## **Supplementary Online Content**

- Baudry J, Assmann KE, Touvier M, et al. Association of frequency of organic food consumption with cancer risk: findings from the NutriNet-Santé prospective cohort study. *JAMA Intern Med.* Published online October 22, 2018. doi:10.1001/jamainternmed.2018.4357
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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. PNNS-GS: Components and Scores According to PNNS Recommendations

	Recommendation	Scoring criteria	Score
	At least 5/d	[0-3.5[	0
1 Fruits and vagatables		[3.5-5[	0.5
1.Fruits and vegetables		[5-7.5[	1
		≥7.5	2
	At each meal	[0-1[	0
	according to appetite		
2.Bread, cereals, potatoes and legumes		[1-3[	0.5
		[3-6[	1
	Chaaga whala aming	≥6	0.5
	Choose whole grains	ΓΟ 1/2Γ	0
2 Whole angin food	and whole-grain breads more often	[0-1/3[	U
3.Whole grain food	oreaus more orien	[1/3-2/3[	0.5
		$\geq 2/3$	1
	3/d (≥55-years-old: 3		1
	to 4/d)	[0-1[	0
	10 174)	[1-2.5[	0.5
43500 111		[2.5-3.5] (≥55-	
4.Milk and dairy products		years-old: [2.5-	1
		4.5])	
		>3.5 (55-years-	0
		old: >4.5)	U
	1 to 2/d	0	0
5.Meat, poultry seafood and eggs		]0-1[	0.5
savieus, poulery seuroou una eggs		[1-2]	1
		>2	0.5
6.Seafood	At least 2/week	<2/week	0
		≥2/week	1
	T: ',	Lipids from added	0
	Limit consumption	fat>16% energy	0
7.Added fat		intake/d	
		Lipids from added fat≤16% energy	1
		intake/d	1
		No use of	
		vegetable oil or	
	Favor fat of	ratio vegetable	0
	vegetable origin	oil/total added	
8.Vegetable added fat		fats≤0.5	
		No use of added	
		fats or ratio	1
		vegetable oil/total	1
		added fats >0.5	
9.Sweetened foods	Limit consumption	Added sugar from	-0.5
3.5 weetelieu 100us	Limit consumption	sweetened foods	-0.5

		\17.50/ amanara		
		≥17.5% energy		
		intake/d		
		Added sugar from		
		sweetened foods	0	
		17.5-12.5% energy		
		intake/d		
		Added sugar from		
		sweetened foods	1	
		<12.5% energy	1	
		intake/d		
Beverages				
	Drink water as	<11 water and	0	
	desired	>250 ml soda/d	U	
	Limit sweetened	\11o4		
	beverages: no more	$\geq$ 11 water and	0.5	
10.Non-alcoholic beverages	than 1 glass/d	>250 ml soda/d		
Ü		<11 water and	0.75	
		≤250 ml soda/d	0.75	
		≥11 water and	1	
		≤250 ml soda/d	1	
	Women advised to			
	drink ≤2 glasses of	Ethanol >20 g/d	0	
	wine/d and $\leq 3$	for women and		
	glasses/d for men	>30g/d for men		
	<u> </u>	Ethanol ≤20 g/d		
11.Alcohol		for women and	0.8	
		≤30g/d for men		
		Abstainers and		
		irregular	4	
		consumers ( <once< td=""><td>1</td></once<>	1	
		a week)		
	Limit consumption	>12g/d	-0.5	
		]10-12]g/d	0	
12.Salt		]8-10]g/d	0.5	
		]6-8]g/d	1	
			1.5	
	At least the	_~ 5/ 4	1.0	
	equivalent of 30		_	
	min/d of brisk	[0-30[ min/d	0	
13.Physical activity	walking			
	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	[30-60[min/d	1	
		≥60 min/d	1.5	
All DNNIG CC 1'C 1D			1.3	

