Legume Consumption and Risk of Coronary Heart Disease in US Men and Women

NHANES I Epidemiologic Follow-up Study

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Background: Soybean protein and dietary fiber supplementation reduce serum cholesterol in randomized controlled trials. Consumption of legumes, which are high in bean protein and water-soluble fiber, may be associated with a reduced risk of coronary heart disease (CHD).

Methods: A total of 9632 men and women who participated in the First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study (NHEFS) and were free of cardiovascular disease (CVD) at their baseline examination were included in this prospective cohort study. Frequency of legume intake was estimated using a 3-month food frequency questionnaire, and incidence of CHD and CVD was obtained from medical records and death certificates.

Results: Over an average of 19 years of follow-up, 1802 incident cases of CHD and 3680 incident cases of CVD were documented. Legume consumption was significantly and inversely associated with risk of CHD ($P = .002$ for trend) and CVD ($P = .02$ for trend) after adjustment for established CVD risk factors. Legume consumption 4 times or more per week compared with less than once a week was associated with a 22% lower risk of CHD (relative risk, 0.78; 95% confidence interval, 0.68-0.90) and an 11% lower risk of CVD (relative risk, 0.89; 95% confidence interval, 0.80-0.98).

Conclusions: Our study indicates a significant inverse relationship between legume intake and risk of CHD and suggests that increasing legume intake may be an important part of a dietary approach to the primary prevention of CHD in the general population.
METHODS

STUDY POPULATION

The NHANES I used a multistage, stratified probability sampling design to select a representative sample of the US civilian noninstitutionalized population aged 1 to 74 years. Certain population subgroups, including those with a low income, women of childbearing age (25-44 years), and elderly persons (65 years or older) were oversampled. The NHEFS is a prospective cohort study of NHANES I participants who were 23 to 74 years old when the survey was conducted between 1971 and 1975. Of the 14,407 persons in this age range at baseline, we excluded (1) 1,347 who had a self-reported history of heart attack, heart failure, or stroke at baseline or had used medication for heart disease during the preceding 6 months, (2) 2,853 NHANES I Augmentation Survey participants for whom the study protocol did not include a dietary assessment, and (3) 190 who lacked legume intake information. Among the remaining participants, 386 (3.9%) were lost to follow-up, leaving a total of 9,632 participants who contributed 159,599 person-years to this analysis.

MEASUREMENT

Baseline data collection included a dietary assessment, standardized medical examination, anthropometric measurements, medical history, and laboratory tests. The dietary assessment included a 3-month food frequency questionnaire on participants’ usual consumption of food groups in 13 major categories including legume intake. The primary item used in this investigation asked participants how often “dry beans and peas like pinto beans, red beans, black-eyed [sic] peas, peanuts and peanut butter” were usually consumed in the past 3 months excluding periods of illness or dieting. Information on portion size was not collected. In addition to the food frequency questionnaire, a single 24-hour dietary recall was conducted by trained NHANES I personnel using a standardized protocol and 51 three-dimensional models to estimate portion size. Trained personnel coded the dietary recall questionnaires using nutrient information from the Department of Agriculture Handbook No. 8 or other resources. Saturated fat and total energy intake was calculated for each participant by the National Center for Health Statistics. Blood pressure, body weight, and height were obtained using standard protocols. Frozen serum samples were sent to the Centers for Disease Control and Prevention for measurement of serum total cholesterol levels.

The baseline questionnaire on medical history included questions about selected health conditions and medications used for these conditions during the preceding 6 months. Data on education, physical activity, and alcohol consumption were obtained by means of interviewer-administered questionnaires. Baseline information on smoking status was obtained for 6,913 participants who underwent a more detailed baseline examination.

RESULTS

Baseline characteristics of the study participants are given by category of legume intake in Table 1. Compared with those with a lower intake, participants with a higher intake of legumes tended to be younger and male. Persons with more frequent legume intake had, on average, a lower systolic blood pressure, less hypertension, lower levels of total cholesterol and hypercholesterolemia, less diabetes, and a lower body mass index (BMI) than their counterparts who consumed legumes less often. In addition, participants with more frequent legume intake tended to be more physically active, more likely to smoke, and less likely to have completed high school. They also tended to consume more saturated fat and to have a higher total energy intake. The average amount of legumes consumed in 24 hours increased with frequency of legume intake from the 3-month food questionnaire. The average serving size of legumes consumed in this cohort calculated from the 24-hour dietary recall was 98.6 g with an SD of 97.6 g.

