

HHS Public Access

Author manuscript *JAMA Intern Med*. Author manuscript; available in PMC 2015 June 19.

Published in final edited form as: *JAMA Intern Med*. 2015 May 1; 175(5): 755–766. doi:10.1001/jamainternmed.2014.8347.

Prospective Evaluation of the Association of Nut/Peanut Consumption With Total and Cause-Specific Mortality

Hung N. Luu, MD, PhD, **William J. Blot, PhD**, **Yong-Bing Xiang, MD, MPH**, **Hui Cai, MD, PhD**, **Margaret K. Hargreaves, PhD**, **Honglan Li, MD, MPH**, **Gong Yang, MD, MPH**, **Lisa Signorello, ScD**, **Yu-Tang Gao, MD**, **Wei Zheng, MD, PhD**, and **Xiao-Ou Shu, MD, PhD** Division of Epidemiology, Department of Medicine, Vanderbilt Epidemiology Center, Vanderbilt University School of Medicine, Nashville, Tennessee (Luu, Blot, Cai, Yang, Zheng, Shu); Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, Tennessee (Luu, Blot, Cai, Yang, Zheng, Shu); International Epidemiology Institute, Rockville, Maryland (Blot); Department of Epidemiology, Shanghai Cancer Institute, Xuhui, Shanghai, China (Xiang, Li, Gao); Department of Internal Medicine, Meharry Medical College, Nashville, Tennessee (Hargreaves); Department of Epidemiology, Harvard School of Public Health, Harvard University, Boston, Massachusetts (Signorello)

Abstract

Importance—High intake of nuts has been linked to a reduced risk of mortality. Previous studies, however, were primarily conducted among people of European descent, particularly those of high socioeconomic status.

Objective—To examine the association of nut consumption with total and cause-specific mortality in Americans of African and European descent who were predominantly of low socioeconomic status (SES) and in Chinese individuals in Shanghai, China.

Copyright 2015 American Medical Association. All rights reserved.

Corresponding Author: Xiao-Ou Shu, MD, PhD, Division of Epidemiology, Department of Medicine, Vanderbilt Epidemiology Center, Vanderbilt University School of Medicine, 2525 W End Ave, Ste 600 (Institute for Medicine and Public Health), Nashville, TN 37203 (xiao-ou.shu@vanderbilt.edu).

Supplemental content at jamainternalmedicine.com

Author Contributions: Dr Shu had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Luu, Blot, Shu.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Luu, Blot, Shu.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Luu, Cai.

Obtained funding: Blot, Signorello, Zheng, Shu.

Administrative, technical, or material support: Xiang, Cai, Li, Gao, Zheng.

Study supervision: Luu, Gao, Zheng, Shu.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank all research teams and participants of the SCCS, SMHS, and SWHS. Bethanie Rammer, BA, and Nan Kennedy, BA (Division of Epidemiology, Department of Medicine, Vanderbilt University), edited the manuscript.

There was no financial compensation.

Disclaimer: Opinions expressed in this article are those of the authors and do not represent the official opinion of the US National Cancer Institute.

Design, Setting, and Participants—Three large cohorts were evaluated in the study. One included 71 764 US residents of African and European descent, primarily of low SES, who were participants in the Southern Community Cohort Study (SCCS) in the southeastern United States (March 2002 to September 2009), and the other 2 cohorts included 134 265 participants in the Shanghai Women's Health Study (SWHS) (December 1996 to May 2000) and the Shanghai Men's Health Study (SMHS) (January 2002 to September 2006) in Shanghai, China. Self-reported nut consumption in the SCCS (approximately 50% were peanuts) and peanut-only consumption in the SMHS/SWHS were assessed using validated food frequency questionnaires.

Main Outcomes and Measures—Deaths were ascertained through linkage with the National Death Index and Social Security Administration mortality files in the SCCS and annual linkage with the Shanghai Vital Statistics Registry and by biennial home visits in the SWHS/SMHS. Cox proportional hazards regression models were used to calculate hazard ratios (HRs) and 95% CIs.

Results—With a median follow-up of 5.4 years in the SCCS, 6.5 years in the SMHS, and 12.2 years in the SWHS, 14 440 deaths were identified. More than half of the women in the SCCS were ever smokers compared with only 2.8% in the SWHS. The ever-smoking rate for men was 77.1% in the SCCS and 69.6% in the SMHS. Nut intake was inversely associated with risk of total mortality in all 3 cohorts (all $P < .001$ for trend), with adjusted HRs associated with the highest vs lowest quintiles of intake being 0.79 (95% CI, 0.73-0.86) and 0.83 (95% CI, 0.77-0.88), respectively, for the US and Shanghai cohorts. This inverse association was predominantly driven by cardiovascular disease mortality (*P* < .05 for trend in the US cohort; *P* < .001 for trend in the Shanghai cohorts). When specific types of cardiovascular disease were examined, a significant inverse association was consistently seen for ischemic heart disease in all ethnic groups (HR, 0.62; 95% CI, 0.45-0.85 in blacks; HR, 0.60; 95% CI, 0.39-0.92 in whites; and HR, 0.70; 95% CI, 0.54-0.89 in Asians for the highest vs lowest quintile of nut intake). The associations for ischemic stroke (HR, 0.77; 95% CI, 0.60-1.00 for the highest vs lowest quintile of nut intake) and hemorrhagic stroke (HR, 0.77; 95% CI, 0.60-0.99 for the highest vs lowest quintile of nut intake) were significant only in Asians. The nut-mortality association was similar for men and women and for blacks, whites, and Asians and was not modified by the presence of metabolic conditions at study enrollment.

Conclusions and Relevance—Nut consumption was associated with decreased overall and cardiovascular disease mortality across different ethnic groups and among individuals from low SES groups. Consumption of nuts, particularly peanuts given their general affordability, may be considered a cost-effective measure to improve cardiovascular health.

