

Prospective association between consumption frequency of organic food and body 2 weight change, risk of overweight or obesity: Results from the NutriNet-Santé Study

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- 1 Prospective association between consumption frequency of organic food and body
- weight change, risk of overweight or obesity: Results from the NutriNet-Santé Study
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- 15 **Running title**: Organic food consumption and corpulence
- 16 **Keywords:** organic food, obesity, prospective cohort study, weight gain

Abbreviations: BMI: body mass index, OS: organic score, mPNNS-GS, PCA: Principal component analysis

Abstract

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A lower body mass index (BMI) has been reported among consumers of organic foods but 18 this relationship has never been examined in a prospective design. Our aim was to 19 prospectively investigate the association between the frequency of organic foods and weight 20 21 change. We analyzed data from 62,224 participants of the NutriNet-Santé cohort (78% women, mean age=45y) with information on consumption frequency of organic foods, dietary 22 intake, and repeated anthropometric data. For 16 products, participants reported their 23 consumption frequency of labeled organic foods (never, occasionally, most of the time). An 24 organic score (OS) with a maximum of 32 points was computed. The associations of the OS 25 (modeled as quartiles (Q)) with change in BMI during follow-up (on average 3·1 y), and with 26 27 the risk of overweight and obesity were estimated ANCOVA and multivariable logistic 28 regression. A lower BMI increase was observed across quartiles of the OS (mean difference (95%CI) Q4 versus Q1= -0·16 (-0·32, -0·01). An increase in OS was associated with a lower 29 risk of overweight and obesity (among non-overweight and non-obese participants at 30 inclusion): odds ratios (95%CI) Q4 versus Q1 were 0.77 (0.68, 0.86) and 0.69 (0.58, 0.82), 31 respectively. Concerning obesity risk, the association was stronger among participants with 32 higher adherence to nutritional guidelines. This study supports a strong protective role of 33 34 consumption frequency of organic foods concerning the risk of overweight and obesity that depends on overall dietary quality. Upon confirmation, these results may contribute to fine-35 36 tune nutritional guidelines by accounting for farming practices in food production.

Introduction

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The global obesity epidemic, involving multifaceted origins, is a major public health issue (1). 38 Overweight and obesity contribute to the global burden of chronic diseases (2) - especially 39 type 2 diabetes and ischemic cardiovascular diseases (3), along with cancers (4,5). 40 41 Among the factors involved in the etiology of obesity, excess caloric consumption, sedentary lifestyle and genetic susceptibility are well-recognized, but there is a growing concern for the 42 identification of novel factors involved such as gut microbiota (6) or environmental chemicals 43 (7-10) 44 Among the different dietary factors, organic food is of major interest since it presents multiple 45 features that could potentially protect from weight gain and obesity. Notably, compared to 46 47 conventional food, organic food has been suggested to present better nutritional values concerning fatty acids profiles and specific micronutrients (11-13). Nonetheless, the possible 48 49 implications at an individual level in terms of daily nutrient intake are unknown due to the lack of food composition tables accounting for farming practices. A small number of clinical 50 studies have been conducted that compared specific nutritional biomarkers according to the 51 type of diet (organic or conventional). However, due to short study durations, these studies 52 were not well-equipped to provide reliable results, and findings were inconsistent (14). 53 54 Organic foods are also characterized by a markedly low level or an absence of pesticide residues, as repeatedly reported in food residue analyses (11,14,15) and in experimental studies 55 showing that adopting an organic diet leads to a drastic reduction in pesticide residues and 56 urine metabolites in children and adults (16-20). For most pesticide families (organochlorines 57 (now banned in the EU but still persistent), organophosphates, and pyrethrynoïds), a large 58 number of molecules have been recognized as endocrine disruptors (21), leading to possible 59 metabolic disorders (22). Indeed, a higher exposure to some of these compounds has been 60 associated with a higher risk for obesity or type 2 diabetes in humans ⁽⁹⁾. 61

