

Citation:

Silvera SA, Rohan TE, Jain M, Terry PD, Howe GR, Miller AB. Glycaemic index, glycaemic load and risk of endometrial cancer: A prospective cohort study. *Public Health Nutr.* 2005 Oct; 8(7): 912-919.

PubMed ID: [16277808](#)

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 examine the association between dietary glycemic load (GL) and glycemic index (GI) and endometrial cancer risk in a cohort of 49,613 Canadian women.

Inclusion Criteria:

Women aged 40 to 59 who were enrolled in the Canadian National Breast Screening Study and completed a self-administered food-frequency questionnaire (FFQ) between 1982 and 1985.

Exclusion Criteria:

- Of the 49,613 women for whom dietary data were available, women were excluded if they had extreme energy intake values [at least three standard deviations (SD) above or below the mean value for \log_e energy intake] (N=502); women with prevalent endometrial cancer at baseline (N=61); and women who had undergone a hysterectomy (N=14,659)
- These exclusions left 34,391 women available for analysis, among whom there were 426 incident cases of endometrial cancer
- Study participants were at risk from their date of enrollment until the date of diagnosis of their endometrial cancer, until the termination of follow-up or death, whichever was earlier.

Description of Study Protocol:**Recruitment**

Between 1980 and 1985, a total of 89,835 women aged 40 to 59 years were recruited from the general population into the Canadian National Breast Screening Study (NBSS), a randomized controlled trial of screening for breast cancer.

Design

Prospective cohort study.

Dietary Intake/Dietary Assessment Methodology

- In 1982 a self-administered FFQ was distributed covering 86 food items
- A comparison between the self-administered questionnaire and a full interviewer-administered questionnaire revealed that the two methods gave estimates of intake of the major macronutrients and dietary fiber that were moderately to strongly correlated (reported correlation coefficients ranged from 0.47 to 0.72).

Statistical Analysis

- Cox proportional hazards models (using age as the time scale) were used to estimate hazard ratios (HR) and 95% CI for the association between energy-adjusted quartile levels of glycemic load and overall glycemic index and endometrial cancer risk; energy adjustment was performed using the residual method. To test for trend we fitted the median value of each quartile as successive integers in the risk models. The authors examined the associations overall and within strata defined BMI [defined as weight (kg)/square of height (m^2); weight and height were measured at baseline], self-reported vigorous physical activity (defined as jogging, running, brisk walking, vigorous sport, bicycling, heavy housework, and so on) and use of hormone replacement therapy (HRT) (ever vs. never). Also examined were the associations within strata defined by menopausal status. Women who reported having regular menstrual periods within the past 12 months were classified as pre-menopausal. Women whose menstrual periods had ceased at least 12 months before enrolment into the study and those who had had a bilateral oophorectomy were considered post-menopausal
- Tests for interaction were based on likelihood ratio tests comparing models with and without product terms representing the variables of interest. Each of the interactions examined in Table 3 was adjusted for the other three factors where appropriate (e.g., the interaction between glycemic load and BMI was adjusted for physical activity, menopausal status and use of HRT, in addition to the variables listed in the footnote to Table 3) so that the various interactions that were examined were independent of each other
- Use of the LIFETEST procedure in SAS^e showed that the proportional hazards assumption was met in this dataset. All analyses were performed using SAS version 8 (SAS Institute, Cary, NC, USA).

Data Collection Summary:

Timing of Measurements

- FFQ distributed beginning in 1982
- 16.6-year follow-up.

Dependent Variables

Endometrial cancer risk.

Independent Variables

- Glycemic load
- Glycemic index
- Total carbohydrate consumption
- Total sugar consumption.

Description of Actual Data Sample:

- *Initial N:* 49,613 women
- *Attrition (final N):* 34,391
- *Age:* 40 to 59 years
- *Location:* Canada.

Summary of Results:

Key Findings

- Hazard ratios (HR) for the highest vs. the lowest quartile level of overall GI and GL were 1.47 (95% CI: 0.90 to 2.41; P=0.14) and 1.36 (95% CI: 1.01 to 1.84; P=0.21), respectively
- No association was observed between total carbohydrate or total sugar consumption and endometrial cancer risk
- Among obese women (BMI higher than 30kg/m²), the HR for the highest vs. the lowest quartile level of GL was 1.88 (95% CI: 1.08 to 3.29; P=0.54) and there was a 55% increased risk for the highest vs. the lowest quartile level of GL among pre-menopausal women
- There was also evidence to support a positive association between GL and endometrial cancer risk among post-menopausal women who had used HRT.

Author Conclusion:

Diets with high GI or high GL may be associated with endometrial cancer risk overall, and particularly among obese women, pre-menopausal women and post-menopausal women who use HRT.

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?	No
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?	Yes
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?	No
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?	???
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?	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?	Yes
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?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	Yes
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?	???
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)?	???
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