> Nuts are rich in nutrients, such as unsaturated fatty acids, fiber, vitamins, phenolic antioxidants, arginine, and other phytochemicals.^{1,2} Cumulative epidemiologic evidence suggests that nut consumption may have beneficial effects with respect to coronary heart disease.³ Indeed, nuts have been found to be inversely associated with various cardiovascular disease (CVD) mediators, such as inflammation, oxidative stress, and endothelial dysfunction, as reviewed by Kris-Etherton et al¹ and Casas-Agustench et al.⁴ Nut consumption was also reported to be associated with a reduced risk of hypertension⁵ and diabetes mellitus.⁶ Although classified as legumes, peanuts have nutrients that are similar to those of many tree nuts and were included as nuts in these and many other epidemiologic studies.

A recent meta-analysis³ of 11 studies of total mortality found that nut consumption was inversely associated with total mortality, but no information was provided for cause-specific mortality. A recent report⁷ from an analysis of 76 464 women in the Nurses' Health Study (NHS) and 42 498 men in the Health Professionals Follow-up Study (HPFS) found that nut consumption was inversely associated with all-cause, cancer-specific, and heart disease– specific mortality. Another report⁸ from a secondary analysis of a randomized clinical trial, Prevencion Con Dieta Mediterranea (PREDIMED), which included 7447 men and women aged 55 to 80 years in Spain, also found that baseline nut consumption was significantly associated with reduced total mortality, an association that was particularly pronounced among people consuming a Mediterranean diet with a nuts intervention arm. These 2

studies, however, were mainly conducted among either well-educated health professionals⁷ and/or populations of European ancestry.^{7,8} This raises a concern as to whether the findings of these studies can be generalized to individuals of other racial/ethnic backgrounds or to Americans of low socioeconomic status (SES), for whom peanuts are the primary nut consumed.

To address this question, we examined the association between nut/peanut consumption and total and cause-specific mortality in 71 764 participants of the Southern Community Cohort Study (SCCS), two-thirds of whom are US residents of African descent and the vast majority of whom have a low income, and 134 265 Chinese participants in the Shanghai Men's Health Study (SMHS) and the Shanghai Women's Health Study (SWHS).

Methods

Study Population

Participants in the SCCS, SWHS, and SMHS provided written informed consent, and the institutional review boards of all participating institutions approved the study protocols. Participants in the SCCS received financial compensation; those in the Shanghai studies did not.

The SCCS is a prospective cohort study conducted in 12 southern US states. It has enrolled more than 85 000 participants aged 40 to 79 years, primarily from low-income communities. Individuals receiving treatment for cancer were excluded at recruitment (March 25, 2002, through September 24, 2009).⁹ The SMHS and SWHS are population-based cohort studies conducted in 8 communities of urban Shanghai, China (January 1, 2002, through September 5, 2006, and December 28, 1996, through May 23, 2000, respectively). Their designs and methods have been described elsewhere.^{10,11} Briefly, between 2002 and 2006, a total of 61 480 men aged 40 to 74 years were recruited for the SMHS, and between 1996 and 2000, a total of 74 741 women aged 40 to 70 years were recruited for the SWHS. Individuals with a history of cancer were excluded from the SMHS.

Dietary Assessment

Dietary assessment in the SCCS used a semiquantitative food frequency questionnaire (FFQ), which was developed based on 24-hour dietary recall data from the US National Health and Nutrition Examination Surveys (NHANES III, NHANES 1999-2000, NHANES

2001-2002, and NHANES 2003-2004) and the Continuing Survey of Food Intakes¹² and included 89 food items covering the main sources of energy and nutrient intakes for African Americans and non–African Americans in the South. Study participants were asked about the frequency of consumption of 13 food groups, including "peanuts and other nuts" and peanut butter, in 9 categories (never, rarely, 1 time/mo, 2-3 times/mo, 1 time/wk, 2-3 times/wk, 4-6 times/wk, 1 time/d, and 2-3 times/d). We used portion-size information from the NHANES and Continuing Survey of Food Intakes, restricted to individuals who lived in the South census region, were aged 30 to 84 years, and self-reported as non-Hispanic blacks or whites, to estimate intake amount of each food item. Intake of total energy and 18 nutrients was derived by summing the product of the number of servings per day for each food with the estimated nutrient content of that food for all foods included in the FFQ.¹³ Nut consumption patterns among southerners reported in the NHANES and Continuing Survey of Food Intakes indicated that peanuts account for approximately 50% of the nuts consumed in this region.14 In the present analysis, we evaluated nut intake and peanut butter intake separately and in combination so that our results could be compared directly with those in previous reports on the same topic.

The SMHS/SWHS used nearly identical validated FFQs to collect information on food intake, including peanut consumption. Because tree nut consumption was very low in the SWHS/SMHS, we collected information only on peanut consumption. The SMHS/SWHS FFQs contain 84 to 87 food items and food groups commonly consumed in urban Shanghai. Study participants were asked how frequently (in 5 categories: daily, weekly, monthly, yearly, or never) they consumed the food or food group, followed by a question on the amount of food consumed in liangs $(1 \text{ Jiang} = 50 \text{ g})$ per unit of time during the previous 12 months. Daily nutrient intakes were then calculated from the FFQ using the nutrient content of each food based on the China Food Composition Tables.¹⁵

The reproducibility and validity of the SCCS FFQ were evaluated in 275 individuals with 3 day, 24-hour dietary recall during a 3- to 5-month period. The correlation between the FFQ and 24-hour dietary recall after adjusting attenuation factors and total energy intake varied from 0.59 to 0.83 for macronutrients and 0.43 to 0.81 for micronutrients. The reproducibility and validity of the FFQs in the SMHS/SWHS were determined using monthly (SMHS; $n =$ 12) or biweekly (SWHS; n = 24) 24-hour dietary recall evaluation over a 1-year period, which covered the same period as the $FFOs.16,17$ The unadjusted correlation coefficients were 0.38 to 0.63 for macronutrients, 0.33 to 0.58 for micronutrients, and 0.35 to 0.72 for major food groups in the SMHS¹⁶ and 0.59 to 0.66 for macronutrients, 0.41 to 0.59 for micronutrients, and 0.41 to 0.66 for major food groups in the SWHS.¹⁷

