Nut and Peanut Butter Consumption and the Risk of Total Cancer

Nut and Peanut Butter Consumption and the Risk of Total Cancer: A Prospective Cohort Study

Lisette Nieuwenhuis[1] and Piet A. van den Brandt[1,2]

ABSTRACT

Background: Nut intake has been associated with reduced cancer-related mortality, but there is very limited evidence on total cancer risk. We investigated the associations of nut and peanut butter intake with the risk of total cancer and smoking- and alcohol-related cancer subgroups.

Methods: In the prospective Netherlands Cohort Study, 120,852 men and women aged 55 to 69 years provided information on lifestyle and dietary habits at baseline in 1986. After 20.3 years of follow-up, 19,255 total cancer cases and 3,499 subcohort members were included in multivariable-adjusted Cox regression analyses, using a case–cohort approach.

Results: No significant associations were found between total nut, tree nut, peanut, and peanut butter intake and total cancer risk in men and women. There were also no significant associations with smoking-(un)related and alcohol-(un)related cancers in both sexes.

Conclusions: Our findings suggest that nut and peanut butter intake are not associated with a reduced risk of total cancer in men or women.

Impact: Nut and peanut butter consumption are not related to the risk of total cancer.

Introduction

Growing scientific evidence has indicated that nut intake might have beneficial effects on cancer-related mortality and the risk of several cancer (sub)types, which might be related to their antioxidative and anti-inflammatory components (1). From a public health perspective, it is also relevant to know whether nut and peanut butter intake might contribute to a reduction of the total cancer burden. To our knowledge, this relation has only been investigated in one prospective cohort study, in which no associations were observed between nut intake and total cancer risk (2).

In this study, we investigated the associations of nut and peanut butter intake with the risk of total cancer in the prospective Netherlands Cohort Study (NLCS). These associations were also studied for smoking- and alcohol-related cancers, because the potential cancer preventive effects of nuts might be stronger for these carcinogen-related cancers.

Materials and Methods

At baseline, in September 1986, 58,279 men and 62,573 women aged 55 to 69 years were included in the NLCS (3). All participants filled in a self-administered baseline questionnaire on potential cancer risk factors. A case–cohort approach was applied, in which cases were derived from the entire cohort and person-time at risk from a subcohort consisting of 5,000 randomly sampled participants. Follow-up of cancer incidence was performed through annual record linkage with the Netherlands Cancer Registry and the Netherlands Pathology Registry (PALGA).

After 20.3 years of follow-up, we included 19,255 cancer cases (of which 765 in the subcohort) and 3,499 subcohort members after excluding participant with prevalent cancer (excluding skin cancer), incomplete or inconsistent dietary data, missing data on exposures and confounders, and cases with noninvasive tumors or without microscopic confirmation. Smoking-related cancers comprised cancers of the oral cavity (including lip), pharynx, esophagus, stomach, colorectum, liver, pancreas, nasal cavity, paranasal sinuses, larynx, trachea, lung, uterine cervix, ovary, kidney, ureter, urinary bladder, and myeloid leukemia (4). Alcohol-related cancers included cancers of the oral cavity (including lip), pharynx, esophageal squamous cell carcinoma, colorectum, liver, larynx, and breast (4). The smoking- and alcohol-unrelated cancer subgroups included all cancers not described above.

Habitual diet was assessed using a validated 150-item self-administered semiquantitative food frequency questionnaire (FFQ). Nut and peanut butter intake was measured as described previously (5).

Cox proportional hazards models were used to estimate multivariable-adjusted HRs and 95% confidence intervals (CI) for the associations between total nut intake and total cancer risk. Associations were also examined for tree nut, peanut, and peanut butter intake, and for smoking- and alcohol-(un)related cancers. SEs were calculated using a robust Huber–White sandwich estimator (6). Scaled Schoenfeld residuals, −ln(−ln) survival plots, and time-varying covariates confirmed that assuming proportional hazards was appropriate. Heterogeneity between the smoking- and alcohol-(un)related subgroups was tested using a competing risk procedure that applies a bootstrapping method to estimate SEs in case–cohort designs.

Results

Mean total nut intake in the subcohort was 7.9 g/day in men and 4.5 g/day in women. Baseline characteristics are presented in **Table 1**. We observed no associations between total nut, tree nut, peanut, and peanut butter intake and total cancer risk in

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Table 1. Baseline characteristics [mean (SD) or %] of subcohort members and total cancer cases, the NLCS, 1986–2006.

	Subcohort	Total cancer	Smoking-related cancer	Smoking-unrelated cancer	Alcohol-related cancer	Alcohol-unrelated cancer
Men						
N	1,834	12,184	6,723	5,461	2,385	9,799
Age (years)	61.2 (4.2)	61.6 (4.1)	61.6 (4.1)	61.6 (4.1)	61.5 (4.1)	61.6 (4.1)
Body mass index (kg/m^2)	24.9 (2.6)	25.0 (2.6)	25.1 (2.7)	25.0 (2.5)	25.2 (2.7)	25.0 (2.6)
Height (cm)	176.6 (6.6)	176.7 (6.7)	176.6 (6.7)	176.7 (6.7)	176.7 (6.6)	176.7 (6.7)
Ever cigarette smoker (%)	86.4	88.8	91.7	85.2	88.3	88.9
University or higher vocational education (%)	20.3	20.0	17.7	22.8	20.4	19.9
Nonoccupational physical activity (minutes/day)	81.0 (67.4)	80.8 (65.7)	81.0 (67.4)	80.5 (63.4)	81.9 (67.0)	80.5 (65.3)
Family history of cancer (%)	45.6	48.6	48.8	48.2	49.5	48.3
Daily energy intake (kcal)	2,167 (499)	2,166 (492)	2,170 (495)	2,161 (487)	2,153 (487)	2,169 (493)
Total nut intake (g/day)	7.9 (13.7)	7.9 (14.4)	7.4 (13.5)	8.4 (15.4)	7.6 (12.9)	7.9 (14.7)
Tree nut intake (g/day)	1.0 (3.4)	1.0 (3.6)	0.9 (3.1)	1.1 (4.2)	1.0 (3.4)	1.0 (3.7)
Peanut intake (g/day)	6.9 (13.0)	6.8 (13.2)	6.5 (12.6)	7.2 (13.8)	6.6 (12.1)	6.9 (13.4)
Peanut butter intake (g/day)	1.4 (4.2)	1.5 (4.3)	1.4 (4.2)	1.6 (4.4)	1.6 (4.3)	1.5 (4.3)
Alcohol intake (g/day)	15.1 (17.1)	16.7 (17.7)	17.8 (18.8)	15.2 (16.1)	18.0 (19.4)	16.3 (17.2)
Women						
N	1,665	7,071	3,013	4,058	3,756	3,315
Age (years)	61.3 (4.2)	61.5 (4.1)	61.7 (4.1)	61.4 (4.1)	61.5 (4.1)	61.6 (4.2)
Body mass index (kg/m^2)	25.0 (3.5)	25.2 (3.6)	24.9 (3.6)	25.3 (3.5)	25.2 (3.5)	25.2 (3.7)
Height (m)	165.3 (6.1)	165.8 (6.4)	165.9 (6.3)	165.8 (6.4)	165.9 (6.4)	165.7 (6.3)
Ever cigarette smoker (%)	41.4	43.9	47.4	41.2	43.4	44.4
University or higher vocational education (%)	9.8	9.7	9.7	9.7	10.1	9.3
Nonoccupational physical activity (minutes/day)	66.1 (50.4)	63.1 (51.0)	64.2 (52.9)	62.4 (49.6)	62.4 (50.7)	64.0 (51.4)
Family history of cancer (%)	47.9	52.3	52.1	52.4	53.1	51.4
Age at menarche (years)	13.7 (1.8)	13.5 (1.7)	13.5 (1.7)	13.5 (1.7)	13.5 (1.7)	13.6 (1.7)
Age at menopause (years)	48.8 (4.4)	49.0 (4.3)	48.7 (4.4)	49.2 (4.3)	49.0 (4.3)	49.0 (4.3)
Parous (%)	81.7	80.8	81.3	80.4	80.9	80.7
Age at first birth (in parous, years)	27.0 (4.2)	27.0 (4.2)	26.9 (4.2)	27.1 (4.2)	27.2 (4.2)	26.9 (4.3)
Number of children (in parous, *n*)	3.4 (1.9)	3.3 (1.8)	3.3 (1.9)	3.2 (1.8)	3.3 (1.8)	3.3 (1.8)
Oral contraceptive use (%)	25.3	24.3	25.2	23.6	25.1	23.4
Hormone replacement therapy (%)	13.5	13.3	12.9	13.6	13.5	13.1
Daily energy intake (kcal)	1,689 (391)	1,689 (386)	1,687 (381)	1,691 (389)	1,688 (389)	1,690 (382)
Total nut intake (g/day)	4.5 (8.6)	4.4 (8.8)	4.2 (8.6)	4.5 (8.9)	4.4 (9.0)	4.4 (8.5)
Tree nut intake (g/day)	1.1 (4.1)	1.0 (3.2)	1.0 (3.1)	1.0 (3.3)	1.0 (3.3)	1.0 (3.1)
Peanut intake (g/day)	3.4 (7.0)	3.4 (7.4)	3.2 (7.3)	3.5 (7.5)	3.4 (7.6)	3.4 (7.3)
Peanut butter intake (g/day)	1.2 (3.5)	1.1 (3.2)	1.0 (3.3)	1.1 (3.2)	1.1 (3.2)	1.1 (3.3)
Alcohol intake (g/day)	6.0 (9.6)	6.7 (11.1)	6.9 (11.6)	6.5 (10.7)	6.9 (11.4)	6.4 (10.7)

