

Citation:

Wang L, Manson JE, Buring JE, Lee IM, Sesso HD. Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged and older women. *Hypertension*. 2008 Apr;51(4):1073-9. Epub 2008 Feb 7.

PubMed ID: [18259007](#)

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 associations between intake of dairy products, from both high-fat and low-fat food sources, as well as the major nutrient components in dairy products, calcium and vitamin D, with the risk of hypertension in a large cohort of middle-aged and older US women.

Inclusion Criteria:

- Women's Health Study participants
- Female US health professionals
- At least 45 years old
- Free from cardiovascular disease, cancer (except nonmelanoma skin cancer)
- Informed written consent

Exclusion Criteria:

- Baseline hypertension, defined as having a self-reported physician diagnosis of hypertension, self-reported systolic BP (SBP) at least 140 mm Hg, diastolic BP (DBP) at least 90 mm Hg or antihypertensive treatment
- Women with insufficient completion of semi-quantitative food frequency questionnaires (SFFQ)
- Women with implausible total energy intake
- Women with missing data on dairy intake
- Prerandomized cardiovascular disease or cancer

Description of Study Protocol:**Recruitment**

The population were participants in the Women's Health Study. Women were recruited from September 1992 to May 1995 and followed for 10 years.

Design: Prospective cohort study

Blinding used: Not applicable

Intervention: Not applicable

Statistical Analysis

- Baseline hypertension risk factors were compared across quintiles of dairy product intake
- Cox regression models were used to estimate the hazard ratio (presented as relative risk (RR) of hypertension across quintiles of dairy intake, with the lowest quintile as the reference
- Models first adjusted for age, race, total energy intake, and randomized treatment, and then additional adjusted for other factors predictive of hypertension, including smoking, alcohol intake, physical activity, menopausal status, multivitamin use, body mass index (BMI), history of diabetes and hypercholesterolemia, and fruit and vegetable, whole grain, and red meat intake.
- The individual effect of adjusting for dietary calcium and vitamin D on the RRs was evaluated. Analyses were further stratified by known hypertension risk factors such as BMI, alcohol intake, physical activity, and baseline BP.
- All of these analyses were repeated for dietary and supplemental calcium and vitamin D.
- Joint association of calcium and vitamin D with risk of hypertension was considered using a priori defined categories.

Data Collection Summary:

Timing of Measurements

Baseline

- Demographics
- Lifestyle characteristics
- Medical history through questionnaires
- SFFQ

Annual follow-ups of medical history through questionnaires

Dependent Variables

- Incident hypertension - defined as meeting one of these 4 criteria from annual follow-up questionnaires:
 - self-reports of a new physician diagnosis of hypertension
 - month and year of diagnosis were provided or, if missing, date was randomly selected between the present and previous questionnaire
 - self-reports of newly initiated antihypertensive treatment
 - self-reported SBP at least 140 mm Hg
 - self-reported DBP at least 90 mm Hg

Independent Variables

- Dietary intake - measured by the SFFQ

- Commonly used unit or portion size was specified for each food item
- Participants asked how often they had consumed that amount, on average, during the previous year, with possible answers ranging from "never or less than once per month" to "6+ per day."
- Average daily intake for the food item was calculated by multiplying the intake frequency by the portion size of the specific items
- Total dairy product intake was calculated by summing the intake of individual dairy items: low-fat dairy items included skim or low-fat milk, sherbet, yogurt, cottage/ricotta cheese, and high fat dairy items include whole milk, cream, sour cream, ice cream, cream cheese, and other cheese.
- Nutrient intake was computed by multiplying the intake frequency by the nutrient content of the specified portion size according to food composition tables from the Harvard School of Public Health. Each nutrient reported has adjusted for total energy intake using the residual method.
- Supplemental calcium and vitamin D were assessed from the self-reported use of individual and multivitamin supplements.

Control Variables

- Age
- Race
- Total energy intake
- Randomized treatment
- Smoking
- Alcohol intake
- Physical activity
- Menopausal status
- Multivitamin use
- Body mass index (BMI)
- History of diabetes and hypercholesterolemia
- Fruit and vegetable, whole grain, and red meat intake.

