Nut consumption in relation to all-cause and cause-specific mortality: a meta-analysis 18 prospective studies

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Supplementary Table 1. Characteristics of included prospective studies on nut consumption and total and cause-specific mortality

Author, year (Country)	Study name, duration	Participants	Type of nut	Diet assessment	No. of death	RR (95% CI)	Nut intake	Statistical adjustment
Mann, 1997[1] (UK)	Oxford Vegetarian Study, 13.3 yr	10 802 M/F aged 16-79 yr	Nuts (not specified)	Self-reported FFQ	Total:392 CHD:64	0.99 (0.72-1.38) 0.87 (0.45-1.68)	≥5 vs.<1 ser/wk	Age, sex, smoking, and social class.
Fraser, 1997[2] (USA)	Adventists Health Study (non-Hispanic White), 12 yr	M/F aged ≥85 yr	Nuts (not specified)	Self-reported FFQ	Total:1387 CHD:364	0.75 (0.65-0.86) 0.55 (0.42-0.73)	≥5 vs.<1 ser/wk	Sex, smoking, physical activity, diabetes, and intakes of fruit, bread, donut, sweet dessert, beef, and fish.
Fraser, 1997[3] (USA)	Adventists Health Study (black), 9yr	1668 M/F aged≥25 yr	Nuts (except those used in recipes)	Self-reported FFQ	Total:153	0.60 (0.30-1.00)	≥5 vs.<1 ser/wk	Age, smoking and physical activity.
Yochum, 2000[4] (USA)	Iowa Women's Health Study, 9 yr	34 492 F aged 55-69 yr	Nuts and seeds	Self-reported FFQ	Stroke:215	0.73 (0.41-1.29)	>4 vs. 0 ser/mo	Age, BMI, smoking, physical activity, waist/hip ratio, BP, diabetes, estrogen use, education, marital status, and intakes of energy, alcohol, cholesterol, saturated fat, fish, vitamin C, carotenoids, dietary fiber, and whole grains.
Blomhoff, 2006[5] (USA)	Iowa Women's Health Study, 15 yr	31 778 F aged 55-69 yr	Nuts and peanut butter	Self-reported FFQ	Total:5451 CVD:1675 CHD:948	0.89 (0.81-0.99) 0.72 (0.60-0.88) 0.71 (0.55-0.91)	≥5 vs. 0 ser/wk	Age, education, physical activity, BMI, waist/hip ratio, estrogen use, multivitamin supplements, and intakes of alcohol, energy, whole or refined grain, red meat, fish, seafood, and fruit and vegetables.
Guasch-Ferré, 2013[6] (Spain)	PREDIMED Study, 4.8 yr	7216 M/F aged 55-80 yr	Nuts (peanuts, almonds, hazelnut, walnut, pine nut, pistachios, Brazil nut, macadamia and cashew)	Interview-based FFQ, validated	Total:323 CVD:81 CHD:15* Stroke:24* Cancer:130	0.61 (0.45-0.83) 0.45 (0.25-0.81) 0.20 (0.04-1.06)* 0.40 (0.12-1.37)* 0.60 (0.37-0.98)	>3 vs. 0 ser/wk	Age, sex, BMI, smoking, education, physical activity, intervention group, recruitment center, history of diabetes or hypercholesterolemia, antidiabetic medication use, antihypertensive medication use, statins use, Mediterranean diet adherence , and intakes of energy, alcohol, fruit, vegetables, red meat, eggs, and fish.
Bao, 2013[7] (USA)	Nurses' Health Study, 30 yr	76 464 F aged 30-55 yr	Nuts (peanuts and other nuts)	Self-reported FFQ, validated	Total:16200 CVD:3086 HD:2208 Stroke:878 Cancer:6535	0.84 (0.77-0.92) 0.82 (0.66-1.01) 0.72 (0.55-0.94) 1.05 (0.73-1.52) 0.94 (0.82-1.09)	≥5 vs. 0 ser/wk	Age, race, BMI, physical activity, smoking, physical examination, menopausal status, hormone use, multivitamin use, current aspirin use, family history of diabetes or MI or cancer, history of diabetes or hypertension or hypercholesterolemia, and intake of energy, alcohol, red and processed meat, fruit, and vegetables.
Bao, 2013[7] (USA)	Health Professionals Follow-up Study, 24 yr	42 498 M aged 40-75 yr	Nuts (peanuts and other nuts)	Self-reported FFQ, validated	Total:11229 CVD:3385 HD:2698 Stroke:687 Cancer:3758	0.82 (0.76-0.88) 0.73 (0.64-0.83) 0.71 (0.61-0.83) 0.78 (0.58-1.06) 0.86 (0.75-0.98)	≥5 vs. 0 ser/wk	Age, race, BMI, physical activity, smoking, physical examination, multivitamin use, current aspirin use, family history of diabetes or MI or cancer, history of diabetes or hypertension or hypercholesterolemia, and intake of energy, alcohol, red/processed meat, fruit, and vegetables,

Reference	Study	Participants	Exposure	Assessment	Cases	RR (95% CI)	Comparison	Adjustments
Fernandez-Montero, 2014[8] (Spain)	SUN Cohort Study, 5 yr	17 184 M/F	Nuts (peanuts, walnut, almonds, and hazelnut)	Self-reported FFQ, validated	Total:119 CVD:19* Cancer:51*	0.44 (0.23-0.86) 0.24 (0.04-1.54)* 0.86 (0.35-2.08)*	≥2 ser/wk vs. never/almost never	Age, sex, BMI, smoking, alcohol intake, physical activity, adherence to the Mediterranean diet, use of special diets, marital status, history of hypercholesterolemia or hypertension or CVD or diabetes or cancer, and length of TV watching,.
Sluik, 2014[9] (10 European countries)	EPIC Study, 9.9 yr	265 295 M/F aged 35-70 yr	Nuts and seeds	Self-reported FFQ, validated	Total:830 (diabetic) 12135 (non-diabetic)	0.94 (0.90-0.97) 0.99 (0.98-1.00)	Per 1 g/d	Age, sex, smoking, alcohol, physical activity study center, prevalence of HD, cancer or stroke, education, diabetes medication use (in diabetic individuals), and underlying dietary patterns.
Luu, 2015[10] (USA)	Southern Community Cohort Study, 5.4 yr	71 764 M/F aged 40-79 yr	Nuts and peanut butter (total and causes-specific death) / Nuts only (total death) / Peanut butter (total death)	Self-reported FFQ, validated	Total:6256 CVD:1309 (African) CVD:548 (European) IHD:501 (African) IHD:292 (European) IS:96 (African) IS:25 (European) HS:75 (African) HS:21(European) Cancer:1052 (African) Cancer:499 (European)	0.79 (0.73-0.86) 0.77 (0.63-0.92) 0.62 (0.46-0.84) 0.62 (0.45-0.85) 0.60 (0.39-0.92) 0.89 (0.45-1.74) 0.47 (0.12-1.76) 1.37 (0.67-2.80) 0.62 (0.12-3.26) 0.74 (0.60-0.92) 0.93 (0.68-1.29) /Nuts and peanut butter	≥18.45 vs.< 0.95 g/d	Age, sex, BMI, smoking, physical activity, race, education, occupation, income, marital status, vitamin supplement, Charlson Comorbidity Index, metabolic conditions (≥1 of the following conditions: history of hypertension or HD, diabetes mellitus, BMI of≥30, or hypercholesterolemia), and intakes of energy, alcohol, red meat, chicken and duck, seafood, fruit, vegetable.
Luu, 2015[10] (China)	Shanghai Men's Health Study, 6.5 yr	61 123 M aged 40-74 yr	Peanuts	Self-reported FFQ, validated	Total:3387 CVD:1117 IHD:306 IS:234 HS:245 Cancer:1492	0.83 (0.75-0.91) 0.78 (0.66-0.93) 0.80 (0.58-1.11) 0.79 (0.54-1.14) 0.80 (0.55-1.16) 0.96 (0.83-1.11)	≥2.54 vs.< 0.14 g/d	Age, BMI, smoking, physical activity, race, education, occupation, income, marital status, vitamin supplement, Charlson Comorbidity Index, metabolic conditions (≥1 of the following conditions: history of hypertension or HD, diabetes mellitus, BMI of≥30, unspecified dyslipidemia), and intakes of energy, alcohol, red meat, chicken and duck, seafood, fruit, and vegetable.
Luu, 2015[10] (China)	Shanghai Women's Health Study, 12.2 yr	73 142 F aged 40-70 yr	Peanuts	Self-reported FFQ, validated	Total:4757 CVD:1479 IHD:325 IS:354 HS:352 Cancer:2040	0.83 (0.75-0.91) 0.72(0.61-0.86) 0.58(0.39-0.87) 0.72(0.51-1.03) 0.77 (0.55-1.07) 0.97 (0.84-1.12)	≥2.54 vs.< 0.14 g/d	As above.
di Giuseppe, 2015[11] (Germany)	EPIC-Potsdam Study, 8.3 yr	10 904 M and 16 644 F with a mean age of 52.5 yr and 49.2 yr, respectively	Nuts (peanuts, walnut and Brazil nut)	Self-reported FFQ, validated	Stroke death: 36	0.31 (0.07-1.38)†	14.2 vs. 0 g/d	Age, sex, BMI, waist circumference, smoking, education, physical activity, hypertension, hyperlipidemia, diabetes, and intakes of energy, alcohol, red meat, whole-grain breads, fruit, vegetable, fish, cakes and cookies, confectionary, fried potatoes, and other beverages.

First author, year (country)	Study, follow-up	Participants	Exposure	Dietary assessment	Outcomes (no. of cases)	RR (95% CI)	Comparison	Adjustments
Hshieh, 2015[12] (USA)	Physicians' Health Study, 9.6 yr	20 742 M with a mean age of 66.6 yr	Nuts and peanut butter	Self-reported FFQ	Total:2732 CVD:760 CAD:405 Stroke:142 Cancer:868	0.76 (0.64-0.89) 0.74 (0.55-1.02) 0.85 (0.56-1.28) 0.87 (0.66-1.15) 0.64 (0.32-1.30)	≥5 ser/wk vs.<1 ser/ wk	Age, BMI, smoking, physical activity, prevalence of hypertension or diabetes, and intakes of energy, alcohol, saturated fat, fruit, vegetable, red meat, magnesium (total mortality), and dietary fiber (total mortality).
van den Brandt, 2015[13] (the Netherlands)	Case-cohort with the Netherlands Cohort Study, 10 yr	12 025 M/F aged 55-69 yr	Nuts and peanut butter / Peanuts / Tree nuts / Peanut butter	Self-reported FFQ, validated	Total: 8823 CVD: 2985 IHD: 1488 Stroke: 565 Cancer: 3917	0.77 (0.66-0.89) 0.83 (0.69-1.00) 0.83 (0.67-1.04) 0.76 (0.56-1.02) 0.79 (0.67-0.93) / Nuts and peanut butter	≥10 vs. 0 g/d	Age, sex, smoking, history of hypertension and diabetes, body height, BMI, physical activity, education, use of nutritional supplements, postmenopausal HRT (for women), and intakes of energy, alcohol, and vegetables and fruit.
Gopinath, 2015[14] (Australia)	Blue Mountains Eye Study, 15 yr	2893 M/F aged ≥49 yr	Nuts (not specified)	Self-reported FFQ	Total: 1044 CVD: 546 IHD: 430 Stroke: 430	0.93 (0.72-1.08) 0.90 (0.73-1.12) 0.95 (0.74-1.21) 0.88 (0.60-1.29)	4.90-100 vs. 0.00-0.50 g/d	Age, sex, BMI, smoking, alcohol, qualifications, total diet score, self-rated health, walking disability, presence of hypertension and/or diabetes, doctor-diagnosed history of cancer, angina, stroke and/or acute MI.
Bonaccio, 2015[15] (Italy)	Moli-Sani Study, 4.3 yr	19 386 M/F	Nuts (peanuts, almonds, hazelnut, and walnut)	Interview-based FFQ, validated	Total: 334 CVD: 104 IHD: 39 Stroke: 19 Cancer: 124	0.55 (0.33-0.92) 0.71 (0.27-1.84)* 0.76 (0.39-1.49) 1.01 (0.37-2.76) 0.56 (0.25-1.27)*	Total mortality: ≥8 times/mo vs. never; CHD and stroke: Intake vs. no intake	Age, sex, education, smoking, leisure-time physical activity, BMI, energy intake, Mediterranean diet score without nut, and biomarkers of inflammation including C-reactive protein, platelet count and the neutrophil to lymphocyte ratio.
Eslamparast, 2016[16] (Iran)	Golestan Cohort Study, 7.0 yr	50 045 M/F aged ≥40 yr	Nuts (peanuts and tree nuts)	Self-reported FFQ, validated	Total: 3981 CVD: 2016 Cancer: 887	0.71 (0.58-0.86) 0.77 (0.58-1.01) 0.62 (0.38-1.01)	≥3 ser/wk vs. never	Age, sex, BMI, education, residence, smoking, opium and alcohol consumption, physical activity, wealth score, diabetes, hypertension, total energy intake, main food groups (fish, red meat, chicken, fruit, vegetable, dairy product, egg, and total fiber), magnesium, zinc and copper.
Wang, 2016[17] (China)	Linxian Nutrition Intervention Trials cohort, 26 yr	2445 M/F aged 40-69 yr	Nuts (peanuts, chestnut, and walnut)	Self-reported FFQ	Total: 1501 HD: 355 Stroke: 452	0.99 (0.96-1.02) 0.89 (0.82-0.98) 0.99 (0.93-1.05)	Per 3 times/mo	Age, sex, BMI, commune, smoking, alcohol, and season.

BMI, body mass index; CAD, coronary artery disease; CHD, coronary heart disease; CVD, cardiovascular disease; d, day; EPIC, European Prospective Investigation into Cancer and Nutrition; F, female; FFQ, Food frequency questionnaire; g, grams; HD, heart disease; HS, hemorrhagic stroke; IHD, ischemic heart disease; IS, ischemic stroke; M, male; MI, myocardial infarction; mo, month; PREDIMED, 'PREvención con DIeta MEDiterránea'; SUN, Seguimiento Universidad de Navarra; wk, week; yr, years

*unpublished data provided by the authors of the primary studies.

†Estimated RR and 95% CI when the lowest category of nut intake was set as the new reference category.

Supplementary Table 2. The quality of included studies assessed by the Newcastle Ottawa Scale*

| Study | Causes of death | Selection | | | | Comparability | Outcome | | | Total stars |
		Representativeness of exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
Mann, 1997[1]	Total+CHD	0	1	0	0	2	1	1	0	5
Fraser, 1997 (AHS-White)[2]	Total+CHD	0	1	0	1	1	1	1	1	6
Fraser, 1997 (AHS-Black)[3]	Total	0	1	0	0	2	1	1	1	6
Yochum, 2000[4]	Stroke	1	1	0	0	2	1	1	1	7
Blomhoff, 2006[5]	Total+CVD	1	1	0	0 for total, 1 for CVD	1	1	1	0	5 for total 6 for CVD
Guasch-Ferré, 2013[6]	Total+CVD +Cancer	0	1	1	1 for CVD, 0 for others	2	1	0	1	7 for CVD,6 for others
Bao, 2013 (NHS)[7]	All 5 causes	0	1	1	1	2	1	1	1	8
Bao, 2013 (HPFS)[7]	All 5 causes	0	1	1	1	2	1	1	1	8
Fernandez-Montero, 2014[8]	Total	0	1	1	0	2	1	0	1	6
Sluik, 2014[9]	Total	1	1	1	0	2	1	1	0	7
Luu, 2015 (SCCS)[10]	All 5 causes	1	1	1	1 for cancer, 0 for others	2	1	1	0	8 for cancer, 7 for others
Luu, 2015 (SMHS)[10]	All 5 causes	1	1	1	1 for cancer, 0 for others	2	1	1	1	9 for cancer, 8 for others
Luu, 2015 (SWHS)[10]	All 5 causes	1	1	1	0	2	1	1	1	8
di Giuseppe, 2015[11]	Stroke	1	1	1	1	2	1	1	1	9
Hshieh, 2015[12]	All 5 causes	0	1	0	0	2	1	1	0	5
Van den Brandt, 2015[13]	All 5 causes	1	1	1	1	2	1	1	1	9
Gopinath, 2015[14]	All 5 causes	1	1	1	0	2	1	1	0	7
Bonaccio, 2015[15]	All 5 causes	1	1	1	1	2	1	0	0	7
Eslamparast, 2016[16]	Total+CVD +Cancer	1	1	1	0	2	1	1	1	8
Wang, 2016[17]	Total+CHD +stroke	0	1	0	0	2	1	1	0	5