Cohort Follow-up and Outcome Ascertainment

In the SCCS, vital status is ascertained using a linkage approach via the National Death Index and Social Security Administration mortality files.⁹ In the SMHS/SWHS, study participants were followed up by annual record linkage with the Shanghai Vital Statistics Registry and in-person surveys every 2 to 3 years. All possible matches from the linkages are checked manually and verified by home visits. Death certificate data from the Shanghai Vital Statistics Unit were used to identify the primary cause of death. Follow-up for survival

status in the SMHS/SWHS was nearly 100% because of the extremely low out-migration rate in Shanghai.10,11

We used the *International Statistical Classification of Diseases, Tenth Revision* (*ICD-10*) 18 in the SCSS and the *International Classification of Diseases, Ninth Revision* (*ICD-9*) ¹⁹ in the SMHS and SWHS to code and classify causes of death into major groups, including cancer (*ICD-10* codes C00-C97 and D00-D48; *ICD-9* codes 140-208), CVD (*ICD-10* codes I00-I99; *ICD-9* codes 390-459), and diabetes mellitus (*ICD-10* codes E10-E14; *ICD-9* code 250). Deaths due to CVD were further classified into the following 4 subgroups: ischemic heart disease (*ICD-10* codes I60-I69; *ICD-9* codes 410-414), ischemic stroke (*ICD-10* codes I63-I64; *ICD-9* codes 433-435), hemorrhagic stroke (*ICD-10* codes I61-I62; *ICD-9* codes 430-431), and other CVD (*ICD-10* codes I00-I10, I12, I14-I19, I25-I59, and I68-I99; *ICD-9* codes 390-409, 415-429, and 436-459).

Statistical Analysis

For the SCCS, 77 975 participants with FFQ data were considered for the present analysis. We excluded individuals who reported a race/ethnicity group other than black (ie, American of African descent) or white (ie, American of European descent) ($n = 3475$) because of low statistical power for estimating risk for these minority groups. We also excluded participants with extreme total energy intake (ie, outside the range of 600-6500 kcal/d; 1777 participants), those who died or were lost to follow-up within the first year of study enrollment (761 participants), and those with no information on nut intake (198 participants). The final sample size for the SCCS analysis was 71 764 participants.

Likewise, we excluded SMHS/SWHS participants from the analysis who reported extreme total energy intake (ie, outside the range of 500-4000 kcal/d; 91 participants in the SMHS and 52 in the SWHS), who were diagnosed as having cancer before the baseline interview (1350 in the SWHS), and who died or were lost to follow-up within the first year (178 in the SMHS and 145 in the SWHS). The final sample size for the SMHS/SWHS analysis was 134 265 participants (61 123 men and 73 142 women). No SWHS/SMHS participants had missing information on nut intake.

Baseline nut/peanut consumption was categorized based on quintile distributions for the combined SMHS/SWHS cohorts and separately for the SCCS. We used Cox proportional hazards regression models to determine the association of nut intake with total and causespecific mortality, using the lowest quintile as the reference group. The follow-up time in all cohorts was calculated beginning 1 year after the date of study enrollment (ie, excluding the first year of cohort observation) and ending at the date of death, loss to follow-up, or December 31, 2011, whichever came first.

In the analysis of SCCS data, the following covariates were included in the final models: age at baseline (40-49, 50-59, 60-69, and 70-79 years), educational level (high school, high school/vocational school, some college or completed college, and more than college), income (low, lower-middle, upper-middle, and high), occupation (professional, clerical, and manual laborer/no formal job), regular use of vitamin supplements (yes/no), smoking packyears (0 to <13, 13 to <22, 22 to <32, and 32 pack-years), alcohol consumption (tertiles),

body mass index (BMI) (underweight, normal, overweight, obese, and morbidly obese), Charlson Comorbidity Index, 20 physical activity in metabolic equivalent tertiles, metabolic conditions, quintiles scale of total energy, and red meat, chicken, seafood, vegetable, and fruit intakes. A similar set of covariates was included in the final adjusted models for the SMHS/SWHS cohorts, with these exceptions: alcohol consumption (ever/never) was adjusted in the SWHS and the combined SWHS/SMHS because of the low alcohol consumption rate in the SWHS; chicken/duck consumption was adjusted in the SWHS/ SMHS because this intake was collected as a group food in the SMHS, and tea drinking was adjusted but vitamin supplementation was not adjusted in both Shanghai cohorts because tea drinking met but vitamin supplementation did not meet the confounding criteria. Metabolic condition was defined as a study participant having self-reported 1 or more of the following conditions: history of hypertension or heart disease, diabetes mellitus, BMI of 30 or higher (calculated as weight in kilograms divided by height in meters squared), unspecified dyslipidemia (SMHS and SWHS only), or hypercholesterolemia (SCCS only).

The proportional hazards assumption was evaluated using Schoenfeld residual plots, and no evidence of violation of assumption was found. Nonlinear associations between nut consumption and total and cause-specific mortality were evaluated using cubic spline analyses. We further performed stratified analysis by race, sex, ever consumption of alcohol, BMI, and presence of a metabolic condition. We performed sensitivity analyses by excluding all participants with a follow-up time of 2 years or less or who had a history of hypertension, diabetes mellitus, or ischemic heart disease. All statistical analyses were conducted using SAS, version 9.3 (SAS Institute Inc). All tests were 2-sided, and *P* < .05 was considered statistically significant. To test for a linear trend across quintiles of nut/ peanut intake, a continuous variable was created with the values of 0, 1, 2, 3, and 4 for the 5 quintiles.

Results

In the SCCS, there were 6256 deaths (men, 3332; women, 2924) during a median follow-up time of 5.4 years. In the SMHS and SWHS, there were 8144 deaths (SMHS, 3387; median follow-up, 6.5 years, and SWHS, 4757; median follow-up, 12.2 years).

