort entry (time of questionnaire completion), and ending at the earliest date of the following dates: Date of pancreatic cancer diagnosis, date of death or December 31, 2002, the closing date of the study
- Models are presented with both sexes (no evidence of interaction by sex), after adjustment for sex and follow-up time on study from baseline (two or less, two to five or more than five years) as strata variables, to allow for different baseline hazard rates
- Median values for quartiles by sex and race-ethnicity were used in the respective models to test for trend
- To reduce measurement error in the dietary assessments, nutrients and foods were analyzed in terms of densities (i.e., by 100 or 1,000kcal per day)
- All models were calculated separately for normal-weight (BMI less than 25kg/m²) or overweight or obese (BMI 25kg/m² or higher) participants
- The likelihood ratio test was used to determine the significance of the interaction between BMI and the main exposure variables with respect to pancreatic cancer.

Data Collection Summary:

Timing of Measurements

- Baseline questionnaires were completed at enrollment between 1993 and 1996 and study follow-up was completed on December 31, 2002
- Eight-year follow-up.

Dependent Variables

- Incident exocrine pancreatic cancer cases were identified by record linkage to the Hawaii Tumor Registry, the Cancer Surveillance Program of Los Angeles County and the California State Cancer Registry
- Linkages to the National Death Index and death certificate files in Hawaii and California provided information on vital status and causes of death.

Independent Variables

Dietary glycemic load, carbohydrate, sucrose, fructose, total sugar and added sugar intake were calculated from a quantitative FFQ.

Control Variables

- Race-ethnicity

- Age at cohort entry
- Smoking status
- Pack-years of smoking
- Family history of pancreatic cancer
- Energy intake
- Intake of red meat and processed meat
- BMI
- Sex and time on study (two or less, two to five or more than five years).

Description of Actual Data Sample:

- *Initial N*: More than 215,000
- *Attrition (final N)*: 162,150 (72,966 men and 89,184 women)
- *Age*: 45 to 75 years at baseline
- *Ethnicity*: African American, Japanese American, Latino, Native Hawaiian, White
- *Anthropometrics*: Mean BMI was slightly elevated in the last quartile of glycemic load only
- *Location*: Hawaii and Los Angeles.

Summary of Results:

Key Findings

- Glycemic load and added sugars were not associated with pancreatic cancer risk in the overall cohort (P=0.65)
- Risk of exocrine pancreatic cancer was significantly increased with high fructose intake (RR=1.35; 95% CI: 1.02 to 1.80; P=0.046)
- Higher (but not significantly higher) risks of pancreatic cancer were seen in the overweight and obese group than in the normal-weight group in the top quartiles of intakes of all dietary variables, and there were stronger trends across quartiles
- Among overweight and obese participants, RR=1.46 for the fourth quartile of sucrose intake compared with the first (95% CI: 0.95 to 2.25; P=0.04); among normal weight participants, RR=1.07 (95% CI: 0.71 to 1.60; P=0.85).

Author Conclusion:

- High sugar intake, specifically fructose, was associated with a greater risk of pancreatic cancer
- A higher risk of pancreatic cancer was also observed in overweight or obese participants with higher sucrose consumption.

Reviewer Comments:

- *Author-identified limitations*: Dietary measurement error was present, glycemic load may not be accurate when using dietary intakes collected with a FFQ and glycemic index values have not been determined for many local foods
- *Author-identified strengths*: Dietary assessment was comprehensive, detailed and specifically designed for the study population; sample size was large; and participants were heterogeneous

- *Limitations: Weight and height were self-reported; diet and covariates were only measured once, at baseline.*

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) | N/A |
| 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) | N/A |

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%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
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?	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?	N/A

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?	N/A
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?	No
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?	No
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
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?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
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