62 In this context, consumption of organic foods might contribute to the management of weight gain and of obesity risk. In a recent cross-sectional analysis based on the NutriNet-Santé 63 cohort, we showed that participants identified as regular consumers of organic food, 64 compared to non-consumers, presented reduced odds of being overweight or obese (-36% and 65 -62% in men and -42% and -48% in women, respectively) (23). Comparable findings were 66 reported in the German National Nutrition Survey II (NVS II), a nationwide food 67 consumption study conducted among 13,074 adults: German buyers of organic food exhibited 68 healthier lifestyles compared with non-buyers, and presented lower body weight ⁽²⁴⁾. 69 To the best of our knowledge, no epidemiologic study has yet investigated the prospective 70 relation between consumption frequency of organic foods and the risk of overweight and 71 72 obesity. The main objective of the present study was thus to investigate the longitudinal 73 association between the frequency consumption of organic foods and change in body mass 74 index, the risk of overweight, and the risk of obesity in a very large adult cohort. Given our previous finding that organic food consumers show a higher level of adherence to nutritional 75 recommendations (23) - especially a higher consumption of fruit and vegetables and a lower 76 consumption of animal products -a secondary objective was to explore a potential modifying 77 effect of the nutritional quality of the diet on the investigated associations. 78

Material and methods

Study population

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The NutriNet-Santé is a web-based prospective observational cohort that was launched in France in May 2009. The objectives, design and methodology have been described elsewhere Commission The study was conducted according to the guidelines laid down in the Declaration of Helsinki and was approved by the Institutional Review Board of the French Institute for Health and Medical Research (IRB Inserm no. 0000388FWA00005831) and the "Commission"

- Nationale de l'Informatique et des Libertés" (CNIL no. 908450 and no. 909216). All subjects
- signed an electronic informed consent.

Data collection and computation

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- 89 Volunteers filled in self-administrated questionnaires using a dedicated website at baseline
- and during follow-up on an approximately monthly basis. The baseline questionnaires,
- 91 inquired sociodemographic data and lifestyles, health status, physical activity,
- 92 anthropometrics and diet. These questionnaires were first pilot-tested and then compared to
- traditional assessment methods or objectively validated (26-28).
- 94 Consumption frequency of organic products data
- 95 Two months after enrollment, volunteers were asked to provide information on their
- consumption frequency of 16 labeled organic products (fruit, vegetables, soya, dairy products,
- 97 meat and fish, eggs, grains and legumes, bread and cereals, flour, vegetable oils and
- 98 condiments, ready-to-eat meals, coffee/tea/herbal tea, wine,
- 99 biscuits/chocolate/sugar/marmalade, other foods, dietary supplements). Initially, the
- 100 collection of these data was related to research questions focused on reasons for non-
- consumptions. Consumption frequencies were presented in 8 modalities: (1) most of the time;
- 2) occasionally; 3) never ("too expensive"); 4) never ("product not available"); 5) never ("I'm
- not interested in organic products"); 6) never ("I avoid such products"); 7) never ("for no
- specific reason"); and 8) "I don't know"). For each product, we allocated two and one points
- to the "most of the time" and "occasionally" modalities, respectively (and 0 otherwise) since
- the objective of the present study was to focus on the level of frequency, and not on reasons
- for non-consumption. The 16 dietary components were summed up to provide an *organic*
- score (ranging from 0 to 32).
 - Anthropometric data

At enrollment and yearly after, participants were asked to report weight and height assessed during a medical or occupational health examination by a physician, or from selfmeasurement guided by standardized procedures (on flat surface, lightly dressed, and without shoes). Self-reported anthropometric data have been shown to present an elevated concordance with clinical assessment (26). Body mass index (kg/m2) was calculated as weight divided by the square of height. Subjects were classified as underweight or normal weight (BMI<25), overweight (including obesity; BMI\ge 25), or obese (BMI\ge 30) according to the World Health Organization (WHO) reference values (1). Dietary data and physical activity At baseline, quantitative dietary intakes were assessed using three 24-hour records (24HR), randomly allocated over a two-week period, including two week-days and one weekend day, using a validated method (27,28). Participants reported all foods and beverages consumed at each eating occasion. Portion sizes were estimated with the help of photographs, derived from a previously validated picture booklet (29) or directly entered as grams, volumes or purchased units. Since alcohol is only episodically consumed by most individuals, alcohol intake was

