

**Citation:**

Thorpe DL, Knutsen SF, Beeson WL, Rajaram S, Fraser GE. Effects of meat consumption and vegetarian diet on risk of wrist fracture over 25 years in a cohort of peri- and postmenopausal women. *Public Health Nutr.* 2008 Jun; 11 (6): 564-572. Epub 2007 Aug 9.

**PubMed ID:** [17686206](#)

**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 effects of foods high in protein and the effect of an absence of meat in the diet relative to low-energy wrist fracture (WF).

**Inclusion Criteria:**

The study participants were peri- and post-menopausal women in a cohort of white female Seventh-day Adventists (SDAs) who completed two life-style questionnaires, the first of which was administered in 1976 and the second initiated in 2002.

**Exclusion Criteria:**

None.

**Description of Study Protocol:****Recruitment**

- The study participants were peri- and post-menopausal women in a cohort of white female Seventh-day Adventists (SDAs) who completed two life-style questionnaires, the first of which was administered in 1976 and the second being initiated in 2002
- 1976: Lifestyle questionnaire sent to SDA census respondents who were 25 years or older. The census of the SDA membership was undertaken to identify all non-Hispanic whites residing in California in 1974
- 2002: Recruitment efforts among church membership included announcements and media presentations at weekly church services, advertisements in SDA periodicals, brochures and

interviews on SDA television networks. Interested members who turned in an enrollment card and were 35 years or older received a questionnaire.

## **Design**

- Cohort study
- In this cohort of women, 1406 were menopausal at baseline (1976). This included women who experienced surgical menopause as early as age 25 years, as well as those experiencing early but natural menopause. Another 459 women were not yet menopausal, but were 45 years of age or older. They were considered perimenopausal in that age 45 was two standard deviations (SD) below the current mean age for menopause in AHS-2. This is consistent with the definition for the peri-menopausal period used in other studies. Together, the total of 1,865 women comprised the study population.

## **Dietary Intake/Dietary Assessment Methodology**

- The dietary analysis included individual food items from the questionnaire.
- In addition, five indices representing different food groups were used. Four of the five indices were constructed by summing the frequency of intake for foods in the group using mid-point frequencies for particular categories. Then those sums were again categorized. The fifth index, meat intake, was constructed using the summed frequency of five items on beef, poultry, fish and pork consumption and the response to a single question on frequency of overall meat consumption.
- The meat intake index reflected the higher meat intake if the summed frequency of various meat intake differed from the single question on meat consumption
- Three levels of intake were specified for each of the selected foods (cheese, cottage cheese, eggs, milk, salad, green vegetables, nuts, beans, vegetarian meat substitute products typically made from wheat gluten or soybean textured protein) and food groups (meat, fruit, fruits and vegetables, vegetable-protein foods, animal-protein foods). In most cases, the low, medium and high categories corresponded to approximately the 20th, 50th and 80th percentiles of intake, respectively.

## **Blinding Used**

Not applicable.

## **Intervention**

Not applicable.

## **Statistical Analysis**

- The independent T-test for means and Pearson's X-test for categorical data were used to test for differences in demographic and lifestyle variables between cases and non-cases.
- The effects of foods high in protein and other covariates on WF risk were assessed using Cox proportional-hazard regression with attained age as the time variable. Attained age for WF cases was estimated at the mid-point of the time interval specified for the event on the AHS-2 questionnaire
- Covariates were entered into univariate and multivariable models as dummy variables except for years since menopause, which was entered as a time-dependent covariate
- In univariate models these included age, BMI, height, weight, education, any fracture since age 35, parity, smoking status, alcohol use, presence of diabetes mellitus, presence of rheumatoid arthritis and physical activity

- All variables were measured at baseline except for fracture since age 35 and years since menopause. For multivariable modelling of main effects, a base model was constructed with the three food variables high in protein (nuts, beans, meat substitutes), physical activity, hormone use and BMI (covariates often shown in the literature to be strongly associated with risk of fracture) and education. The last variable was forced into the model to control for socio-economic status. Correlates that altered the main effect of vegetarian status (vegetarian, semi-vegetarian, non-vegetarian) by 10% or that showed an independent effect on WF ( $P < 0.05$ ) were retained in the final multivariable model for all subjects
- Multivariable high-protein foods-only models with interactions between the food variables were also explored
- Significant food interaction terms were added to the final multivariable model. SAS (Statistical Analysis System, version 8.0) was used for all analyses. Visual inspection of the log-log survival plot, and also a non-significant interaction term between the three-level vegetarian status and log time temporarily added to the final model, confirmed that the proportional hazards assumption for the Cox regression model was met.