Over the course of 139,599 person-years of follow-up between 1971 and 1992, 1,802 CHD events and 3,680 CVD events were documented. Relative risks (RRs) and corresponding 95% confidence intervals (CIs) for CHD and CVD by category of legume intake are given in Table 2. In age-, sex-, race-, and energy-adjusted analyses, risk of CHD was significantly and inversely related to frequency of legume consumption at baseline (P = .02 for trend). After additional adjustment for history of diabetes, recreational physical activity, level of education, regular alcohol consumption, and current cigarette smoking, frequency of legume consumption at baseline was again significantly and inversely related to risk of CHD (P = .002 for trend). In the latter model, those with an intake of legumes at least 4 times a week had a 22% lower risk of CHD (RR, 0.78; 95% CI, 0.68-0.90) compared with their counterparts consuming legumes less than once a week. Further adjustment for systolic blood pressure, total serum cholesterol, BMI, frequency of meat and poultry consumption, frequency of fruit and vegetable consumption, and saturated fat intake did not materially alter the risk estimates. For instance, those consuming legumes at least 4 times a week had a 20% lower risk of CHD (RR, 0.80; 95% CI, 0.69-0.91) compared with those consuming legumes less than once a week. Risk of CVD was inversely related to participants’ frequency of legume consumption with borderline significance (P = .07 for trend) in models adjusted for age, sex, race, and energy intake. After additional adjustment for history of diabetes, recreational physical activity, level of education, regular alcohol consumption, and current cigarette smoking, risk of CVD was significantly and inversely related to legume consumption at baseline (P = .02 for trend). Intake of legumes at least 4 times per week was associated with a 11% lower risk of CVD events compared with intake of legumes less than once a week (RR, 0.89; 95% CI,
study participants, information on smoking status at baseline was derived from responses to questions on lifetime smoking history obtained at their follow-up interviews from 1982 to 1984 or later.11 The validity of information obtained using this approach has been documented.13,14

FOLLOW-UP PROCEDURES

Follow-up data were collected between 1982 and 1984 and in 1986, 1987, and 1992.11,12,15,16 Each follow-up examination included tracking a participant or his/her proxy to a current address; performing an in-depth interview; obtaining hospital and nursing home records, including pathology reports and electrocardiograms; and, for decedents, acquiring a death certificate. Incident CVD was based on documentation of an event that met prespecified study criteria and occurred during the period between the participant’s baseline examination and last follow-up interview. Validity of study outcome data has been documented.17

Incident CHD was based on a death certificate report in which the underlying cause of death was coded as an International Classification of Diseases, Ninth Revision (ICD-9) code of 410 to 414, or by 1 or more hospital and/or nursing home stays in which the participant had a discharge diagnosis with these codes. Incident CVD was based on a death certificate report in which the underlying cause of death was recorded using an ICD-9 code of 390 to 459, or 1 or more hospital and/or nursing home stays in which the participant had a discharge diagnosis with these codes.

0.80-0.98). Further adjustment for systolic blood pressure, serum cholesterol, BMI, frequency of meat and poultry consumption, frequency of fruit and vegetable consumption, and saturated fat intake produced little change in risk estimates but was associated with borderline statistical significance (P = .06 for trend).

Relative risks and 95% CIs for the comparison of legume intake at least 4 times a week to less than once a week by selected subgroups are given in Table 3. Relative risks for CHD and CVD were lower among persons consuming legumes at least 4 times a week than for their counterparts consuming legumes less than once a week across subgroups based on sex, recreational physical activity, smoking status, vitamin use, hypertension status, serum cholesterol levels, and BMI.

However, estimates of risk differed significantly by category of age at entry. When participants were stratified by age at entry into 2 groups (60 years or older at the baseline examination and younger than 60 years at baseline) significant associations were detected in the older group but not in the younger group. For instance, in the older group, those with an intake of legumes at least 4 times a week had a 38% lower risk of CHD (RR, 0.62; 95% CI, 0.50-0.77) and a 27% lower risk of CVD (RR, 0.73; 95% CI, 0.62-0.87) compared with those whose intake of legumes was less than once a week. However, after adjustment for time from dietary measurement to event, effect modification was no longer statistically significant for either CHD or CVD (P > .05), while estimates of risk associated with legume consumption categories were not considerably changed.

The date of record for incident events was identified by the date of first hospital admission with an established study event or date of death from a study event in the absence of hospital or nursing home documentation of such an event.