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121 122 123 124 125 126 calculated using either the 24HR or a frequency questionnaire for those identified as abstainers in the three 24HR days. Moreover, since fish and seafood are infrequently 127 consumed by many individuals, the weekly consumption of this food group was assessed by a 128 129 specific frequency question. Individual daily mean food consumption was calculated from the three 24HR, weighted for the type of day (week or weekend day). Nutrient intakes were 130 calculated using the NutriNet-Santé composition table (30). Under-reporters were identified 131 and excluded using the validated method developed by Black (31). To assess nutritional diet 132 quality, a modified version of the validated PNNS-GS (without physical activity) was 133 computed. This modified score, the mPNNS-GS, reflects adherence to the official French 134

nutritional recommendations ⁽³²⁾. The score includes 12 components: eight refer to food-serving recommendations (fruit and vegetables; starchy foods; whole grain products; dairy products; meat, eggs and fish; fish and seafood; vegetable fat; water vs soda) and four refer to moderation in consumption (added fat; salt; sweets; alcohol). Moreover, points are deducted for overconsumption of salt, added sugars, or when energy intake exceeds the estimated energy needs by more than 5%.

In order to also account for *a posteriori* dietary patterns, we performed a principal component analysis (PCA), on 31 aggregated food groups. Dietary patterns obtained by PCA are independent linear combinations of the 31 food group consumptions, maximizing the explained variance. Two dietary patterns were retained based on Cattel's Scree plots and the interpretability of the factors. **Supplementary table S1** presents all factor loading coefficients (corresponding to the correlations between the different food groups and the two dietary patterns) > 0·3. For each participant, the individual pattern score was calculated by summing the intake of the 31 food groups, weighted by their factor loading.

Covariates

At baseline, self-administered questionnaires were used to collect data including age, gender, formal education (≤ high school diploma, high school, post-secondary graduate), occupation (managerial staff, intermediate profession, employee/manual worker, retired, unemployed, never employed/homemaker and self-employed), marital status (cohabiting or single), income, number of children and smoking status (never, former and current). Income per household unit was calculated by dividing the household's total monthly income by the number of consumption units (CU), using the following coefficients: 1 CU for the first adult in the household, 0.5 CU for all other household members aged 14 or older and 0.3 CU for children under 14 (33). The following categories of monthly income were used: <1,200, 1,200-1,800, 1,800-2,700 and >2,700 euros per household unit.

Physical activity was assessed by the International Physical Activity Questionnaire (IPAQ) 160 (34). Metabolic equivalents (MET) measured in minutes per week were computed. The 161 recommended IPAQ categories of physical activity were used: low (<30 min of brisk 162 walking/day), moderate (30 - <60 min/day of brisk walking /day or equivalent) and high (≥60 163 164 min of brisk walking /day or equivalent). The inquired baseline health data included use of medication and self-reported history of 165 diseases (cancer, cardiovascular diseases, hypertension, dyslipidemia and diabetes). 166 Statistical analysis 167 For the present study, we used data from volunteers who were included before June 2014 and 168 169 initially aged 18-74 y. Among them, we selected those 1) who completed the organic 170 questionnaire, 2) with baseline anthropometric data and at least one measurement during follow-up, 3) with available data to compute PNNS-GS and 4) who were not identified as 171 energy underreporters (Figure 1). Follow-up anthropometric data were collected until June 172 2015. 173 The participants included (N=62,224) into our analyses were compared to those excluded, 174 using Mann-Whitney-U tests and Chi square tests. 175 176 Baseline characteristics were presented by quartiles of the organic score. Values represent 177 means (±SD) or percentages, and P-values were calculated using linear contrast tests (for continuous variables) or Chi square trend tests (for categorical variables). 178 The association of the organic score with BMI change was assessed by covariance analysis 179 180 (ANCOVA), modeling change in BMI as a percentage of the baseline value. Mean differences (95% confidence intervals) were presented across quartiles of the organic score. Three 181 different models were performed. The first model was adjusted for baseline age and gender. 182 The second model was further adjusted for year and month of inclusion, follow-up duration, 183 occupation, marital status, education, monthly income per household unit, baseline use of 184