There was no significant difference in age between male and female participants in the SCCS, whereas Shanghai men were approximately 3 years older than women at the baseline survey (mean, 55.3 vs 52.5 years; $P < .05$). In the SCCS, two-thirds of the participants were self-identified as black, and most were classified as having a low income. More than half of the women in the SCCS were ever smokers compared with only 2.8% in the SWHS. In addition, although 33.7% of the Shanghai men reported drinking alcohol, this rate was only 2.2% for women. The SCCS population had a higher prevalence of metabolic conditions than did the combined SMHS/SWHS population (76.8% vs 33.2%). Men in both the US and Chinese cohorts consumed more peanuts than did women (Table 1). Several sociodemographic characteristics differed across quintiles of nut/peanut intake in the 3 cohorts (eTables 1A and B and eTable 2 in the Supplement); these factors were adjusted for in subsequent analyses.

Nut/peanut consumption was inversely associated with the risk of total mortality across all study groups (Table 2). In the SCCS, a reduced risk of total mortality of 21% was observed for individuals in the highest compared with the lowest quintiles of peanut consumption. Despite having a similar association pattern, the separate analysis of nuts and peanut butter intake did not reach statistical significance. Therefore, subsequent analyses in the SCCS were focused on combined nut and peanut butter intake. No apparent difference between blacks and whites was observed in the association of nut intake with total mortality. In the Shanghai cohorts, the corresponding risk reduction associated with high nut intake was 17% in the combined analysis (hazard ratio [HR], 0.83; 95% CI, 0.77-0.88), with identical data for men and women (17% risk reduction; HR, 0.83; 95% CI, 0.75-0.91).

No apparent association between nut/peanut intake and risk of death due to cancer or diabetes was observed in Americans of European descent or in the Asian populations studied (Table 3). However, an inverse association of nut intake with CVD mortality was seen in all 3 ethnic groups. When specific types of CVD were examined, a significant inverse association was consistently seen for ischemic heart disease in all ethnic groups (HR, 0.62; 95% CI, 0.45-0.85 in blacks; HR, 0.60; 95% CI, 0.39-0.92 in whites; and HR, 0.70; 95% CI, 0.54-0.89 in Asians for the highest vs lowest quintile of nut intake). The associations for ischemic stroke (HR, 0.77; 95% CI, 0.60-1.00 for the highest vs lowest quintile of nut intake) and hemorrhagic stroke (HR, 0.77; 95% CI, 0.60-0.99 for the highest vs lowest quintile of nut intake) were significant only in Asians. The results were similar between men and women in the stratified analyses for each ethnic population. In the second and third quintiles of nut consumption in the SWHS, nut intake was inversely associated with diabetes mortality. However, a null association was observed for the fourth and fifth quintiles (eTable 3 in the Supplement).

In stratified analyses, the associations between nut/peanut consumption and total mortality were similar for participants with or without metabolic conditions, although in the SCCS, the association reached statistical significance only among participants with a metabolic condition. Nut/peanut consumption was also inversely associated with deaths due to CVD in similar patterns among participants with a metabolic condition (Table 4). Sensitivity analyses excluding participants with a follow-up time of 2 years or less and participants with a history of hypertension, diabetes, or ischemic heart disease showed similar patterns to major findings (eTables 4-7 in the Supplement).

Discussion

In this analysis of 3 large population-based cohort studies involving 71 764 low-income black and white men and women living in the southeastern United States and 134 265 Chinese men and women living in Shanghai, China, we found consistent evidence that high nut/peanut consumption was associated with a reduced risk of total mortality and CVD mortality. This inverse association was observed among both men and women and across each racial/ethnic group and was independent of metabolic conditions, smoking, alcohol consumption, and BMI. We observed no significant associations between nut/peanut consumption and risk of death due to cancer and diabetes mellitus.

To our knowledge, this is the first study that has examined the association between nut/ peanut consumption and the risk of total and cause-specific mortality in Americans of African descent or in Asians, although a recent meta-analysis³ and 2 original studies^{7, 8} evaluated this association with total mortality in populations of European descent. We found that the highest quartile of nut/peanut consumption vs the lowest nut quintile intake was associated with a 21% and 17% reduction in mortality in the SCCS and SWHS/SMHS, respectively; these findings are consistent with those from the meta-analysis,³ NHS/HPFS,⁷ and PREDIMED trial⁸ that showed a 15% to 39% reduced risk of total mortality associated with nut consumption.³

Our finding of an inverse association between nut/peanut consumption and deaths due to CVD is also consistent with previous reports.^{7,8} Hence, despite large differences in the populations under study (ie, low-SES white and black, as well as Chinese individuals in our study vs predominantly white and high-SES populations in the NHS/HPFS⁷ or low-SES and high-risk population in the PREDIMED trial^{8,21}) and in peanut/nut intake assessments (ie, semiquantitative measurement in our study and in the PREDIMED trial⁸ vs frequency measurement in the NHS/HPFS⁷), the findings from all of these studies with respect to total mortality and CVD mortality are remarkably similar.

Noteworthy in both the prior report³ and in our study is the general flatness of the doseresponse trends; the major difference occurred between individuals with no or low peanut intake and those with some peanut intake, with only minimal decreases in mortality with increasing nut consumption thereafter. The lack of a clear dose-response pattern is particularly evident in the SMHS/SWHS population, which could be the result of generally low intake levels and small variations in this population (median intake, 10.1 g/wk in men and 5.0 g/wk in women). In addition, although we have carefully evaluated and adjusted for a wide range of sociodemographic characteristics and lifestyle factors, we cannot completely rule out a residual confounding effect.