Abbreviations: mPNNS-GS, modified Programme National Nutrition Santé-Guideline Score;

PNNS, Programme National Nutrition Santé

**eTable 2.** Baseline Characteristics Among Included and Excluded Participants, NutriNet-Santé Cohort, France<sup>a</sup>

	Included	Excluded	P <sup>b</sup>
Organic food score (0-32)	8.87 (7.36)	8.53 (7.39)	< 0.0001
Age (years)	44.23 (14.49)	43.39	<0.0001
		(14.60)	
Female (%)	78.0	77.1	<0.0001
Education level (%)			<0.0001
Primary	0.7	0.6	
Secondary	18.2	23.7	
Undergraduate	16.6	18.6	
Postgraduate	64.5	57.1	
Occupational status (%)			< 0.0001
Unemployed	5.9	7.0	
Student	7.7	9.4	
Self-employed, farmer	1.9	2.6	
Employee, manual worker	19.3	21.8	
Intermediate professions	17.6	15.7	
Managerial staff, intellectual profession	23.6	21.2	
Retired	18.4	15.9	
Never employed	5.7	6.4	
Monthly income per household unit (%)			<0.0001
<1,200€	16.2	20.8	
1,200-1,800€	24.6	25.3	

> 1,800-2,700€	23.7	21.2	
> 2,700€	24.2	20.0	
Unwilling to answer	11.2	12.7	
Cohabiting (%)	81.8	80.0	<0.0001
Body mass index (kg/m²)	23.73 (4.49)	24.45	<0.0001
		(5.16)	
Baseline use of dietary supplement (%)	45.4	31.3	<0.0001
Energy intake (kcal/d) <sup>c</sup>	1912.87 (495.00)	1874.28	<0.0001
		(519.96)	
mPNNS-GS (/13.5)	7.81 (1.73)	7.38 (1.67)	<0.0001
Smoking status (%)			<0.0001
Never smoker	50.9	47.7	
Former smoker	33.7	32.2	
Current smoker	15.4	20.1	
Physical activity (%)			0.025
Low	28.7	28.6	
Moderate	37.6	34.4	
High	20.3	20.7	
Missing data	13.4	16.3	
Postmenopausal status (%) <sup>d</sup>	20.8	19.3	<0.0001
Use of hormonal treatment for menopause (%) <sup>d</sup>	4.6	3.8	0.01
Use of oral contraception (%) <sup>d</sup>	20.2	19.6	<0.0001

Abbreviations: mPNNS-GS, modified Programme National Nutrition Santé-Guideline Score

<sup>&</sup>lt;sup>a</sup>Values are means (SD) or % as appropriate

<sup>b</sup>P-value based on linear trend for continuous variables or Mantel-Haenszel chi-square test for categorical variables

<sup>c</sup>Energy intake without alcohol

<sup>d</sup>Among women

**eTable 3.** Parameter Estimates and Hazard Ratios (HR) with 95% Confidence Intervals (95% CI) for All Variables Included in the Main Model, NutriNet-Santé Cohort, France

Variable	Coding	Parameter	HR	Lower CI	Upper CI
		estimate			
Organic food score					
(ref=Q1)					
	Q2	-0.06277	0.939	0.810	1.088
	Q3	-0.08157	0.922	0.793	1.071
	Q4	-0.2926	0.746	0.632	0.882
Sex (ref=Female)	Male	-0.43015	0.650	0.496	0.854
Occupational status					
(ref=Self-employed,					
farmer)					
	Unemployed	0.01231	1.012	0.601	1.706
	Student	-0.12301	0.884	0.368	2.125
	Employee,	0.11235	1.119	0.702	1.785
	manual worker				
	Intermediate	0.23246	1.262	0.794	2.006
	professions				
	Managerial	0.02602	1.026	0.646	1.631
	staff, intellectual				
	profession				
	Retired	0.48144	1.618	1.012	2.588