men or women (**Table 2**). Also no associations were found for smoking- and alcohol-(un)related cancers, except for a borderline significant positive association between 0.1–<5 g peanut butter intake/day and smoking-unrelated cancer in men [HR (95% CI), 1.17 (1.00–1.37)].

Heterogeneity tests between smoking-related and smoking-unrelated cancers were significant for all nut variables in men ($P_{heterogeneity} < 0.001$). This is probably the result of the large number of cases and the opposite directions of the nonsignificant associations in the smoking-related and smoking-unrelated subgroups in men.

Discussion

Our results are in line with the only other cohort study that investigated the relation between nut intake and total cancer risk, in which also no significant associations were observed (2). Prospective evidence on total cancer is thus very limited. In a recent meta-analysis, a significantly reduced "overall" cancer risk was observed after pooling 33 prospective cohort studies that investigated the relations between nut intake and several cancer (sub)types (7). However, this pooled estimate is not informative, because it does not include all cancer types and might be affected by publication bias.

Here, we presented results for total cancer, but associations for several cancer (sub)types have been investigated previously in the NLCS, for example, ref. 5. Strengths of the NLCS include the prospective design, the inclusion of all cancer types (except skin cancer), the large number of cases, and the long and complete follow-up of 20.3 years. Unfortunately, we only have baseline measurements. Nevertheless, the FFQ showed adequate reproducibility (8) and the NLCS consists of an older population with relatively stable dietary

Table 2. Multivariable-adjusted HRs and 95% CI for total cancer and for smoking-(un)related and alcohol-(un)related cancers, according to nut and peanut butter consumption, the NLCS, 1986–2006.