Although we observed a consistent association between nut/peanut intake and deaths due to CVD, particularly ischemic heart disease, we found no significant associations for the risk of death due to cancer or diabetes, particularly in the Americans of European descent and Asian populations. Two recent meta-analyses^{3,6} also found no association between nut consumption and incidence of stroke or type 2 diabetes mellitus. Although the methods for measuring the outcome in our study (cause-specific mortality) vs the other studies (specific disease incidence) 3 were different, the similar findings support an overall null association for diabetes. The null association for cancer mortality, on the other hand, is in contrast with the finding of the NHS/HPFS, 7 which showed reductions in cancer mortality risk of 7% to 11% associated with different frequencies of peanut consumption vs nonconsumption. This inconsistency may be the result of differences in the distribution of the major types of cancer death in our study populations. Smoking-related and upper gastrointestinal cancers accountedfor80% of cancer deaths in the SMHS/SWHS and 60% in the SCCS, whereas in the NHS/HPFS, which did not include information on the major types of cancer deaths, it can be postulated that many cancer deaths were hormonal and metabolic associated. In addition, the shorter follow-up time in our study (medians: SCCS, 5.4 years; SMHS, 6.5 years; and

SWHS, 12.2 years vs NHS, 30 years and HPFS, 24 years) may also have contributed to the discrepancy.

The most noticeable strengths of our study are the inclusion of multiple ethnicities (ie, African, European, and Asian ancestry), as well as a large population of individuals from a low SES background who have a high prevalence of obesity and obesity-related metabolic conditions and thus a high risk of mortality. Because of the standardized dietary measurements, nut/peanut consumption in our study could be quantified (grams per day) rather than using frequency as reported in previous studies.^{7,8,22-26} Our study is also among very few to have investigated the association of nut/peanut consumption with total and cause-specific mortality by stroke subtypes, which are known to have different mechanisms driving their etiology and risk factor profiles, and by several other causes of death.^{27,28} Finally, because very few women (2.8%) in our Asian population were smokers, we were able to evaluate associations between peanuts and total and cause-specific mortality without the confounding effect of smoking in that population.

Our study also has some limitations. The short follow-up time, particularly for the SMHS and SCCS cohorts, may have contributed to the low statistical power encountered in some subgroup analyses. Another concern is that preclinical conditions at baseline might have influenced baseline dietary intake. However, we excluded the first-year follow-up data for all study participants. Additional sensitivity analyses that excluded the first 2 years of follow-up observation and participants with comorbidities (ie, hypertension, diabetes, or ischemic heart disease) at baseline did not materially change the results. The other limitation is the lack of information on tree nut consumption in the SMHS/SWHS, although the intake is infrequent in this population.

The unique characteristics of our 3 cohorts complement the participants of previous studies, especially the NHS/HPFS. In particular, the low-SES background and high prevalence of metabolic conditions in the SCCS allowed us to evaluate the influence of nut/peanut consumption on total and cause-specific mortality in a high-risk population (ie, >76% had metabolic conditions, >75% were either overweight or obese/morbidly obese, 55%had hypertension,21%had diabetes, and 34% had high cholesterol). Together, our study provides strong evidence that the association of nut/peanut consumption with mortality does not vary by ethnicity or SES.

Conclusions

We found that high nut/peanut consumption was associated with a reduced risk of total mortality and death due to CVD compared with consumption of few or no nuts/peanuts among low-income men and women of either African or European descent living in the southeastern United States and among Chinese men and women living in Shanghai, China. We also found that this association was not modified by the presence of metabolic conditions. Our findings, and their similarity to those previously observed in other race and SES groups, raise the possibility that a diet including peanuts may offer some CVD protection. We cannot, however, make etiologic inferences from these observational data, especially with the lack of a clear dose-response trend in many of the analyses.

Nevertheless, the findings highlight a substantive public health impact of nut/peanut consumption in lowering CVD mortality given the affordability of peanuts to individuals from all SES backgrounds.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding/Support: This work was supported by grants from the US National Cancer Institute (R37 CA070867 (principal investigator: Dr Zheng), R01 CA082729 and UM1 CA173640 (principal investigator: Dr Shu), and R01 CA092447 (principal investigators: Drs Blot and Zheng).

Role of the Funder/Sponsor: The funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

References

- 1. Kris-Etherton PM, Hu FB, Ros E, Sabaté J. The role of tree nuts and peanuts in the prevention of coronary heart disease: multiple potential mechanisms. J Nutr. 2008; 138(9):1746S–1751S. [PubMed: 18716180]
- 2. González CA, Salas-Salvadó J. The potential of nuts in the prevention of cancer. Br J Nutr. 2006; 96(suppl 2):S87–S94. [PubMed: 17125538]
- 3. Luo C, Zhang Y, Ding Y, et al. Nut consumption and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: a systematic review and meta-analysis. Am J Clin Nutr. 2014; 100(1):256– 269. [PubMed: 24847854]
- 4. Casas-Agustench P, Bulló M, Salas-Salvadó J. Nuts, inflammation and insulin resistance. Asia Pac J Clin Nutr. 2010; 19(1):124–130. [PubMed: 20199997]
- 5. Djoussé L, Rudich T, Gaziano JM. Nut consumption and risk of hypertension in US male physicians. Clin Nutr. 2009; 28(1):10–14. [PubMed: 18834651]
- 6. Afshin A, Micha R, Khatibzadeh S, Mozaffarian D. Consumption of nuts and legumes and risk of incident ischemic heart disease, stroke, and diabetes: a systematic review and meta-analysis. Am J Clin Nutr. 2014; 100(1):278–288. [PubMed: 24898241]
- 7. Bao Y, Han J, Hu FB, et al. Association of nut consumption with total and cause-specific mortality. N Engl J Med. 2013; 369(21):2001–2011. [PubMed: 24256379]
- 8. Guasch-Ferré M, Bulló M, Martínez-González MA, et al. PREDIMED study group. Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. BMC Med. 2013; 11:164. [PubMed: 23866098]
- 9. Signorello LB, Hargreaves MK, Blot WJ. The Southern Community Cohort Study: investigating health disparities. J Health Care Poor Underserved. 2010; 21(1 suppl):26–37. [PubMed: 20173283]
- 10. Cai H, Zheng W, Xiang YB, et al. Dietary patterns and their correlates among middle-aged and elderly Chinese men: a report from the Shanghai Men's Health Study. Br J Nutr. 2007; 98(5): 1006–1013. [PubMed: 17524168]
- 11. Zheng W, Chow WH, Yang G, et al. The Shanghai Women's Health Study: rationale, study design, and baseline characteristics. Am J Epidemiol. 2005; 162(11):1123–1131. [PubMed: 16236996]
- 12. Signorello LB, Munro HM, Buchowski MS, et al. Estimating nutrient intake from a food frequency questionnaire: incorporating the elements of race and geographic region. Am J Epidemiol. 2009; 170(1):104–111. [PubMed: 19451177]
- 13. Schlundt DG, Buchowski MS, Hargreaves MK, Hankin JH, Signorello LB, Blot WJ. Separate estimates of portion size were not essential for energy and nutrient estimation: results from the Southern Community Cohort food-frequency questionnaire pilot study. Public Health Nutr. 2007; 10(3):245–251. [PubMed: 17288621]