	Never	0.16101	1.175	0.715	1.930
	employed				
Education level (ref=					
Post-secondary					
graduate)					
	Unidentified	-0.09839	0.906	0.469	1.752
	<high school<="" td=""><td>0.00102</td><td>1.001</td><td>0.868</td><td>1.155</td></high>	0.00102	1.001	0.868	1.155
	diploma				
	High school	0.075	1.078	0.921	1.155
	diploma				
Marital status	Cohabiting	-0.08531	0.918	0.742	1.137
(ref=Single)					
Monthly income per					
household unit					
(ref=Unwilling to					
answer)					
	< 1,200€	0.04262	1.044	0.815	1.336
	1,200-1,800€	-0.03457	0.966	0.781	1.195
	> 1,800-2,700€	0.01629	1.016	0.826	1.251
	> 2,700€	0.06034	1.062	0.864	1.306
Physical activity					
(ref=Low)					
	Moderate	-0.02769	0.973	0.832	1.137
	High	-0.07358	0.929	0.791	1.091
	Missing data	-0.10322	0.902	0.739	1.102

Smoking status					
(ref=Never smoker)					
	Former smoker	0.12268	1.131	1.004	1.273
	Current smoker	0.07954	1.083	0.901	1.301
Alcohol intake (g/d)		0.00511	1.005	1.001	1.009
Family history of	No family	-0.24121	0.786	0.703	0.878
cancer (ref=Yes)	history of cancer				
Body mass index		0.01067	1.011	0.998	1.024
(kg/m²)					
Height (cm)		0.01477	1.015	1.006	1.024
Energy intake (kcal/d)		0.0000127	1	1	1
mPNNS-GS (/13.5)		0.00511	1.005	1.001	1.009
Fiber intake (g/d)		-0.00548	0.995	0.984	1.005
Processed meat intake		-0.00147	0.999	0.996	1.001
(g/d)					
Red meat intake (g/d)		0.0004484	1	0.999	1.002
Parity (ref=0)					
	1 child	-0.0756	0.927	0.735	1.169
	2 children	-0.02871	0.972	0.789	1.197
	>2 children	-0.1705	0.843	0.671	1.060
Postmenopausal status		-0.30295	0.739	0.609	0.896
(ref=No)					
Use of hormonal		0.16575	1.180	0.963	1.446
treatment for					
menopause (ref=No)					

Use of contraception	Yes	0.08115	1.085	0.867	1.356
(ref=No)					

**eTable 4.** Factor Loadings of the Two First PCA-Extracted Factors, NutriNet-Santé Cohort, France<sup>a</sup>

	Factor 1	Factor 2
Food group		
Vegetables	0.59	0.27
Fruit	0.49	0.14
Wholegrain bread	0.39	0.06
Nuts	0.39	0.11
Water and non-sweet beverages (excluding juices)	0.31	0.18
Dried fruits	0.31	0.08
Vegetable oils	0.20	0.32
Sweet products	0.01	0.38
Potatoes	-0.08	0.36
Butter	-0.14	0.39
Alcoholic beverages	-0.18	0.38
Cheese	-0.19	0.41
Bread, rusks	-0.30	0.48
Processed meat	-0.32	0.28

Abbreviation: PCA, principal component analysis

 $^{a}$ Only food groups with a factor loading >|0.3| for at least one of the two factors are displayed in the table

**eTable 5.** Multivariable Associations Between the Organic Food Score (Modeled as a Continuous Variable and as Quartiles) and Overall Cancer Risk, Additional Models, NutriNet-Santé Cohort, France, 2009 to 2016