### Data Collection Summary:

#### Timing of Measurements

Recruitment: 1976 -1988, 2002-2006.

#### Dependent Variables

Wrist fracture risk.

#### Independent Variables

- Consumption of foods high in protein
- Absence of meat.

#### Control Variables

None.

### Description of Actual Data Sample:

- *Initial N*: 34,198 in 1976
- *Attrition (final N)*: 1,865 women
  - 1,406 menopausal at baseline
  - 459 women who were not yet menopausal, but were 45 years of age or older
- *Age*:
  - 1976: 25 years or older
  - 2002: 35 years or older
- *Ethnicity*: Not reported
- *Other relevant demographics*: Seventh-Day Adventists
- *Anthropometrics*: None
- *Location*: California.

## Summary of Results:

- Subjects who experienced fractures during the study time period were more likely to be older, have a history of fractures, report low or no vigorous physical activity, have experienced menopause more than 15 years earlier, never used hormones and nulliparous
- There were no differences in height, weight, BMI, education, co-morbidity, alcohol use or smoking
- Cases also consumed more cheese and less meat than non-cases
- Interaction of effects of vegetable protein and meat intake on risk of a wrist fracture among women in the Adventist Health Study who were postmenopausal or 45 years and older at baseline
  - Cheese intake more than three times per week reduced risk of fracture by 58%
  - Meat consumption more than four times per week reduced fracture risk by 56%
  - The vegetable protein food group did not show an independent effect on fracture risk
  - The group at highest risk of fracture were those who never consume meat (vegetarians) and in the lowest category of vegetable protein intake
  - Among vegetarians, increasing vegetable protein clearly reduced risk of fracture by 68% in the highest intake group
  - Among the lower vegetable protein consumers, increase meat intake decreased risk of fractures by 80% in the highest consumption group
  - In medium and high meat consumer, higher vegetable protein intake appeared to increase risk.

			Meat Intake			
			None	Less Than one to Four Times per Week	More Than Four Times per Week	
Vegetable protein	Number of Women	Number of Fractures	HR (95% CI)	HR (95% CI)	HR (95% CI)	P for Interaction
Less than three times per week	304	22	1.00	0.39 (0.15-1.07)	0.20 (0.06-0.66)	0.005
Three times per week-one time per day	1,218	120	0.62 (0.30-1.32)	0.49 (0.23-1.06)	0.32 (0.12-0.86)	
More than one time per day	343	29	0.32 (0.13-0.79)	0.66 (0.27-1.60)	--	

HR=hazard ratio

### Author Conclusion:

- The finding that higher consumption frequencies of foods rich in protein were associated with reduced WF supports the importance of adequate protein for bone health
- The similarity in risk reduction by vegetable protein foods compared with meat intake suggests that adequate protein intake is attainable in a vegetarian diet.

### Reviewer Comments:

### 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.   | <b>Was the research question clearly stated?</b>  | 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.   | <b>Was the selection of study subjects/patients free from bias?</b>   | 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
<b>3.</b>	<b>Were study groups comparable?</b>	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.)	Yes
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.)	No
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
<b>4.</b>	<b>Was method of handling withdrawals described?</b>	Yes
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
<b>5.</b>	<b>Was blinding used to prevent introduction of bias?</b>	No
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.)	No
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
<b>6.</b>	<b>Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were intervening factors described?</b>	<b>Yes</b>
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?	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?	N/A
<b>7.</b>	<b>Were outcomes clearly defined and the measurements valid and reliable?</b>	<b>Yes</b>
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?	???
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
<b>8.</b>	<b>Was the statistical analysis appropriate for the study design and type of outcome indicators?</b>	<b>Yes</b>
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)?	N/A
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?	No
<b>9.</b>	<b>Are conclusions supported by results with biases and limitations taken into consideration?</b>	<b>Yes</b>
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
<b>10.</b>	<b>Is bias due to study's funding or sponsorship unlikely?</b>	<b>Yes</b>
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes