

SUPPLEMENTAL MATERIAL

Table S1. Multivariable adjusted relative risk (95% confidence intervals) for incident cardiovascular disease according to the joint categories of total nuts intake at the first and fourth year of each period in NHS, NHS II, and HPFS.

1 st year intakes	Total nuts intake (serving/day)								
	0	0.1-0.49	≥0.5	0	0.1-0.49	≥0.5	0	0.1-0.49	≥0.5
4 th year intakes	0	0	0	0.1-0.49	0.1-0.49	0.1-0.49	≥0.5	≥0.5	≥0.5
HPFS									
Person Years	61875	47484	3988	53113	187483	33991	6949	46258	44362
Cases	487	361	28	370	1205	245	47	295	254
Crude rate	787	760	702	697	643	721	676	638	573
Model 1	1.0 (ref.)	1.00 (0.88-1.15)	0.78 (0.53-1.15)	0.91 (0.79-1.04)	0.87 (0.78-0.97)	0.90 (0.77-1.05)	0.81 (0.60-1.09)	0.79 (0.68-0.91)	0.69 (0.59-0.81)
Model 2	1.0 (ref.)	1.03 (0.89-1.18)	0.82 (0.56-1.21)	0.94 (0.82-1.08)	0.92 (0.83-1.02)	0.97 (0.83-1.13)	0.86 (0.63-1.16)	0.86 (0.74-0.99)	0.77 (0.66-0.89)
Model 3	1.0 (ref.)	1.02 (0.89-1.17)	0.81 (0.55-1.19)	0.94 (0.82-1.07)	0.91 (0.81-1.01)	0.95 (0.81-1.1)	0.85 (0.63-1.15)	0.85 (0.73-0.99)	0.77 (0.65-0.90)
NHS									
Person Years	345186	164227	9989	176580	352732	46207	19123	73350	49085
Cases	1447	623	47	600	1134	150	65	231	136
Crude rate	419	379	471	340	321	325	340	315	277
Model 1	1.0 (ref.)	0.96 (0.88-1.06)	1.04 (0.78-1.40)	0.84 (0.76-0.92)	0.85 (0.78-0.92)	0.77 (0.65-0.91)	0.72 (0.56-0.93)	0.71 (0.62-0.82)	0.59 (0.49-0.70)
Model 2	1.0 (ref.)	1.03 (0.93-1.13)	1.14 (0.85-1.53)	0.91 (0.82-1.00)	0.97 (0.89-1.05)	0.91 (0.77-1.08)	0.83 (0.65-1.07)	0.86 (0.74-0.99)	0.74 (0.61-0.88)
Model 3	1.0 (ref.)	1.02 (0.93-1.12)	1.15 (0.86-1.54)	0.91 (0.82-1.00)	0.97 (0.89-1.05)	0.92 (0.77-1.09)	0.85 (0.66-1.09)	0.88 (0.76-1.01)	0.76 (0.63-0.92)
NHSII									
Person Years	311193	115799	5055	191070	299703	33812	22711	72669	41764
Cases	201	61	2	135	222	31	13	49	21
Crude rate	65	53	40	71	74	92	57	67	50
Model 1	1.0 (ref.)	0.74 (0.56-0.99)	0.39 (0.10-1.59)	0.93 (0.74-1.15)	0.85 (0.70-1.04)	0.84 (0.57-1.24)	0.62 (0.35-1.09)	0.65 (0.47-0.89)	0.42 (0.27-0.67)
Model 2	1.0 (ref.)	0.74 (0.56-0.99)	0.39 (0.10-1.59)	0.97 (0.77-1.20)	0.91 (0.74-1.11)	0.94 (0.63-1.39)	0.70 (0.39-1.23)	0.75 (0.54-1.04)	0.50 (0.32-0.80)
Model 3	1.0 (ref.)	0.74 (0.55-0.99)	0.40 (0.10-1.63)	0.96 (0.77-1.20)	0.92 (0.75-1.13)	0.98 (0.66-1.46)	0.73 (0.41-1.28)	0.79 (0.56-1.10)	0.58 (0.36-0.93)

Model 1 was stratified by age, sex, and calendar year in 4-year intervals;

Model 2 was stratified by age, sex, and calendar year in 4-year intervals, further adjusted for initial total nut intake, race (white, non-white), family history of MI, initial and change in smoking status (never to never, never to current, past to past, current to past, current to current, missing indicator), menopausal status and postmenopausal hormone use (premenopausal, postmenopausal + current use, postmenopausal + past use, postmenopausal + never use, missing indicator, in NHS and NHSII), number of tooth at baseline (0, 1-16, 17-24, 25-32, in NHS and HPFS) and updated teeth loss during follow-up (continuous, in NHS and HPFS), oral contraceptive use (never, current, past, missing indicator, in NHSII), initial (g/d, 0, 0.1-4.9, 5-14.9, 15-29.9 and ≥30) and change in alcohol intake (decrease, no-change or increase), initial (MET-h/week, quintiles) and change in physical activity level (MET-h/week, <-5, -5~4.9, ≥5). **Model 3** was model 2 further adjusted for initial BMI (<21.0, 21.0-24.9, 25.0-29.9, 30.0-31.9, >32.0 kg/m²), initial history of hypercholesterolemia and high blood pressure at the start of each 4-year interval, initial (quintiles) and changes in energy intakes (kcal/day: <-250, -250~250, ≥250), initial (calculated without the alcohol component and nuts, quintile) and change in AHEI score (<-2, -2~5, ≥5) over each 4-year period

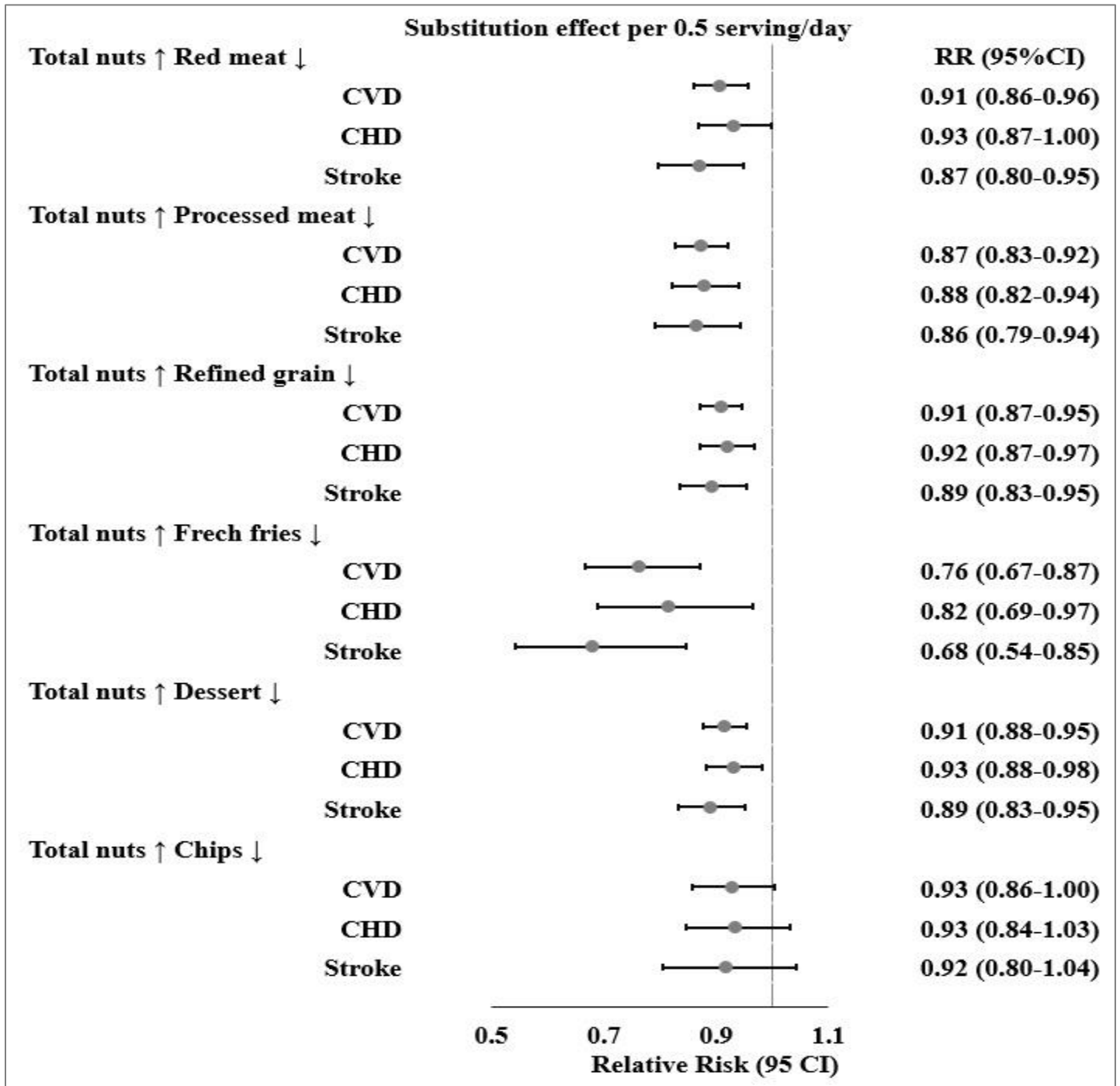
Table S2. Stratified analysis of the multivariable adjusted relative risk (RR, 95% confidence intervals) for incident cardiovascular disease associated with per 0.5 serving/day increase of total nuts based on pooled data of NHS, NHS II, and HPFS.