STATISTICAL ANALYSIS

Based on the distribution of participants’ responses, legume intake was grouped into the following 4 categories: intake less than once a week, once a week, 2 to 3 times a week, and at least 4 times a week. For each baseline characteristic, the mean value or corresponding percentage of study participants was calculated by category of legume intake. The statistical significance of differences was examined by analysis of variance (continuous variables) and by the χ² test (categorical variables). The cumulative incidence of CVD by category of legume intake was calculated using the Kaplan-Meier method,20 and differences in the cumulative rates were examined using the log-rank test for trend.19 Cox proportional hazard models were used to explore the relationship between categories of legume intake and risk of CVD.20 Age was used as the time scale in all time-to-event analyses.21 Cox proportional hazard models were stratified by birth cohort using 10-year intervals to control for calendar period and cohort effects.22 Methods to estimate variance that take into account sample clustering and stratification of the NHANES I sample were used in the Cox proportional hazards models.23 Data from the small number of participants who had reached 85 years of age were censored.

Our study found a strong and independent inverse association between dietary intake of legumes and risk of CHD in a representative sample of the noninstitutionalized adult US population. These findings have important clinical and public health implications. Coronary heart disease is the single largest killer of men and women in the United States, and although improved, the CHD case-fatality rate is still high.1 In addition, CHD is one of the leading causes of premature, permanent disability in the US population, accounting for 19% of disability allowances by the Social Security Administration.3 Moreover, Medicare beneficiaries were paid $10.5 billion in 1996 for CHD events and, per discharge, amounts ranged from $3843 to $11 130.2 Because of the high mortality from CHD, high prevalence of disability due to CHD, and substantial financial burden to individual patients and for society, the primary prevention of CHD is an essential element of any attempt to tackle the problem of CVD in the United States. Our findings suggest that increasing legume intake may be an important part of dietary interventions to reduce heart disease.

To our knowledge, this is the first study examining the relationship between legume intake as foods and the development of CVD. Most studies of legume intake have focused on specific nutritional components of legumes, such as protein, fiber, and phytochemicals,2,22,23 or have not used clinical events as end points. However, it may be more instructive and useful to investigate of the relationship between dietary patterns or specific food in-
takes and risk of CHD events because the results of such studies may have more direct public health implications. In addition, studies focusing on nutrient intake may fail to consider the biochemical complexity and possibility of nutrient interactions in food items.

The present study was conducted in a representative sample of the adult noninstitutionalized US population, so our findings are highly generalizable. Additional strengths include the assessment of incidence of CVD over an average of 19 years of follow-up, with experience available for more than 96% of the study participants. Moreover, because legume intake was measured at baseline, temporal relationships can be established with confidence. Further, the use of a food frequency

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<th>Table 1. Baseline Characteristics of 9632 NHEFS Participants According to Frequency of Legume Intake*</th>
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<td>Dietary intake of saturated fat, g/24 h</td>
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<td>Dietary intake of energy, kcal/24 h</td>
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*Data are given as mean ± SD or percentage of participants. NHEFS indicates First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study; BP, blood pressure.
†Systolic blood pressure ≥160 mm Hg and/or diastolic blood pressure ≥95 mm Hg and/or use of antihypertensive medication.
‡Serum cholesterol level ≥240 mg/dL (≥6.2 mmol/L).
§Vitamin supplement use includes regular and irregular use of any vitamin supplement.
| From 24-hour dietary recall. |

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<th>Table 2. Relative Risk of Coronary Heart Disease and Cardiovascular Disease According to Frequency of Legume Intake in 9632 NHEFS Participants*</th>
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<td>Multivariate model 2‡</td>
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*NHEFS indicates First National Health and Nutrition Examination Survey Epidemiologic Follow-up Study; RR, relative risk; and CI, confidence interval.
†Stratified by birth cohort and adjusted for age, sex, race, history of diabetes, recreational physical activity, level of education, regular alcohol consumption, current cigarette smoking, and total energy intake; n = 9178.
‡Additionally adjusted for total serum cholesterol level, systolic blood pressure, body mass index, saturated fat intake, frequency of meat and poultry intake, and frequency of fruit and vegetable intake; n = 9078.
Limitations of the study include a lack of portion size information for legume intake. We were not able to estimate the RR of CVD associated with servings of legumes per day using data derived from the food frequency questionnaire. However, several studies have shown that portion size estimation using food frequency methods may not be accurate and may introduce measurement error. Average portion size was estimated using data from the 24-hour dietary recall.

Additionally, changes in legume intake during follow-up were not measured. This might have contributed to misclassification of legume intake because dietary practices may have changed during the 19-year follow-up period. Consequently, the interaction observed here between legume intake and age may be due to greater measurement error in legume intake for persons whose age at entry to the study was younger than 60 years. While the median time from baseline dietary assessment to CVD events was 7.6 years in participants 60 years or older at baseline, the median time to events was 10.3 years in participants younger than 60 years at baseline. Moreover, in models adjusted for time from dietary measurement to event, age interactions were not statistically significant.