AHS, Adventists Health Study; CVD, cardiovascular disease; CHD, coronary heart disease; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; SCCS, Southern Community Cohort Study; SMHS, Shanghai Men's Health Study; SWHS, Shanghai Women's Health Study.

*A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories and a maximum of two stars for comparability.

Selection:
1) Representativeness of exposed cohort
Star assigned if cohort was truly or somewhat representative of the average nut-consumer in the community/population. Note that stars were not assigned where study population was sampled from a special population (i.e. participants of clinical trials or health examinations, nurses, health professionals, Adventists, university graduates).
2) Selection of non-exposed cohort
Star assigned where non-exposed persons were drawn from the same population as the exposed participants.
3) Ascertainment of exposure
Star assigned where diets were assessed using structured interviews, or where articles stated that the self-administered questionnaires had been validated.
4) Demonstration that outcome was not present at start of study:
Star assigned where participants with prevalent cardiovascular disease and/or cancer were excluded. For total mortality, stars assigned where both prevalent cardiovascular disease and cancer were excluded.

Comparability:

1) <u>Comparability of cohorts on the basis of the design or analysis</u>

One star assigned where aged and smoking was controlled for in analyses.

Second star assigned where other important potential confounders were controlled for in analyses.

Outcome:

1) <u>Assessment of outcome</u>

Star assigned where outcomes were identified through medical records/ record linkage.

2) <u>Was follow-up long enough for outcomes to occur</u>

Star assigned where mean years of follow-up was >5 years

3) <u>Adequacy of follow up of cohorts</u>

Star assigned where the follow-up rate was >80%. Note that stars were not assigned where these data were not available.

Supplementary Table 3. Subgroup analysis for the association of nut consumption with all-cause mortality, high vs. low consumption

		N*	RR (95% CI)	P†	I² (%)	P‡
Geographic areas						
USA		7	0.82 (0.79-0.86)	0.49	0	Ref.
Europe		5	0.70 (0.60-0.81)	0.26	25.0	0.07
Asia-Pacific		4	0.83 (0.77-0.89)	0.31	16.7	0.91, 0.11§
Sex of participants						
Men		9	0.79 (0.74-0.84)	0.22	25.0	0.45
Women		9	0.81 (0.75-0.88)	0.05	49.2	
Duration of follow-up						
≥10 years		8	0.84 (0.80-0.87)	0.73	0	0.07
<10 years		8	0.76 (0.70-0.82)	0.16	33.5	
Number of deaths						
≥3000		8	0.82 (0.79-0.85)	0.49	0	0.29
<3000		8	0.75 (0.67-0.85)	0.13	37.8	
Range of nut intake‖						
≥5 servings/week		8	0.82 (0.79-0.85)	0.58	0.0	0.57
<5 servings/week		8	0.78 (0.71-0.85)	0.07	46.6	
Exposure assessment						
FFQ with validation		10	0.80 (0.76-0.84)	0.19	27.9	0.30
FFQ without validation		6	0.84 (0.79-0.91)	0.38	5.4	
Quality score						
≥ 7		9	0.81 (0.79-0.84)	0.47	0	0.97
< 7		7	0.77 (0.69-0.87)	0.07	48.3	
Type of nuts						
Total nuts		11	0.79 (0.73-0.85)	0.002	63.6	Ref.
Nuts plus peanut butter		4	0.81 (0.75-0.87)	0.19	36.8	0.75
Peanut butter		2	0.89 (0.80-0.99)	0.23	31.2	0.17
Peanuts		5	0.85 (0.81-0.89)	0.19	34.1	0.27
Tree nuts		3	0.83 (0.77-0.89)	0.95	0	0.53, 0.46#
Adjustment						
Age	*Yes*	15	0.81 (0.78-0.84)	0.16	27.2	0.95
	No	1	0.82 (0.70-0.96)	NA	NA	
Smoking	*Yes*	15	0.80 (0.77-0.84)	0.32	12.2	0.11
	No	1	0.89 (0.81-0.98)	NA	NA	
Alcohol	*Yes*	12	0.81 (0.78-0.85)	0.15	30.3	0.53
	No	4	0.78 (0.68-0.88)	0.41	0	
BMI/weight/height	*Yes*	13	0.81 (0.78-0.85)	0.11	33.6	0.76
	No	3	0.80 (0.71-0.91)	0.60	0	
Physical activity	*Yes*	14	0.81 (0.78-0.84)	0.18	25.4	0.50
	No	2	0.87 (0.73-1.04)	0.28	13.8	
Education	*Yes*	8	0.80 (0.75-0.85)	0.11	41.1	0.77
	No	8	0.82 (0.78-0.86)	0.41	3.2	
Diabetes	*Yes*	12	0.81 (0.78-0.84)	0.31	13.6	0.36
	No	4	0.78 (0.64-0.95)	0.15	43.8	
Hypertension	*Yes*	11	0.81 (0.77-0.84)	0.24	21.3	0.40
	No	5	0.82 (0.73-0.92)	0.24	27.7	
Dyslipidemia	*Yes*	8	0.82 (0.78-0.86)	0.15	34.6	0.26
	No	8	0.78 (0.73-0.84)	0.45	0	
Energy intake	*Yes*	12	0.81 (0.77-0.84)	0.13	33.1	0.72
	No	4	0.83 (0.75-0.93)	0.45	0	
Vitamin supplements	*Yes*	7	0.83 (0.80-0.85)	0.64	0	0.13
	No	9	0.75 (0.67-0.83)	0.16	32.7	
Fruit/vegetables	*Yes*	11	0.82 (0.79-0.84)	0.37	7.6	0.75
	No	5	0.71 (0.55-0.91)	0.08	51.6	
Red/processed meat	*Yes*	10	0.82 (0.79-0.85)	0.33	11.8	0.48
	No	6	0.75 (0.64-0.89)	0.14	40.0	
Fish/seafood	*Yes*	7	0.81 (0.77-0.86)	0.17	34.1	0.87
	No	9	0.81 (0.76-0.86)	0.26	20.8	
Dietary fiber	*Yes*	2	0.74 (0.65-0.84)	0.60	0	0.17
	No	14	0.82 (0.79-0.85)	0.22	21.2	
Whole grain	*Yes*	1	0.89 (0.81-0.98)	NA	NA	0.11
	No	15	0.80 (0.77-0.84)	0.32	12.2	

BMI, body mass index; NA, not applicable

*Number of studies

†P value for heterogeneity among studies

‡P value for differences between groups

§Asia-Pacific vs. Europe

‖Range between mean/median of the highest and lowest categories of nut intake

#Tree nuts vs. peanuts

Supplementary Table 4. Subgroup analysis for the associations of nut consumption with cardiovascular disease and cancer mortality, high vs. low consumption

		CVD mortality					Cancer mortality			
		N*	RR (95% CI)	P†	I² (%)	P‡	N*	RR (95% CI)	P†	I² (%)	P‡
Geographic areas											
USA		6	0.73 (0.68-0.79)	0.77	0	Ref.	4	0.87 (0.79-0.94)	0.38	2.1	Ref
Europe		6	0.65 (0.48-0.88)	0.15	38.4	0.75	4	0.76 (0.66-0.89)	0.63	0	0.21
Asia-Pacific		4	0.78 (0.71-0.86)	0.47	0	0.31, 0.54§	3	0.93 (0.82-1.07)	0.22	33.9	0.28, 0.07§
Sex of participants											
Men		7	0.77 (0.70-0.84)	0.35	10.6	0.59	5	0.85 (0.75-0.96)	0.23	29.5	0.33
Women		7	0.74 (0.68-0.81)	0.65	0		4	0.93 (0.84-1.04)	0.32	14.3	
Duration of follow-up											
≥10 years		8	0.76 (0.71-0.82)	0.43	0	0.47	4	0.89 (0.82-0.97)	0.24	28.9	0.33
<10 years		8	0.73 (0.66-0.80)	0.44	0		7	0.80 (0.68-0.93)	0.20	29.9	
Number of deaths											
≥1500		6	0.75 (0.70-0.81)	0.79	0	0.81	5	0.87 (0.81-0.95)	0.21	31.2	0.54
<1500		10	0.73 (0.65-0.82)	0.22	24.3		6	0.76 (0.59-0.96)	0.17	35.1	
Range of nut intake‖											
≥ 5 servings/week		7	0.73 (0.68-0.79)	0.83	0	0.36	4	0.87 (0.79-0.94)	0.38	2.1	0.96
< 5 servings/week		9	0.76 (0.69-0.85)	0.22	25.3		7	0.85 (0.74-0.97)	0.11	41.8	
Exposure assessment											
FFQ with validation		11	0.75 (0.70-0.80)	0.49	0	0.81	10	0.87 (0.80-0.94)	0.18	29.4	0.44
FFQ without validation		5	0.76 (0.66-0.87)	0.30	18.0		1	0.64 (0.32-1.29)	NA	NA	
Quality score											
≥ 7		11	0.76 (0.72-0.81)	0.49	0	0.23	8	0.88 (0.81-0.95)	0.17	32.4	0.15
< 7		5	0.69 (0.60-0.79)	0.51	0		3	0.65 (0.45-0.93)	0.79	0	
Type of nuts											
Total nuts		10	0.75 (0.68-0.84)	0.16	31.2	Ref.	6	0.85 (0.74-0.96)	0.27	21.5	Ref.
Nuts plus peanut butter		4	0.75 (0.68-0.83)	0.66	0	0.72	3	0.79 (0.70-0.88)	0.85	0	0.24
Peanut butter		1	0.99 (0.80-1.23)	NA	NA	0.11	1	0.98 (0.82-1.17)	NA	NA	0.33
Peanuts		5	0.78 (0.73-0.85)	0.30	18.0	0.73	5	0.93 (0.87-0.99)	0.30	18.5	0.29
Tree nuts		3	0.81 (0.74-0.89)	0.62	0	0.42, 0.53#	3	0.82 (0.76-0.90)	0.99	0	0.45, 0.06#
Adjustment											
Age	Yes	15	0.75 (0.71-0.80)	0.56	0	0.20	11	0.87 (0.80-0.93)	0.20	26.0	NA
	No	1	0.61 (0.45-0.83)	NA	NA		0	NA	NA	NA	
Smoking	Yes	15	0.75 (0.71-0.80)	0.43	1.5	0.68	11	0.87 (0.80-0.93)	0.20	26.0	NA
	No	1	0.72 (0.59-0.87)	NA	NA		0	NA	NA	NA	
Alcohol	Yes	13	0.75 (0.71-0.80)	0.41	3.2	0.33	10	0.87 (0.81-0.94)	0.19	27.1	0.34
	No	3	0.65 (0.50-0.85)	0.62	0		1	0.56 (0.25-1.26)	NA	NA	
BMI/weight/height	Yes	14	0.75 (0.71-0.80)	0.49	0	0.32	11	0.87 (0.80-0.93)	0.20	26.0	NA
	No	2	0.65 (0.49-0.86)	0.34	0		0	NA	NA	NA	
Physical activity	Yes	14	0.74 (0.70-0.78)	0.60	0	0.09	11	0.87 (0.80-0.93)	0.20	26.0	NA
	No	2	0.90 (0.73-1.10)	0.92	0		0	NA	NA	NA	
Education	Yes	9	0.74 (0.69-0.80)	0.62	0	0.78	7	0.84 (0.74-0.95)	0.07	48.6	0.64
	No	7	0.76 (0.67-0.85)	0.23	25.5		4	0.89 (0.81-0.98)	0.43	0	
Diabetes	Yes	13	0.75 (0.70-0.80)	0.30	14.3	0.77	10	0.87 (0.81-0.94)	0.19	27.1	0.34
	No	3	0.73 (0.61-0.87)	0.86	0		1	0.56 (0.25-1.26)	NA	NA	
Hypertension	Yes	12	0.76 (0.71-0.81)	0.35	9.5	0.34	10	0.87 (0.81-0.94)	0.19	27.1	0.34
	No	4	0.70 (0.60-0.81)	0.74	0		1	0.56 (0.25-1.26)	NA	NA	
Dyslipidemia	Yes	8	0.73 (0.68-0.79)	0.34	11.3	0.35	7	0.90 (0.83-0.97)	0.28	19.1	0.07
	No	8	0.78 (0.71-0.85)	0.59	0		4	0.76 (0.65-0.88)	0.65	0	
Energy intake	Yes	13	0.74 (0.70-0.79)	0.65	0	0.46	11	0.87 (0.80-0.93)	0.20	26.0	NA
	No	3	0.77 (0.58-1.03)	0.12	52.8		0	NA	NA	NA	
Vitamin supplements	Yes	7	0.75 (0.71-0.80)	0.83	0	0.84	6	0.89 (0.83-0.96)	0.22	29.2	0.04
	No	9	0.71 (0.60-0.84)	30.5		0.17	5	0.63 (0.48-0.83)	0.96	0	
Fruit/vegetables	Yes	12	0.74 (0.70-0.79)	0.65	0	0.25	10	0.87 (0.81-0.94)	0.19	27.1	0.34
	No	4	0.77 (0.57-1.06)	0.24	28.9		1	0.56 (0.25-1.26)	NA	NA	
Red/processed meat	Yes	11	0.73 (0.69-0.78)	0.71	0	0.10	8	0.88 (0.81-0.96)	0.16	33.3	0.23
	No	5	0.83 (0.72-0.96)	0.38	5.3		3	0.78 (0.67-0.92)	0.70	0	
Fish/seafood	Yes	8	0.72 (0.67-0.78)	0.56	0	0.18	5	0.86 (0.74-0.99)	0.07	54.6	0.76
	No	8	0.78 (0.72-0.85)	0.48	0		6	0.86 (0.79-0.93)	0.51	0	
Dietary fiber	Yes	1	0.77 (0.58-1.02)	NA	NA	0.85	1	0.62 (0.38-1.01)	NA	NA	0.22
	No	15	0.75 (0.71-0.79)	0.42	2.4		10	0.87 (0.81-0.94)	0.24	22.2	
Whole grain	Yes	2	0.66 (0.40-1.09)	0.27	17.2	0.57	0	NA	NA	NA	NA
	No	14	0.75 (0.71-0.80)	0.46	0		11	0.87 (0.80-0.93)	0.20	26.0	

BMI, body mass index; CVD, cardiovascular disease; NA, not applicable
*Number of studies
†P value for heterogeneity among studies
‡P value for differences between groups
§Asia-Pacific vs. Europe
‖Range between mean/median of the highest and lowest categories of nut intake.
#Tree nuts vs. peanuts

Supplementary Table 5. Subgroup analysis for the associations of nut consumption with coronary heart disease and stroke mortality, high vs. low consumption