			Total cancer		Smoking-related cancer		Smoking-unrelated cancer		Alcohol-related cancer		Alcohol-unrelated cancer	
	Median intake[a]	Person-years	Cases	Multivariable-adjusted[b] HR (95% CI)	Cases	Multivariable-adjusted[b] HR (95% CI)	Cases	Multivariable-adjusted[b] HR (95% CI)	Cases	Multivariable-adjusted[b] HR (95% CI)	Cases	Multivariable-adjusted[b] HR (95% CI)
Men												
Total nut intake (g/day)												
0	0.0	8,231	3,889	1.00 (reference)	2,292	1.00 (reference)	1,597	1.00 (reference)	761	1.00 (reference)	3,128	1.00 (reference)
0.1–<5	2.5	8,972	3,990	0.96 (0.84–1.11)	2,175	0.94 (0.80–1.09)	1,815	1.01 (0.86–1.17)	789	0.96 (0.81–1.14)	3,201	0.97 (0.83–1.12)
5–<10	8.5	3,679	1,527	0.91 (0.75–1.09)	816	0.88 (0.72–1.08)	711	0.95 (0.78–1.16)	305	0.90 (0.71–1.12)	1,222	0.91 (0.75–1.10)
10+	21.4	6,496	2,778	0.96 (0.82–1.13)	1,440	0.88 (0.74–1.05)	1,338	1.08 (0.91–1.28)	530	0.91 (0.75–1.11)	2,248	0.97 (0.83–1.14)
P_{trend}				0.69		0.18		0.38		0.38		0.82
Continuous, per 5 g/day increment				1.00 (0.98–1.02)		0.99 (0.96–1.01)		1.01 (0.99–1.03)		0.99 (0.96–1.01)		1.00 (0.98–1.02)
$P_{heterogeneity}$								<0.001				0.88
Tree nuts (g/day)												
0	0.0	19,756	8,951	1.00 (reference)	5,056	1.00 (reference)	3,895	1.00 (reference)	1,754	1.00 (reference)	7,197	1.00 (reference)
0.1–<5	1.6	6,251	2,660	0.98 (0.85–1.12)	1,385	0.95 (0.82–1.10)	1,275	1.00 (0.87–1.16)	514	0.95 (0.81–1.12)	2,146	0.98 (0.85–1.13)
5+	8.9	1,372	573	1.02 (0.79–1.31)	282	0.95 (0.72–1.26)	291	1.08 (0.83–1.42)	117	1.03 (0.76–1.40)	456	1.01 (0.78–1.31)
P_{trend}				0.98		0.60		0.58		0.96		0.99
Continuous, per 5 g/day increment				1.01 (0.94–1.10)		1.00 (0.91–1.09)		1.02 (0.93–1.12)		1.01 (0.92–1.11)		1.01 (0.93–1.10)
$P_{heterogeneity}$								<0.001				0.81
Peanuts (g/day)												
0	0.0	9,277	4,311	1.00 (reference)	2,524	1.00 (reference)	1,787	1.00 (reference)	862	1.00 (reference)	3,449	1.00 (reference)