	Q1	Q2	Q3	Q4	P-	HR for a	P
					trenda	5-point	
						increase	
Cases/non-cases	360/16471	358/17286	353/16887	269/16962			
Suppl. model 4 <sup>b</sup>	1 (ref)	0.94	0.92	0.74	0.0005	0.92	<0.0001
		(0.81-	(0.79-	(0.63-		(0.88-	
		1.09)	1.07)	0.87)		0.96)	
Suppl. model 5 <sup>c</sup>	1 (ref)	0.95	0.93	0.76	0.002	0.92	0.0002
		(0.82-	(0.80-	(0.64-		(0.89-	
		1.10)	1.09)	0.89)		0.96)	
Suppl. model 6 <sup>d</sup>	1 (ref)	0.91	0.89	0.70	0.004	0.91	0.001
		(0.75-	(0.72-	(0.56-		(0.86-	
		1.11)	1.09)	0.88)		0.96)	

Abbreviations: HR, hazard ratio; mPNNS-GS, Programme National Nutrition Santé Guideline Score without the physical activity component; Q, quartile

<sup>a</sup>P-value for linear trend obtained from the quartile classification by modeling organic food score quartiles as an ordinal variable

<sup>b</sup>Suppl. model 4 is adjusted for age (time-scale) and sex, occupational status, education, marital status, monthly income, physical activity, smoking status, alcohol consumption, family history of cancer, month of inclusion, body mass index, height, energy intake, mPNNS-GS and for women, parity, menopausal status, hormonal replacement treatment and oral contraception

<sup>c</sup>Suppl. model 5 is Suppl. model 4 + further adjustments for fiber, processed meat and meat consumption and ultra-processed food

<sup>d</sup>Suppl. model 6 is Suppl. model 4 + further adjustments for fiber, processed meat and meat consumption, with cases occurring during the first two-years of follow-up removed (numbers of cases across quartiles were: 204, 195, 187, 136)

**eTable 6.** Parameter Estimates and Hazard Ratios (HR) with 95% Confidence Intervals (95% CI) for a 'Tandem' Variable Combining Both Different Diet Quality Levels (Reflected by the mPNNS-GS) and Organic Food Consumption Frequencies, NutriNet-Santé Cohort, France

'Tandem' variable <sup>a</sup>	Parameter	HR	Lower CI	Upper CI
	estimate			
High organic food score + high	-0.27	0.78	0.58	1.01
mPNNS-GS vs. low organic food				
score + low mPNNS-GS				
High organic food score + medium	-0.34	0.71	0.53	0.95
mPNNS-GS vs. low organic food				
score + low mPNNS-GS				
High organic food score + low	-0.46	0.63	0.45	0.88
mPNNS-GS vs. low organic food				
score + low mPNNS-GS				

Abbreviations: mPNNS-GS, modified Programme National Nutrition Santé-Guideline Score 
<sup>a</sup>High organic food score: belonging to quartile 4 of the organic food score; low organic food score: belonging to quartile 1 of the organic food score; high mPNNS-GS: belonging to tertile 3 of the mPNNS-GS; medium mPNNS-GS: belonging to tertile 2 of the mPNNS-GS; low mPNNS-GS: belonging to tertile 1 of the mPNNS-GS

**eTable 7.** Dietary Characteristics of Participants According to Quartiles of the Organic Food Score, NutriNet-Santé Cohort, France<sup>a</sup>