		CHD mortality				Stroke mortality			
	N*	RR (95% CI)	P†	I² (%)	P‡	N*	RR (95% CI)	P†	I² (%)	P‡
Geographic areas										
USA		6	0.69 (0.63-0.76)	0.73	0	Ref.	5	0.87 (0.74-1.02)	0.73	0	Ref.
Europe		4	0.81 (0.66-0.99)	0.40	0	0.16	4	0.73 (0.55-0.96)	0.44	0	0.30
China		3	0.79 (0.60-1.03)	0.12	53.1	0.14, 0.98§	3	0.79 (0.67-0.93)	0.78	0	0.42, 0.64§
Sex of participants										
Men		6	0.74 (0.67-0.83)	0.68	0	0.65	5	0.85 (0.73-0.99)	0.58	0	0.70
Women		6	0.71 (0.61-0.81)	0.36	0		5	0.81 (0.69-0.97)	0.47	0	
Duration of follow-up										
≥10 years		8	0.74 (0.67-0.82)	0.28	18.7	0.62	6	0.81 (0.71-0.92)	0.72	0	0.78
<10 years		5	0.71 (0.57-0.87)	0.29	19.6		6	0.83 (0.70-0.99)	0.67	0	
Number of deaths										
≥500		5	0.72 (0.65-0.79)	0.50	0	0.51	4	0.80 (0.69-0.93)	0.47	0	0.73
<500		8	0.75 (0.63-0.90)	0.19	29.7		8	0.83 (0.72-0.97)	0.77	0	
Range of nut intake‖										
≥5 servings/week		7	0.69 (0.63-0.77)	0.77	0	0.09	4	0.89 (0.75-1.05)	0.65	0	0.23
<5 servings/week		6	0.79 (0.67-0.95)	0.21	30.2		8	0.77 (0.67-0.88)	0.84	0	
Exposure assessment										
FFQ with validation		8	0.71 (0.65-0.79)	0.41	0	0.38	9	0.80 (0.71-0.91)	0.63	0	0.64
FFQ without validation		5	0.78 (0.65-0.93)	0.22	30.5		3	0.85 (0.69-1.05)	0.85	0	
Quality score										
≥7		9	0.74 (0.66-0.83)	0.16	31.8	0.73	11	0.81 (0.72-0.90)	0.77	0	0.63
<7		4	0.71 (0.60-0.84)	0.57	0		1	0.87 (0.66-1.15)	NA	NA	
Type of nuts										
Total nuts		7	0.75 (0.67-0.84)	0.22	26.8	Ref.	7	0.89 (0.77-1.02)	0.52	0	Ref.
Nuts plus peanut butter		4	0.73 (0.63-0.85)	0.28	22.5	0.80	3	0.84 (0.70-1.01)	0.66	0	0.67
Peanut butter		1	0.97 (0.75-1.25)	NA	NA	0.15	1	0.86 (0.60-1.23)	NA	NA	0.89
Peanuts		5	0.76 (0.69-0.82)	0.65	0	0.88	5	0.83 (0.71-0.97)	0.12	46.2	0.59
Tree nuts		3	0.79 (0.69-0.82)	0.25	27.5	0.65, 0.70#	3	0.93 (0.77-1.13)	0.44	0	0.69, 0.44#
Adjustment										
Age	Yes	12	0.74 (0.68-0.81)	0.33	12.0	0.27	12	0.82 (0.73-0.91)	0.82	0	NA
	No	1	0.61 (0.45-0.83)	NA	NA		0	NA	NA	NA	
Smoking	Yes	12	0.74 (0.67-0.81)	0.24	20.9	0.83	12	0.82 (0.73-0.91)	0.82	0	NA
	No	1	0.71 (0.55-0.91)	NA	NA		0	NA	NA	NA	
Alcohol	Yes	10	0.74 (0.67-0.82)	0.20	26.6	0.51	11	0.81 (0.73-0.90)	0.77	0	0.68
	No	3	0.66 (0.51-0.86)	0.58	0		1	1.01 (0.37-2.76)	NA	NA	
BMI/weight/height	Yes	11	0.74 (0.67-0.82)	0.27	18.5	0.45	12	0.82 (0.73-0.91)	0.82	0	NA
	No	2	0.65 (0.49-0.86)	0.34	0		0	NA	NA	NA	
Physical activity	Yes	11	0.71 (0.65-0.77)	0.54	0	0.05	11	0.81 (0.73-0.90)	0.77	0	0.69
	No	2	0.94 (0.75-1.18)	0.81	0		1	0.88 (0.60-1.29)	NA	NA	
Education	Yes	7	0.71 (0.62-0.81)	0.30	16.6	0.52	8	0.77 (0.67-0.89)	0.79	0	0.28
	No	6	0.76 (0.66-0.86)	0.27	22.2		4	0.88 (0.75-1.03)	0.68	0	
Diabetes	Yes	10	0.73 (0.65-0.82)	0.14	34.1	0.97	11	0.81 (0.73-0.90)	0.77	0	0.68
	No	3	0.73 (0.59-0.91)	0.85	0		1	1.01 (0.37-2.76)	0.97	0	
Hypertension	Yes	9	0.75 (0.66-0.84)	0.15	34.1	0.50	10	0.82 (0.73-0.91)	0.70	0	0.90
	No	4	0.69 (0.57-0.82)	0.75	0		2	0.79 (0.48-1.30)	0.58	0	
Dyslipidemia	Yes	9	0.72 (0.66-0.78)	0.45	0	0.36	9	0.80 (0.71-0.90)	0.64	0	0.46
	No	4	0.79 (0.61-1.02)	0.17	39.7		3	0.88 (0.71-1.10)	0.96	0	
Energy intake	Yes	10	0.72 (0.66-0.78)	0.55	0	0.36	11	0.81 (0.73-0.90)	0.77	0	0.69
	No	3	0.79 (0.57-1.09)	0.08	59.6		1	0.88 (0.60-1.29)	NA	NA	
Vitamin supplements	Yes	8	0.72 (0.66-0.79)	0.60	0	0.45	6	0.81 (0.72-0.92)	0.68	0	0.89
	No	5	0.75 (0.56-1.01)	0.10	48.0		6	0.83 (0.68-1.01)	0.61	0	
Fruit/vegetables	Yes	10	0.71 (0.65-0.77)	0.45	0	0.05	9	0.81 (0.73-0.91)	0.62	0	0.81
	No	3	0.92 (0.74-1.14)	0.82	0		3	0.85 (0.62-1.15)	0.81	0	
Red/processed meat	Yes	9	0.69 (0.63-0.76)	0.59	0	0.03	8	0.82 (0.73-0.92)	0.53	0	0.86
	No	4	0.87 (0.75-1.02)	0.84	0		4	0.80 (0.65-0.99)	0.88	0	
Fish/seafood	Yes	6	0.66 (0.58-0.75)	0.45	0	0.06	6	0.77 (0.66-0.90)	0.60	0	0.39
	No	7	0.78 (0.71-0.86)	0.57	0		6	0.85 (0.74-0.98)	0.81	0	
Dietary fiber	Yes	0	NA	NA	NA	NA	1	0.73 (0.41-1.29)	NA	NA	0.71
	No	13	0.73 (0.67-0.80)	0.30	14.2		11	0.82 (0.74-0.91)	0.76	0	
Whole grain	Yes	1	0.71 (0.55-0.91)	NA	NA	0.83	2	0.63 (0.34-1.18)	0.29	9.5	0.43
	No	12	0.74 (0.67-0.81)	0.24	20.9		10	0.82 (0.74-0.92)	0.84	0	