- 14. US Centers for Disease Control and Prevention. [Accessed September 25, 2014] National Health and Nutrition Examination Survey: nut consumption of US adults, 2009-2010. Dec 17. 2010 [http://](http://www.cdc.gov/nchs/pressroom/calendar/2014_schedule.htm#Subject) www.cdc.gov/nchs/pressroom/calendar/2014_schedule.htm#Subject
- 15. Yang, Y.; Wang, G.; Pan, X., editors. China Food Composition Tables Beijing. China: Peking University Medical Press; 2002.
- 16. Villegas R, Yang G, Liu D, et al. Validity and reproducibility of the Food-Frequency Questionnaire used in the Shanghai Men's Health Study. Br J Nutr. 2007; 97(5):993–1000. [PubMed: 17381986]
- 17. Shu XO, Yang G, Jin F, et al. Validity and reproducibility of the Food Frequency Questionnaire used in the Shanghai Women's Health Study. Eur J Clin Nutr. 2004; 58(1):17–23. [PubMed: 14679362]
- 18. World Health Organization. International Statistical Classification of Diseases, Tenth Revision. Geneva, Switzerland: World Health Organization; 1992.
- 19. World Health Organization. International Classification of Diseases, Ninth Revision. Geneva, Switzerland: World Health Organization; 1977.
- 20. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40(5):373– 383. [PubMed: 3558716]
- 21. Estruch R, Ros E, Salas-Salvadó J, et al. PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013; 368(14):1279–1290. [PubMed: 23432189]
- 22. van den Brandt PA. The impact of a Mediterranean diet and healthy lifestyle on premature mortality in men and women. Am J Clin Nutr. 2011; 94(3):913–920. [PubMed: 21795445]
- 23. Baer HJ, Glynn RJ, Hu FB, et al. Risk factors for mortality in the Nurses' Health Study: a competing risks analysis. Am J Epidemiol. 2011; 173(3):319–329. [PubMed: 21135028]
- 24. Ellsworth JL, Kushi LH, Folsom AR. Frequent nut intake and risk of death from coronary heart disease and all causes in postmenopausal women: the Iowa Women's Health Study. Nutr Metab Cardiovasc Dis. 2001; 11(6):372–377. [PubMed: 12055701]
- 25. Fraser GE, Sumbureru D, Pribis P, Neil RL, Frankson MA. Association among health habits, risk factors, and all-cause mortality in a black California population. Epidemiology. 1997; 8(2):168– 174. [PubMed: 9229209]
- 26. Fraser GE, Shavlik DJ. Risk factors for all-cause and coronary heart disease mortality in the oldestold: the Adventist Health Study. Arch Intern Med. 1997; 157(19):2249–2258. [PubMed: 9343002]
- 27. Leppälä JM, Virtamo J, Fogelholm R, Albanes D, Heinonen OP. Different risk factors for different stroke subtypes: association of blood pressure, cholesterol, and antioxidants. Stroke. 1999; 30(12): 2535–2540. [PubMed: 10582974]
- 28. Warlow CP. Epidemiology of stroke. Lancet. 1998; 352(suppl 3):I1–I4.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 1

Sociodemographic Characteristics of Study Participants

Sociodemographic Characteristics of Study Participants

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

 \mathbf{r}

 \mathbf{r}

JAMA Intern Med. Author manuscript; available in PMC 2015 June 19.

 $\overline{1}$

 \mathbf{r}

 \mathbf{r}

 \mathbf{r}

ï

 \mathbf{r}

Author Manuscript

 \mathbf{I}

 \mathbf{r}

 \mathbf{r}

 \mathbf{r}

ï

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

"Educational levels were as follows: SCCS: high school or less, high school/vocational school, some or completed college; and beyond college. SMHS/SWHS: elementary or less, middle school, high *a*Educational levels were as follows: SCCS: high school or less, high school/vocational school, some or completed college; and beyond college. SMHS/SWHS: elementary or less, middle school, high school or less, and some or completed college. school or less, and some or completed college.

*b*Income levels were as follows: SCCS: low (<\$15 000/y per household), lower-middle (\$15 000-\$24 999/y per household), middle (\$25 000-\$49 999/y per household), upper-middle (\$50 000-\$99 999/y per household), and high (≥\$100 000/y per household). SMHS: low (<500 yuan/mo per capita), lower-middle (500-999 yuan/mo per capita), upper-middle (1000-1999 yuan/mo per capita), and high (>2000 yuan/mo per capita). SWHS: low (<10 000 yuan/y per household), lower-middle (10 000-19 999 yuan/y per household), upper-middle (20 000-29 999 yuan/y per household), and high (≥30 000 yuan/y per b ncome levels were as follows: SCCS: low (<\$15 000/y per household), lower-middle (\$15 000-\$24 999/y per household), middle (\$25 000-\$49 999/y per household), upper-middle (\$50 000-\$99 999/y
per household), and high (

Author Manuscript

Charlson Comorbidity Index was calculated based on number of existing chronic diseases. *c*Charlson Comorbidity Index was calculated based on number of existing chronic diseases.

 $d_{\rm Self-reported.}$

Prevalence of disease conditions. *e*Prevalence of disease conditions.

Chicken intake in the SCCS and chicken/duck intake in the SMHS/SWHS. *f*Chicken intake in the SCCS and chicken/duck intake in the SMHS/SWHS.

⁸Nut/peanut intake quintile (Q) out points (grams/day) were as follows: SMHS/SWHS data: Q1 (<0.14), Q2 (0.14 to <0.72), Q3 (0.72 to <1.45), Q4 (1.45 to <2.54), and Q5 (2.54). SCCS data: Total nuts
and peanut butter: Q1 $\frac{g_N}{g_N}$ Nut/peanut intake quintile (Q) cut points (grams/day) were as follows: SMHS/SWHS data: Q1 (<0.14), Q2 (0.14 to <0.72), Q3 (0.72 to <1.45), Q4 (1.45 to <2.54), and Q5 (2.54). SCCS data: Total nuts and peanut butter: Q1 (4.14), Q2 (0.95), Q3 (0.95to <0.96), Q3 (20.36), Q3 (3.08 to <0.80), Q2 (2.30), Q3 (3.08 to <0.86), Q3 (3.08 to <0.869), Q3 (3.08 to <0.869), Q4 (4.14), Q4 (4.14), Q4 (4.14), Q4 (4.14), Q4 (4.14), Q4 (8.63). Peanut butter only: Q1 (<0.19), Q2 (0.19 to <0.59), Q3 (0.59 to <2.18), Q4 (2.18 to <6.32), and Q5 (6.32). (≥8.63). Peanut butter only: Q1 (<0.19), Q2 (0.19 to <0.59), Q3 (0.59), Q4 (2.18 to <6.32), and Q5 (≥6.32).

*h*One or more of the following conditions: history of hypertension or heart disease, diabetes mellitus, BMI of 30 or higher, unspecified dyslipidemia (SMHS and SWHS only), or hypercholesterolemia hone or more of the following conditions: history of hypertension or heart disease, diabetes mellitus, BMI of 30 or higher, unspecified dyslipidemia (SMHS and SWHS only), or hypercholesterolemia (SCCS only). (SCCS only). Author Manuscript

Author Manuscript

Table 2
Association of Nut and Peanut Butter Intake With Total Mortality in the SCCS and Peanut Intake With Total Mortality in the SMHS/ **Association of Nut and Peanut Butter Intake With Total Mortality in the SCCS and Peanut Intake With Total Mortality in the SMHS/ SWHS** *a*

Abbreviations: HR, hazard ratio; SCCS, Southern Community Cohort Study; SMHS, Shanghai Men's Health Study; SWHS, Shanghai Women's Health Study.

JAMA Intern Med. Author manuscript; available in PMC 2015 June 19.

butter: Q1 (<0.95 to <3.08), Q2 (0.95 to <3.08 Q5 (2.08), Q3 (0.30 to <18.45), and Q5 (1.345), and Q5 (0.36 to <0.30), Q3 (0.308 to <1.30), Q3 (0.308 to <0.30), Q3 (0.30, Q3 (0.30, Q3 (0.30), Q3 (0.30), Q4 (4.14to <8.63), butter: Q1 (<0.95), Q2 (0.95 to <3.08),Q3 (3.08 to <7.30), Q4 (7.30 to <18.45), and Q5 (18.45). Nuts only: Q1 (<0.36), Q2 (0.56 to <4.814), Q4 (4.14to <8.63), and Q5 (8.63). Peanut 0 Nut/peanut intake quintile (Q) cut-points (grams/day): SMHS/SWHS data: Q1 (<0.14), Q2 (0.14 to <0.72), Q3 (0.72 to <1.45), Q4 (1.45 to <2.54), and Q5 (2.54). SCCS data: Total nuts and peanut α ^NNut/peanut intake quintile (Q) cut-points (grams/day): SMHS/SWHS data: Q1 (<0.14), Q2 (0.14 to <0.72), Q3 (0.72 to <1.45), Q4 (1.45 to <2.54), and Q5 (2.54). SCCS data: Total nuts and peanut butter only: Q1 (<0.19), Q2 (0.19 to <0.59), Q3 (0.59 to <2.18), Q4 (2.18 to <6.32), and Q5 (6.32). butter only: Q1 (<0.19), Q2 (0.19), Q2 (0.59), Q3 (0.59), Q3 (0.59), Q4 (2.18 to <6.32), and Q5 (ρ 6.32). b Nodel adjusted for age, sex, race, education, occupation, household income, marial status, smoking pack-years, alcohol consumption, body mass index (BMI; calculated as weight in kilograms divided by *b*Model adjusted for age, sex, race, education, occupation, household income, marital status, smoking pack-years, alcohol consumption, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), physical activity, vitamin supplement use, Charlson Comorbidity Index, metabolic conditions (1 of the following conditions: history of hypertension or heart disease, diabetes height in meters squared), physical activity, vitamin supplement use, Charlson Comorbidity Index, metabolic conditions (1 of the following conditions: history of hypertension or heart disease, diabetes mellitus, BMI of 30 or higher, unspecified dyslipidemia [SMHS and SWHS only], or hypercholesterolemia [SCCS only]), total energy intake, red meat intake, chicken and duck intake, seafood intake, mellitus, BMI of 30 or higher, unspecified dyslipidemia [SMHS and SWHS only], or hypercholesterolemia [SCCS only]), total energy intake, red meat intake, chicken and duck intake, seafood intake, vegetable intake, and fruit intake. vegetable intake, and fruit intake.

 $\,^{\rm c}$ Model adjusted for all variables mentioned in footnote b except for sex. *c*Model adjusted for all variables mentioned in footnote *b* except for sex.

Table 3

Association of Nut/Peanut Intake With Cause-Specific Mortality by Race/Ethnicity Association of Nut/Peanut Intake With Cause-Specific Mortality by Race/Ethnicity^a

JAMA Intern Med. Author manuscript; available in PMC 2015 June 19.

l.