0.1–<5	2.5	9,777	4,321	0.98 (0.86–1.12)	2,332	0.94 (0.81–1.08)	1,989	1.05 (0.91–1.22)	847	0.94 (0.80–1.11)	3,474	0.99 (0.86–1.14)
5–<10	8.5	2,978	1,249	0.95 (0.77–1.16)	655	0.87 (0.70–1.08)	594	1.07 (0.86–1.32)	241	0.90 (0.71–1.15)	1,008	0.96 (0.78–1.17)
10+	21.4	5,346	2,303	0.98 (0.83–1.16)	1,212	0.91 (0.76–1.09)	1,091	1.10 (0.92–1.31)	435	0.90 (0.73–1.09)	1,868	1.01 (0.85–1.19)
P_{trend}				0.87		0.34		0.37		0.33		0.93
Continuous, per 5 g/day increment				1.00 (0.97–1.02)		0.99 (0.96–1.01)		1.01 (0.98–1.03)		0.99 (0.96–1.01)		1.00 (0.97–1.02)
$P_{heterogeneity}$								<0.001				0.71
Peanut butter (g/day)												
0	0.0	19,616	8,687	1.00 (reference)	4,891	1.00 (reference)	3,796	1.00 (reference)	1,725	1.00 (reference)	6,962	1.00 (reference)
0.1–<5	1.2	4,696	2,095	1.09 (0.94–1.27)	1,086	1.03 (0.88–1.21)	1,009	1.17 (1.00–1.37)	374	0.98 (0.82–1.18)	1,721	1.12 (0.96–1.30)
5+	9.6	3,066	1,402	1.09 (0.91–1.31)	746	1.05 (0.86–1.28)	656	1.14 (0.94–1.38)	286	1.15 (0.93–1.42)	1,116	1.08 (0.90–1.30)
P_{trend}				0.35		0.66		0.19		0.21		0.44
Continuous, per 5 g/day increment				1.05 (0.99–1.13)		1.05 (0.97–1.13)		1.06 (0.99–1.14)		1.08 (1.00–1.17)		1.05 (0.98–1.12)
$P_{heterogeneity}$								<0.001				0.07
Women												
Total nut intake (g/day)												
0	0.0	11,028	2,865	1.00 (reference)	1,268	1.00 (reference)	1,597	1.00 (reference)	1,533	1.00 (reference)	1,332	1.00 (reference)
0.1–<5	2.1	10,290	2,615	1.03 (0.90–1.18)	1,101	1.02 (0.88–1.19)	1,514	1.04 (0.90–1.20)	1,389	1.00 (0.87–1.16)	1,226	1.06 (0.92–1.23)
5–<10	7.8	2,942	720	1.05 (0.85–1.29)	294	1.01 (0.80–1.28)	426	1.08 (0.86–1.34)	377	0.98 (0.79–1.23)	343	1.12 (0.89–1.41)
10+	15.7	3,797	871	0.89 (0.74–1.08)	350	0.83 (0.66–1.03)	521	0.94 (0.77–1.16)	457	0.85 (0.69–1.04)	414	0.95 (0.77–1.18)
P_{trend}				0.26		0.09		0.59		0.11		0.66
Continuous, per 5 g/day increment				0.99 (0.96–1.03)		0.98 (0.94–1.02)		1.00 (0.96–1.04)		0.99 (0.95–1.03)		1.00 (0.96–1.03)
$P_{heterogeneity}$								0.07				0.91