BMI, body mass index; CHD, coronary heart disease; NA, not applicable.
*Number of studies.
†P value for heterogeneity among studies
‡P value for differences between groups
§Asia-Pacific vs. Europe.
‖Range between mean/median of the highest and lowest categories of nut intake
#Tree nuts vs. peanuts

Supplementary Table 6. Regression coefficients between frequency of nut consumption and background risk factors

Study	Nut consumption (serving/wk)				
	Body Mass Index (kg/m^2)	Nonsmoker (%)	Fruits (servings/d)	Vegetables (servings/d)	Fruits and vegetables (servings/d)
Guasch-Ferré, 2013	-0.3000002	1.25	0.1999999	0.1	0.3
Bao (NHS), 2013	-0.2284412	0.383591	0.0927986	0.0762078	0.1690065
Bao (HPFS), 2013	-0.0787603	0.0129444	0.101185	0.1028259	0.2040108
Fernandez-Montero, 2014	-0.013312	1.861329	0.5835995	0.4421959	1.025796
Luu (SCCS), 2015	-0.2744174	-0.8596053	0.2292825	0.1284098	0.3576923
Luu (SWHS+SMHS), 2015	0.8367419	2.910357	0.4631369	1.667956	2.131093
Hshien-2015	-0.0884664	-0.0173318	NA	NA	0.2206113
van den Brandt (men), 2015	0.0299128	-0.3513159	0.0358321	-0.0090018	0.0268303
van den Brandt (women), 2015	-0.1628382	-2.224359	0.0492473	0.0567429	0.1059902
Bonaccio, 2015	NA	1.063461	NA	NA	NA
Eslamparast,2016	0.4580643	-1.665807	0.4954839	0.2374194	0.7329033
Median	**-0.08**	**0.01**	**0.20**	**0.10**	**0.26**

Supplementary Table 7. Sensitivity analyses of nut consumption (high vs. low) and risk of all-cause mortality by regression coefficients between nut consumption and background risk factors

	N*	RR (95% CI)	P†	I² (%)	P‡
Regression coefficient for BMI					
≥ median	5	0.80 (0.75-0.86)	0.20	33.9	0.70
< median	5	0.80 (0.75-0.85)	0.33	13.7	
Regression coefficient for percentage of nonsmokers					
≥ median	7	0.80 (0.74-0.87)	0.08	48.7	0.21
< median	4	0.77 (0.73-0.82)	0.90	0	
Regression coefficient for fruits					
≥ median	5	0.79 (0.72-0.86)	0.12	48.2	0.80
< median	4	0.81 (0.76-0.86)	0.34	11.1	
Regression coefficient for vegetables					
≥ median	6	0.80 (0.76-0.85)	0.20	33.2	0.97
< median	3	0.79 (0.70-0.87)	0.22	32.0	
Regression coefficient for fruits and vegetables					
≥ median	6	0.76 (0.69-0.84)	0.07	54.7	0.63
< median	4	0.81 (0.77-0.88)	0.78	0	

*Number of studies
†P value for heterogeneity among studies
‡P value for differences between groups

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