Stratified variables	CVD		CHD		Stroke	
	Cases	RR (95%CI)	Cases	RR (95%CI)	Cases	RR (95%CI)
Age (years)						
< 60	1634	0.90 (0.81-1.00)	1007	0.90 (0.79-1.03)	627	0.90 (0.76-1.07)
≥ 60	6826	0.92 (0.87-0.96)	3970	0.94 (0.89-0.99)	2856	0.88 (0.82-0.95)
<i>P</i> for interaction		0.35		0.24		0.99
Smoking status						
Never smoking	3550	0.94 (0.88-1.00)	2023	0.92 (0.85-1.00)	1527	0.96 (0.88-1.06)
Ever smoking	4840	0.89 (0.84-0.94)	2911	0.95 (0.88-1.02)	1929	0.81 (0.73-0.88)
<i>P</i> for interaction		0.15		0.74		0.008
Changes of alcohol intake						
No changes or decreased	5889	0.91 (0.87-0.96)	3422	0.93 (0.88-1.00)	2467	0.88 (0.81-0.95)
Increased	2571	0.92 (0.85-0.98)	1555	0.93 (0.85-1.02)	1016	0.89 (0.79-1.00)
<i>P</i> for interaction		0.71		0.81		0.78
Changes of physical activity						
No changes or decreased	4009	0.92 (0.86-0.97)	2444	0.91 (0.84-0.98)	1565	0.93 (0.84-1.02)
Increased	3154	0.96 (0.89-1.03)	1933	0.98 (0.90-1.07)	1221	0.92 (0.82-1.03)
<i>P</i> for interaction		0.34		0.33		0.77
Changes of energy intake						
No changes or decreased	4445	0.92 (0.86-0.99)	2622	0.93 (0.86-1.01)	1823	0.90 (0.82-1.00)
Increased	4015	0.91 (0.86-0.96)	2355	0.93 (0.86-0.99)	1660	0.88 (0.81-0.96)
<i>P</i> for interaction		0.53		0.71		0.59
Changes of AHEI score						
No changes or decreased	3793	0.89 (0.84-0.95)	2243	0.91 (0.84-0.99)	1550	0.86 (0.78-0.96)
Increased	4667	0.93 (0.88-0.98)	2734	0.95 (0.88-1.01)	1933	0.90 (0.83-0.98)
<i>P</i> for interaction		0.31		0.45		0.46
Changes of body weight						
No changes or decreased	4058	0.91 (0.86-0.97)	2393	0.91 (0.85-0.99)	1665	0.91 (0.83-1.00)
Increased	3446	0.91 (0.85-0.97)	1988	0.96 (0.88-1.05)	1458	0.84 (0.75-0.93)
<i>P</i> for interaction		0.98		0.64		0.57

Multivariate adjusted model was stratified by age, sex, and calendar year in 4-year intervals and adjusted for initial total nut intake, race (white, non-white), family history of MI, initial and change in smoking status (never to never, never to current, past to past, current to past, current to current, missing indicator), menopausal status, postmenopausal hormone use (premenopausal, postmenopausal + current use, postmenopausal + past use, postmenopausal + never use, missing indicator, in NHS and NHSII), number of tooth at baseline (0, 1-16, 17-24, 25-32, in NHS and HPFS) and updated teeth loss during follow-up (continuous, in NHS and HPFS), oral contraceptive use (never, current, past, missing indicator, in NHSII), initial (g/d, 0, 0.1-4.9, 5-14.9, 15-29.9 and ≥30) and change in alcohol intake (decrease, no-change or increase), initial (MET-h/week, quintiles) and change in physical activity level (MET-h/week, <-5, -5~4.9, ≥5), initial BMI (<21.0, 21.0-24.9, 25.0-29.9, 30.0-31.9, >32.0 kg/m²), initial (quintiles) and changes in energy intakes (kcal/day: <-250, -250~250, ≥250), initial (calculated without the alcohol component and nuts, quintile) and change in AHEI score (<-2, -2~5, ≥5) over each 4-year period, and initial history of hypercholesterolemia and high blood pressure at the start of each 4-year interval, with the exclusion of stratified variable.

^{*}*P* for interaction between the initial year and the fourth-year nut consumption over each 4-year period

Figure S1. Multivariable adjusted relative risk and 95% confidence intervals for incident cardiovascular disease associated with substitution of 0.5 serving of nuts with equal amount of other food items.



Multi-variables model stratified by age, sex, and calendar year in 4-year intervals, and adjusted initial total nut intake, race (white, non-white), family history of MI, initial and change in smoking status (never to never, never to current, past to past, current to past, current to current, missing indicator), menopausal status and postmenopausal hormone use (premenopausal, postmenopausal + current use, postmenopausal + past use, postmenopausal + never use, missing indicator, in NHS and NHSII), number of tooth at baseline (0, 1-16, 17-24, 25-32, in NHS and HPFS) and updated teeth loss during follow-up (continuous, in NHS and HPFS), oral contraceptive use (never, current, past, missing indicator, in NHSII), initial (g/d, 0, 0.1-4.9, 5-14.9, 15-29.9 and ≥ 30) and change in alcohol intake (decrease, no-change or increase), initial (MET-h/week, quintiles) and change in physical activity level (MET-h/week, < -5 , $-5 \sim -4.9$, ≥ 5), initial BMI (< 21.0 , $21.0 \sim 24.9$, $25.0 \sim 29.9$, $30.0 \sim 31.9$, > 32.0 kg/m²), initial history of hypercholesterolemia and high blood pressure at the start of each 4-year interval, initial energy intake (quintiles) as well as initial (continuous) and changes (continuous) in red meat, processed meat, whole grain, refined grain, French fries, dessert and chips.