

Citation:

Nakamura K, Nagata C, Oba S, Takatsuka N, Shimizu H. Fruit and vegetable intake and mortality from cardiovascular disease are inversely associated in Japanese women but not in men. *J Nutr*. 2008 Jun;138(6):1129-34.

PubMed ID: [18492845](#)

Study Design:

Population-based, 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 fruit and vegetable intake and cardiovascular disease mortality in Japanese men and women.

Inclusion Criteria:

- Nonhospitalized residents of Takayama, Japan
- Aged 35 years or older

Exclusion Criteria:

- Subjects who did not fully complete the food frequency questionnaire
- Subjects who moved out of the area after the initial study
- Subjects who reported a medical history of cancer, stroke, or ischemic heart disease

Description of Study Protocol:**Recruitment**

Subjects were cohort members from the Takayama Study, a population-based cohort study conducted in Takayama, Gifu, Japan in September of 1992.

Design - Population-based, prospective cohort study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis

- Spearman correlation coefficients between the food frequency questionnaire and twelve 1-day food records for 1 year for fruit and vegetable intake were 0.57 ($p < 0.05$) and 0.51 ($p < 0.05$) in men and 0.74 ($p < 0.001$) and 0.41 ($p = 0.069$) in women.
- The food frequency questionnaire used in this study measured relative intake of foods and nutrients instead of absolute

values.

- Metabolic equivalent (MET) was used to represent physical activity, and added to produce a MET hours/week amount.
- Cox proportional hazard models assessed hazard ratios and 95% CI of death from cardiovascular disease (CVD) and were used to determine association of fruit and vegetable intake with CVD death. Person years started at the beginning of the study and continued until date of CVD-related or other death.
- The residual method proposed by Willett was used to adjust estimated food and nutrient intake for individual total energy. Energy-adjusted fruit and vegetable intake was sorted by quartiles.
- Multivariate analysis included variables that changed the risk estimate of CVD mortality. The analysis also included variables in fruit and vegetable intake that are known to affect CVD.
- Intake of total protein, saturated fat, and sodium were covariates.
- SAS program were used for statistical analysis.

Data Collection Summary:

Timing of Measurements - follow-up period of seven years (1992 - 1999). Dietary intake assessed at baseline in 1992.

Dependent Variables

- Risk of CVD death
- All deaths in Takayama and their causes were ascertained using data from the office of National Vital Statistics

Independent Variables

- Fruit and vegetable intake
- Dietary intake was assessed with a food frequency questionnaire. The Standard Tables of Food Composition in Japan were used to analyze individual intake of specific nutrients. Validity/reproducibility of the questionnaire was determined by comparison with other similar tools and assessment methods.

Control Variables

- Age
- Total energy intake
- Tobacco use
- Alcohol use
- Intake of total protein, saturated fat, and sodium

Description of Actual Data Sample:

Initial N: 31,452 (14,427 males and 17,125 females)

Attrition (final N): 29,079 (13,355 males and 15,724 females). 200 men and 184 women died from CVD during 7 years of follow-up.

Age: aged >35 years at baseline

Ethnicity: None mentioned

Other relevant demographics

Anthropometrics

Location: Takayama, Gifu, Japan

Summary of Results:

Key Findings

- At the start of the study, subjects with the highest fruit and vegetable intake were generally older and less likely to use tobacco and alcohol and more likely to be married and educated with hypertension.
- In the 7-year follow-up, 384 deaths were from cardiovascular disease (200 men, 184 women), with 269 due to cerebrovascular disease and 115 ischemic heart disease.
- Adjustment for age and total energy resulted in CVD mortality not being associated with men's total fruit and vegetable intake.
- For women, a significant linear association was found between vegetable intake and risk of death from CVD (p -trend = 0.02). This linear trend remained significant even after exclusion of subjects with CVD deaths during the first 2 years of the study (p -trend = 0.04).
- Stratified analysis among men who never smoked showed that vegetable intake had inverse association with CVD death. Hazard ratio (HR) and 95% CI of CVD deaths in males with lowest intake were 0.48 (95% CI, 0.13-1.73), 0.91 for 2nd quartile (95% CI, 0.32-2.65), and 1.19 (95% CI, 0.62 - 3.59) for highest quartile of vegetable intake. For male smokers, HR values were 0.89 (95% CI, 0.48 -1.63), 1.14 (95% CI, 0.65 - 2.00), and 1.24 (95% CI, 0.73 - 2.11), respectively. The association between smoking and vegetable intake was not significant for CVD mortality (p = 0.53).
- A significant association was noted between vegetable intake and CVD mortality in females but not males. Women with the highest vegetable intake had lower risk of CVD death.
- For women, the highest quartile of vegetable intake compared with the lowest was marginally significant and inversely associated with CVD mortality after adjusting for total energy, age, and nondietary and dietary covariates (hazard ratio = 0.62, 95% confidence interval: 0.36 - 1.08, P for trend = 0.007).

Author Conclusion:

In conclusion, our results suggest that high intake of fruits and vegetables is associated with a modest reduction in CVD in Japanese women. Larger studies should be conducted with more food categories to further assess any association.

Reviewer Comments:

Large population. Dietary intake only assessed at baseline. Inclusion criteria was >35 years old; only 200 men and 184 women died from CVD during 7 years of follow-up. Authors note that the duration of follow-up may have been too short to assess the relationship between diet and death from CVD.

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?	N/A
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?	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?	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.)	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 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?	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?	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

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