	Quartiles of the Organic Food Score				
	Q1	Q2	Q3	Q4	Pb
N	16831	17644	17240	17231	
Organic food score (0-	0.72 (0.82)	4.95 (1.41)	10.36 (1.69)	19.36 (4.28)	< 0.0001
32)					
Nutrient intakes					
% carbohydrates <sup>c</sup>	42.60 (6.90)	42.97 (6.82)	43.10 (7.01)	43.53 (7.18)	< 0.0001
% lipids <sup>c</sup>	39.29 (6.62)	39.00 (6.47)	38.99 (6.60)	39.56 (6.78)	0.0004
% proteins <sup>c</sup>	17.80 (3.97)	17.72 (3.93)	17.58 (4.04)	16.60 (3.95)	< 0.0001
MUFA (g/d)	30.76 (11.21)	30.28 (10.78)	30.35 (11.12)	31.35 (11.74)	< 0.0001
PUFA (g/d)	11.46 (5.37)	11.28 (5.03)	11.44 (5.36)	12.48 (6.22)	< 0.0001
SFA (g/d)	34.54 (13.33)	33.50 (12.66)	32.95 (12.83)	31.74 (12.56)	< 0.0001
Animal proteins (g/d)	58.56 (19.90)	56.47 (19.42)	54.33 (19.84)	46.79 (20.35)	< 0.0001
Vegetable proteins (g/d)	23.69 (7.90)	24.31 (7.87)	25.47 (8.57)	28.40 (10.52)	< 0.0001
Alcohol (g/d)	8.34 (13.84)	8.18 (13.11)	8.17 (12.19)	7.54 (11.30)	< 0.0001
Beta-carotene (g/d)	3057.31	3287.75	3544.41	4102.32	< 0.0001
	(2479.4)	(2523.8)	(2657.4)	(3224.9)	
Calcium (mg/d)	943.26	939.26	941.71	916.81	< 0.0001
	(319.41)	(312.57)	(315.80)	(305.90)	
Cholesterol (mg/d)	329.76	319.67	313.47	289.95	< 0.0001
	(146.68)	(142.60)	(142.45)	(141.84)	
Iron (mg/d)	12.74 (4.69)	13.05 (4.78)	13.64 (4.94)	14.97 (5.57)	< 0.0001
Fibers (g/d)	17.88 (6.55)	18.87 (6.84)	20.05 (7.20)	22.60 (8.31)	< 0.0001

Sodium (mg/d)	2764.38	2722.91	2701.14	2624.57	< 0.0001
	(950.43)	(912.94)	(920.35)	(911.11)	
Folates (µg/d)	312.09	324.22	337.50	361.93	<0.0001
	(113.27)	(114.62)	(119.16)	(130.77)	
Vitamin C (mg/d)	110.62	117.15	121.75	126.34	< 0.0001
	(82.54)	(74.90)	(75.03)	(96.72)	
Vitamin E (mg/d)	11.46 (4.99)	11.44 (4.71)	11.58 (4.85)	12.55 (5.53)	<0.0001
Main food group intakes					
(g/d)					
Vegetables	196.94	213.20	228.70	255.95	<0.0001
	(120.71)	(121.39)	(121.94)	(131.37)	
Fruit	168.80	185.35	199.97	215.65	< 0.0001
	(147.33)	(150.51)	(154.83)	(158.03)	
Vegetable oils	7.97 (8.21)	8.25 (8.34)	8.62 (8.53)	10.49 (10.11)	<0.0001
Legumes	9.11 (22.54)	9.93 (23.16)	11.38 (25.09)	18.31 (33.89)	<0.0001
Nuts	1.55 (7.35)	1.90 (7.34)	3.16 (10.59)	6.69 (15.29)	<0.0001
Potatoes	47.26 (50.96)	44.26 (48.69)	44.12 (49.45)	44.05 (49.59)	<0.0001
Fish	28.16 (35.74)	30.41 (36.90)	31.91 (38.10)	31.45 (37.14)	< 0.0001
Processed meat	23.67 (29.40)	21.15 (27.12)	18.85 (24.92)	15.12 (22.49)	<0.0001
Meat	48.72 (44.51)	44.59 (41.44)	40.77 (40.67)	31.44 (36.81)	<0.0001
Poultry	26.50 (33.39)	25.92 (32.89)	24.69 (32.21)	20.08 (29.20)	<0.0001
Eggs	13.20 (20.99)	13.02 (20.36)	13.36 (20.66)	14.23 (21.21)	<0.0001
Milk	93.46	83.30	73.03	50.45 (94.82)	< 0.0001
	(126.66)	(119.36)	(114.51)		

Abbreviations: MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids

<sup>a</sup>Values are means (SD)

<sup>b</sup>P-value based on linear trend

<sup>c</sup>As % of energy intake (without alcohol)

## eAppendix. Cancer Risk Modeling

Data were analyzed by cancer sites with significant numbers of cases, namely breast, prostate, skin (melanoma and spinocellular carcinoma) and colorectal cancers. Lymphomas were also investigated as of relevance in relation to organic food consumption.