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Table 2. Multivariable-adjusted HRs and 95% CI for total cancer and for smoking-(un)related and alcohol-(un)related cancers, according to nut and peanut butter consumption, the NLCS, 1986–2006. (Cont'd)

			Total cancer		Smoking-related cancer		Smoking-unrelated cancer		Alcohol-related cancer		Alcohol-unrelated cancer	
	Median intake[a]	Person-years	Cases	Multivariable-adjusted[b] HR (95% CI)	Cases	Multivariable-adjusted[b] HR (95% CI)	Cases	Multivariable-adjusted[b] HR (95% CI)	Cases	Multivariable-adjusted[b] HR (95% CI)	Cases	Multivariable-adjusted[b] HR (95% CI)
Tree nuts (g/day)												
0	0.0	19,752	5,030	1.00 (reference)	2,178	1.00 (reference)	2,852	1.00 (reference)	2,688	1.00 (reference)	2,342	1.00 (reference)
0.1–<5	1.6	6,686	1,712	1.05 (0.91–1.20)	692	1.02 (0.87–1.19)	1,020	1.07 (0.92–1.24)	891	0.99 (0.85–1.16)	821	1.11 (0.95–1.29)
5+	8.9	1,619	329	0.83 (0.64–1.08)	143	0.85 (0.63–1.15)	186	0.82 (0.62–1.08)	177	0.82 (0.62–1.08)	152	0.86 (0.64–1.14)
P_{trend}				0.24		0.34		0.23		0.17		0.44
Continuous, per 5 g/day increment				0.97 (0.90–1.05)		0.96 (0.87–1.06)		0.97 (0.90–1.05)		0.96 (0.88–1.05)		0.98 (0.90–1.06)
$P_{heterogeneity}$								0.09				0.57
Peanuts (g/day)												
0	0.0	13,081	3,363	1.00 (reference)	1,473	1.00 (reference)	1,890	1.00 (reference)	1,781	1.00 (reference)	1,582	1.00 (reference)
0.1–<5	2.0	10,269	2,593	1.04 (0.91–1.18)	1,088	1.03 (0.89–1.19)	1,505	1.04 (0.91–1.20)	1,395	1.03 (0.90–1.19)	1,198	1.05 (0.91–1.21)
5–<10	8.5	2,108	502	0.97 (0.77–1.23)	205	0.95 (0.72–1.24)	297	1.00 (0.78–1.28)	263	0.94 (0.73–1.21)	239	1.01 (0.78–1.31)
10+	17.1	2,598	613	0.93 (0.75–1.15)	247	0.86 (0.67–1.11)	366	0.98 (0.78–1.23)	317	0.88 (0.69–1.11)	296	0.99 (0.78–1.26)
P_{trend}				0.43		0.21		0.75		0.21		0.88
Continuous, per 5 g/day increment				1.00 (0.96–1.04)		0.98 (0.94–1.03)		1.01 (0.96–1.05)		0.99 (0.95–1.04)		1.00 (0.95–1.05)
$P_{heterogeneity}$								0.20				0.79
Peanut butter (g/day)												
0	0.0	20,261	5,166	1.00 (reference)	2,212	1.00 (reference)	2,954	1.00 (reference)	2,757	1.00 (reference)	2,409	1.00 (reference)
0.1–<5	1.2	5,092	1,285	1.04 (0.90–1.22)	550	1.05 (0.88–1.25)	735	1.04 (0.88–1.22)	672	1.03 (0.87–1.21)	613	1.06 (0.90–1.25)
5+	5.3	2,703	620	0.96 (0.78–1.18)	251	0.93 (0.74–1.18)	369	0.98 (0.79–1.22)	327	0.95 (0.76–1.18)	293	0.97 (0.77–1.21)
P_{trend}				0.76		0.63		0.91		0.70		0.86
Continuous, per 5 g/day increment				0.96 (0.88–1.05)		0.95 (0.86–1.05)		0.98 (0.89–1.07)		0.95 (0.86–1.04)		0.98 (0.89–1.07)
$P_{heterogeneity}$								0.50				0.76

[a]Median intake (g/day) in the subcohort.

[b]Adjusted for age (years; continuous), cigarette smoking [status (never, former, and current), frequency (*n*/day; continuous and centered), and duration (years; continuous and centered)], body mass index (<18.5, 18.5–<25, 25–<30, and ≥30 kg/m^2), height (cm; continuous), nonoccupational physical activity (≤30, >30–60, >60–90, and >90 minutes/day), daily energy intake (kcal/day; continuous), alcohol intake (0, 0.1–<5, 5–<15, 15–<30, and 30+ g/day), educational level (low, medium, and high), family history of cancer (no and yes), age at menarche (years; continuous; in women only), age at menopause (years; continuous; in women only), parity and age at first child birth (nulliparous; 1–2 children, <25 years; 1–2 children, ≥25 years; ≥3 children, <25 years; and ≥3 children, ≥25 years; in women only), oral contraceptive use (never and ever; in women only), and hormone replacement therapy use (never and ever; in women only).

habits. Furthermore, we cannot completely exclude residual confounding by (un)measured factors.

In conclusion, the results of this prospective cohort study do no support the hypothesis that nut intake is associated with a reduced total cancer risk in men or women.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

L. Nieuwenhuis: Formal analysis, investigation, writing–original draft, writing–review and editing. **P.A. van den Brandt:** Conceptualization, resources, supervision, funding acquisition, investigation, methodology, project administration, writing–review and editing.

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