 \mathbf{r}

Author Manuscript

Author Manuscript

Descent (SCCS) Descent ($SCCS$)^{b}

Descent (SCCS)^b

height in meters squared), physical activity, vitamin supplement use, Charlson Comorbidity Index, metabolic conditions (1 of the following conditions: history of hypertension or heart disease, diabetes height in meters squared), physical activity, vitamin supplement use, Charlson Comorbidity Index, metabolic conditions (1 of the following conditions: history of hypertension or heart disease, diabetes mellitus, BMI of 30 or higher, unspecified dyslipidemia [SMHS and SWHS only], or hypercholesterolemia [SCCS only]), total energy intake, red meat intake, chicken intake, seafood intake, vegetable mellitus, BMI of 30 or higher, unspecified dyslipidemia [SMHS and SWHS only], or hypercholesterolemia [SCCS only]), total energy intake, red meat intake, chicken intake, seafood intake, vegetable Model adjusted for age, sex, education, occupation, household income, marial status, smoking pack-years, alcohol consumption, body mass index (BMI; calculated as weight in kilograms divided by *b*Model adjusted for age, sex, education, occupation, household income, marital status, smoking pack-years, alcohol consumption, body mass index (BMI; calculated as weight in kilograms divided by intake, and fruit intake. intake, and fruit intake.

butter only: Q1 (<0.19), Q2 (0.19 to <0.59), Q3 (0.59), Q4 (2.18 to <6.32), and Q5 (ρ 6.32).

consumption, Charlson Comorbidity Index, metabolic conditions (10 fthe following conditions: history of hypertension or heart disease, diabetes mellitus, BMI of 30 or higher, unspecified dyslipidemia
[SMHS and SWHS only], consumption, Charlson Comorbidity Index, metabolic conditions (1 of the following conditions: history of hypertension or heart disease, diabetes mellitus, BMI of 30 or higher, unspecified dyslipidemia Model adjusted for age, sex, education, occupation, household income (SMHS) or income per capita (SWHS), smoking status, alcohol consumption (ever/never), BMI, physical activity, regular tea *c*Model adjusted for age, sex, education, occupation, household income (SMHS) or income per capita (SWHS), smoking status, alcohol consumption (ever/never), BMI, physical activity, regular tea [SMHS and SWHS only], or hypercholesterolemia [SCCS only]), total energy intake, red meat intake, chicken/duck intake, seafood intake, vegetable intake, and fruit intake.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Association of Nut/Peanut Intake With Total Mortality and Cause-Specific Mortality by Race/Ethnicity and Presence/Absence of Metabolic Conditions *a*

At Least 1
Metabolic Condition **Metabolic Condition**

JAMA Intern Med. Author manuscript; available in PMC 2015 June 19.

P value for interaction

d

Abbreviations: CVD, cardiovascular disease; HR, hazard ratio; SCCS, Southern Community Contort Study; Shanghai Men's Health Study; Study; Shanghai Women's Health Study; Study; Shanghai Women's Health Study. Abbreviations: CVD, cardiovascular disease; HR, hazard ratio; SCCS, Southern Community Cohort Study; Shanghai Men's Health Study; SWHS, Shanghai Women's Health Study, Shanghai Women's Health Study.

<18.45), and Q5 (18.45). Nuts only: Q1 (<0.36), Q2 (0.36 to <0.66), Q3 (0.66 to <4.14), Q4 (4.14 to <8.63), and Q5 (8.63). Peanut butter only: Q1 (<0.19), Q2 (0.19 to <0.59), Q3 (0.59 to <2.18), Q4 (2.18 to <6.32), and Q5 $(8.45), \, (0.36), (0$ were considered metabolic conditions: history of hypertension or heart disease, diabetes mellitus, BM of 30 or higher (calculated as weight in kilograms divided by height in meters squared), unspecified dyslipidemia (SMHS were considered metabolic conditions: history of hypertension or heart disease, diabetes mellitus, BMI of 30 or higher (calculated as weight in kilograms divided by height in meters squared), unspecified dyslipidemia (SMHS 0 Nut/peanut intake quintile (Q) cut-points (grams/day): SMHS/SWHS data: Q1 (<0.14), Q2 (0.14 to <0.72), Q3 (0.72 to <1.45), Q4 (1.45 to <2.54), and Q5 (2.54), SCCS data: Total nuts and peanut butter: Q1 (<0.95), Q2 6 Nut/peanut intake quintile (Q) cut-points (grams/day): SMHS/SWHS data: Q1 (<0.14), Q2 (0.14 to <0.14), Q2 (0.14 to <0.72), Q3 (0.72 to <1.45), Q4 (1.45 to <2.54), and Q5 (2.54). SCCS data: Total nuts and peanut butte only),

Author Manuscript

Author Manuscript

b Nodel adjusted for age, sex, education, occupation, household income, marital status, smoking pack-years, alcohol consumption, (BMI, physical activity, vitamin supplement use, Charlson Comorbidity Index, total energy int Model adjusted for age, sex, education, occupation, household income, marital status, smoking pack-years, alcohol consumption, (BMI, physical activity, vitamin supplement use, Charlson Comorbidity Index, total energy intak vegetable intake, and fruit intake. vegetable intake, and fruit intake. Model adjusted for age, sex, education, occupation, household income (SMHS) or income per capita (SWHS), smoking status, alcohol consumption (ever/never), BML, physical activity, regular tea consumption, Charlson Comorbidi Model adjusted for age, sex, education, occupation, household income (SMHS), or income per capita (SWHS), smoking status, alcohol consumption (ever/never), BMI, physical activity, regular tea consumption, Charlson Comorbid chicken/duck intake, seafood intake, vegetable intake, and fruit intake. chicken/duck intake, seafood intake, vegetable intake, and fruit intake.

d P interaction: between nut and peanut butter (SCCS) or peanut (SMHS/SWHS) consumption with metabolic conditions.