Participants contributed person-time until the date of cancer diagnosis, the date of the last completed questionnaire, the date of death, or November 30, 2016, whichever occurred first. For analysis by cancer site, other cases than the one of interest were censored at the diagnosis date. Thus, other cancer events were considered to be non-cases for the cancer studied and participants contributed person time until the date of diagnosis of their cancer. For breast cancer, supplemental analyses stratified by menopausal status were performed among women. Women contributed person-time to each model according to age at menopause.

Proportional hazards assumption was assessed graphically. A first model was adjusted for age (time-scale) and sex. A second model (main model) was further adjusted for month of inclusion, occupational status, educational level, marital status, monthly income, physical activity, smoking status, alcohol intake, family history of cancer, body mass index (BMI), height, energy intake without alcohol, mPNNS-GS, dietary fiber intake and consumption of meat and processed meat. For women, additional adjustments were performed for the number of biological children, menopausal status at baseline, hormonal treatment for menopause at baseline and oral contraception use at baseline. **eTable 3** provides the parameter estimates and HR (95%CI) for all the independent variables entered into the main model.

Further adjustments for ultra-processed food, fruit and vegetable consumption, dietary supplement use and sun exposure were performed but did not substantially change the risk estimates (data not shown).

In order to consider potential residual confounding related to dietary patterns not captured by the mPNNS-GS, an additional model was adjusted for ultra-processed food consumption, fruit and vegetable consumption, and western and healthy dietary patterns (model 3). To do so, we performed a principal component analysis (PCA) on 59 food groups. Dietary patterns extracted by PCA are independent linear combinations of the food group consumptions, maximizing the explained variance. For each participant, the individual pattern score was calculated by summing the intake of the 59 food groups, weighted by their factor loading. **eTable 4** provides the loadings of the two first PCA-extracted factors.

Additional models (Suppl. models 4 and 5) with different types of adjustments were also performed. Analyses were also performed after excluding cancer cases diagnosed during the two first years of individual follow-up to restrict potential reverse causality bias (Suppl. model 6) (eTable 5).

In addition, to examine the combined effects of various diet quality levels and high frequency of organic food consumption on cancer risk, we created a 'tandem' variable based on both quartiles of the organic food score and tertiles of the mPNNS-GS, consisting of 12 modalities. Each modality represented a particular combination of the two aforementioned scores. For instance, a high-quality diet and high frequency of organic food consumption (defined as belonging to both Q4 of the organic food score and tertile 3 of the mPNNS-GS) was modality 1 while low-quality diet and low frequency of organic food consumption (defined as belonging to both Q1 of the organic food score and tertile 1 of the mPNNS-GS) was modality 12. Analyses were performed using model 2 covariates (reference=belonging to Q1 of the organic food score and tertile 1 of the mPNNS-GS) (eTable 6).

Additionally, as the different food categories included in the organic food score represent different exposure levels to residual pesticides (plant products are more likely to contain pesticide residues than animal products) <sup>1</sup>, a simplified score relying on the main plant-based food groups (fruit; vegetables; flour; soy-based products; bread and cereals; grains and legumes) was also computed in a sensitivity analysis. The association between the simplified

organic food score and risk of cancer was examined using models adjusted for model 2 covariates.

To determine whether the associations varied according to major confounders, we also conducted tests for interactions. In addition, in order to identify vulnerable subgroups, we investigated the association between the organic food score (modeled as quartiles, Q4 vs. Q1, using model 2 covariates) and overall cancer risk stratified by the following factors: sex, age (using median-age as a cut-off), education level, family history of cancer, overall dietary quality, BMI and tobacco status.