Given the above information, it is likely that changes in dietary pattern over the course of prolonged follow-up reduced our ability to assess the relationship between legume intake and CVD in younger participants. Therefore, the apparent age group interaction should be interpreted with caution.

It is possible that persons with a more frequent intake of legumes may have other dietary and nondietary habits that promote health, such as not smoking, regular exercise, and a low dietary intake of cholesterol and saturated fat. However, in our study population, persons consuming legumes more frequently were also more likely to smoke and consumed higher levels of saturated fat than their counterparts with a less frequent intake of legumes, while vitamin use was not significantly different across categories of legume consumption.

Additionally, the estimates of risk in this study were adjusted for important potential confounders of CVD, such as age, sex, race, recreational physical activity, education level, cigarette smoking status, diabetic status, regular alcohol consumption, and total energy intake. Further adjustment for dietary factors (such as frequency of intake of meat, frequency of intake of fruits and vegetables, and intake of saturated fat) and biological factors (such as serum cholesterol level, BMI, and systolic blood pressure) resulted in minimal change in risk estimates and linear trends. The inverse association between legume intake and risk of CHD and CVD was consistent across strata of vitamin use and level of recreational activity, both markers of a healthy lifestyle. These findings suggest that legume intake may be related to a lower risk of CHD and CVD, independent of other health habits.

Many constituents of legumes could contribute to the potential protective effect of legume intake on CVD. For instance, soybean protein has been shown to reduce serum total and low-density lipoprotein cholesterol levels in a meta-analysis of 29 clinical trials. Soybean protein intake averaged 47 g/d across the studies. In 19 of the 29 studies, intakes of energy, total fat, saturated fat, and cholesterol were similar between the control and soybean-containing diets. In a pooled analysis of the results from all 29 trials, soybean protein administration was associated with a reduction in serum total cholesterol concentrations (a decrease of 2.2 mg/dL [95% CI, 1.3-3.2 mg/dL]; 0.56 mmol/L [0.35-0.85 mmol/L]), and a net reduction in serum low-density lipoprotein cholesterol of 21.7 mg/dL (0.56 mmol/L) [95% CI, 1.12-3.17 mg/dL; 0.29-0.82 mmol/L].

In addition, soybean protein diets significantly decreased serum triglyceride concentrations by 13.3 mg/dL (0.15 mmol/L) [95% CI, 0.3-25.7 mg/dL; 0.003-0.29 mmol/L]). While soybean protein did not significantly affect serum high-density lipoprotein cholesterol levels, a net increase of 1.2 mg/dL (0.03 mmol/L) was seen across the 29 trials. Legume intake other than soybean has also been associated with a reduction in serum cholesterol in clinical studies, possibly due to the high soluble fiber content of legumes. A half cup of cooked beans contains an average of 6 g of total fiber and 2 g of soluble fiber, which is more total fiber than the same amount of soluble fiber as
is contained in one-third cup of dry oat bran.31 Soluble fiber has been associated with reduced cholesterol levels and risk of CHD as well as better glycemic control.3,23,31,35

Furthermore, legumes are a major source of dietary folate.36 Both folate and vitamin B12 are important for the metabolism of homocysteine, and dietary intake of folate has been inversely associated with plasma homocysteine levels.3,23,31,35 Elevated levels of plasma homocysteine have been related to an increased risk of CHD.3,37 In addition, serum folate levels have been inversely associated with mortality from CHD and CVD.40,41

In conclusion, our study found a strong inverse relationship between legume intake and risk of CHD. Future specifically designed prospective studies with detailed measurements of legume intake at baseline and during follow-up will provide more definitive information on this association. However, based on our current knowledge and national and international recommendations to increase fruit and vegetable intake, increasing legume consumption may be an important part of dietary interventions to reduce the risk of CHD. Additionally, increasing legume consumption may be a novel approach to culturally tailor dietary interventions aimed at reducing CHD.

Accepted for publication April 10, 2001.

This study was supported by grant R03 HL61954 (Dr He) and in part by grant RO1HL63030 from the National Heart, Lung, and Blood Institute.

The NHES has been developed and funded by the National Center for Health Statistics, Hyattsville, Md; the National Institute on Aging, National Cancer Institute, National Institute of Child Health and Human Development, National Heart, Lung, and Blood Institute, National Institute of Mental Health, National Institute of Diabetes and Digestive and Kidney Diseases, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institute of Allergy and Infectious Diseases, and the National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, Md; the Centers for Disease Control and Prevention, Atlanta, Ga; and the US Department of Agriculture, Washington, DC.

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