Description of Actual Data Sample:

Initial N: 39, 876 females in the Women's Health Study

Attrition (final N): 28,886 women after exclusion criteria

Age: mean ~ 54 years

Ethnicity: over 90% white

Other relevant demographics: less than 20% currently smoked; ~half were postmenopausal

Anthropometrics: BMI mean ~25 kg/m²

Location: Boston, Massachusetts

Summary of Results:

Key Findings:

- Incident cases of hypertension (n=8710) were identified during 10 years of follow-up.
- After adjusting for major hypertension risk factors, the RRs of incident hypertension across increasing quintiles of low-fat dairy product intake were 1.00 (reference), 0.98, 0.97, 0.95, and 0.89 (P for trend = 0.001).
- The risk of hypertension decreased in the higher quintiles of dietary calcium (multivariate RR in the highest quintile: 0.87) and dietary vitamin D (multivariate RR in the highest quintile: 0.95), but did not change with calcium or vitamin D supplements.
- Adjustment for dietary calcium significantly attenuated the inverse association of low-fat dairy intake with risk of hypertension, whereas adjustment for dietary vitamin D did not change the association.
- The multivariate relative risks across increasing quintiles of high-fat dairy product intake, in contrast, were 1.00, 1.02, 1.01, 1.00, and 0.97 (not significant trend).

Variables	First Quintile Measures and confidence intervals	Fifth quintile Measures and confidence intervals	Statistical Significance of Group Difference
Low-fat dairy	0.13	2.71	p = 0.001
Median, servings/day	1.00 (reference)	0.89 (0.82 to 0.96)	
Multivariate model (with adjustments)			
High-fat dairy	0.13	1.49	p = 0.17
Median, servings/day	1.00 (reference)	0.97 (0.90 to 1.04)	
Multivariate model			
Total dairy	0.56	3.69	p = .0003
Median, servings/day	1.00 (reference)	0.86 (0.79 to 0.93)	
Multivariate model			
Dietary calcium			
Median, mg/day	483.5	1170.4	p<.0001
Multivariate model	1.00 (reference)	0.87 (0.81 to 0.93)	
Supplemental calcium			
Median, mg/day	0	1162	p=0.38
Multivariate model	1.00 (reference)	1.07 (0.97 to 1.18)	
Dietary vitamin D			
Median, IU/day	110.1	381.0	p=0.02
Multivariate model	1.00 (reference)	0.95 (0.88 to 1.02)	

Supplemental vit D

Median, IU/day	0	800	p=0.27
Multivariate model	1.00 (reference)	1.09 (0.93 to 1.27)	

Other Findings

- Women who consumed low-fat dairy were older, less likely to smoke and drink alcohol, more likely to be physically active, use multivitamins, and had a higher prevalence of diabetes and hypercholesterolemia. Low-fat dairy intake was also positively associated with fruit and vegetable and whole grain intake and energy-adjusted potassium, fiber, calcium, and vitamin D intake, while inversely associated with red meat and cholesterol intakes.
- Low-fat dairy intake was not associated with baseline BP, but high-fat dairy intake was positively associated with baseline DBP.
- For all 4 major low-fat dairy products, a reduction of 10% to 15% in hypertension risk comparing the highest to the lowest intake categories was observed in the initial model, but the reduction was statistically significant only for skim milk and yogurt. Multivariate adjustment attenuated the inverse association for yogurt, but not for RR for skim milk.

Author Conclusion:

In this large prospective cohort study of middle-aged and older women, we found an inverse association between low-fat dairy product intake and the subsequent risk of hypertension. The association was moderate, graded, and independent of known risk factors for hypertension. In contrast, we found no association between high-fat dairy and subsequent risk of hypertension. Calcium and vitamin D intake in the diet, but not supplements, were inversely associated with risk of hypertension. The association between low-fat dairy intake and reduced risk of hypertension was substantially attenuated by adjustment for dietary calcium.

Reviewer Comments:

Strengths

- *Well-defined dependent variable*

Weaknesses

- *Dietary intake was assessed from a single measurement of SFFQ, which is subject to random error that would tend to underestimate a true association*
- *SFFQ was not designed for a calcium/dairy product study (Pearson correlation coefficient for the SFFQ versus dietary records was referenced at 0.51); a FFQ specific to dairy foods may have provided a more accurate dietary analysis appropriate for this study*
- *Incident hypertension was identified based on self-reported information*
- *Residual confounding factors cannot be completely ruled out, despite all the covariates used*
- *Vitamin D intake from the sun was not assessed*
- *There may be other hypotensive components of dairy products not assessed in this study: dairy protein, lactose, potassium, magnesium, and other minerals*
- *Generalizability is limited to white health professional women*

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?	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
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?	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?	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?	N/A
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?	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?	???
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

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