185 dietary supplements, the mPNNS-GS, PCA-extracted dietary patterns scores, energy intake, physical activity and smoking status. The final model was further adjusted for history of 186 diseases (cancer, cardiovascular diseases, diabetes, hypertension and dyslipidemia). 187 In a second set of analyses, we estimated odds ratios (OR) and 95% confidence intervals (CI) 188 for becoming overweight or obese after exclusion of overweight and obese subjects at 189 baseline, respectively (leading to new study samples of n= 43,301 and n=56,806). Three 190 191 multivariate logistic regression models were computed with similar covariables to those used 192 in the covariance analysis. A set of supplementary analyses was performed for the obesity risk outcome. First, stratified 193 194 analyses were conducted according to physical activity level/day brisk walking versus ≥30 195 min/day brisk walking or equivalent), use of dietary supplements (yes versus no), tobacco status (never and former smokers versus current smokers), education level, and level of 196 197 adherence to nutritional guidelines (using tertiles of the mPNNS-GS). Second, we used an 198 alternative method of accounting for potential confounder bias: adjustment for a 'propensity score' that contains information on potential confounders in a combined manner (35). To 199 obtain the propensity score, a multinomial logistic regression model was used to estimate the 200 201 predicted probability of organic food consumption (using quartiles of the 16-point organic score) as a function of a wide range of factors (sociodemographic, health characteristics, food 202 group consumptions). Finally, we used inverse probability weighting to correct the estimates 203 for potential selection bias ⁽³⁶⁾. All tests of statistical significance were two-sided and the type 204 I error was set at 5%. Statistical analyses were performed using SAS® software (version 9.3, 205 206 SAS Institute Inc, Cary, NC, USA).

207 Results

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Comparison of included and excluded participants

209 Compared with excluded subjects, included subjects (N=62,224) were older, had a higher education level and income, were less often smokers and less physically active. They also 210 presented a lower BMI and a higher nutritional quality of the diet (all P-values<0.05, data not 211 212 tabulated). Baseline Characteristics of the sample 213 Baseline characteristics across quartiles of organic score are shown in **Table 1**. Higher levels 214 of the organic score were related to higher proportions of women, participants who were 215 cohabiting, former smokers, physically active participants, individuals reaching a post-216 secondary educational level, and participants with a high income or occupational level. A 217 positive association was also observed with age, follow-up duration and the mPNNS-GS 218 219 (reflecting the nutritional quality of the diet), while there was a negative association with 220 energy intake, alcohol consumption and BMI. Components of the organic score across quartiles of the organic score are shown in **Table 2.** 221 In the first quartile (Q1), participants mostly reported no consumption of any organic 222 products. In the 4th quartile (Q4), participants reported more frequently consuming organic 223 products, especially products of the following food groups: eggs, starchy food, vegetables, 224 vegetable oil, fruits and flour. 225 226 Then mean follow-up time in our study sample was 3.12 (SD=1.37) years. Results on the prospective association between the organic score and change in BMI over time are presented 227 in **Table 3**. In the second model, higher organic score levels were related to a substantially 228 229 lower increase in BMI over time (mean difference Q4 versus Q1= -0·15; confidence interval= -0.31, -0.01, P for trend =0.05). After further adjustment for history of chronic diseases 230 (third model), an even stronger association was observed (mean difference Q4 versus Q1= -231

0.16; confidence interval= -0.32, -0.01, P for trend =0.04).

Results on the prospective association between the organic score and the risk of overweight and obesity are presented in **Table 4**. In the fully-adjusted model, accounting for sociodemographic data, lifestyles and history of chronic diseases, a linear decrease in the risk of overweight was observed across quartiles of the organic score, with risk reduction of 23% in Q4 compared to Q1. Findings concerning the risk of obesity were similar, with a risk reduction of 31% in Q4 compared to Q1. Stratified analyses are presented in Figure 2 and in Supplemental Table S2. We observed that the association between the organic score and the risk of obesity was stronger among participants with a higher nutritional quality of the diet. Overall, in the different stratified analyses, the association between the organic score and the risk of obesity was observed in each sub-group, except for dietary supplement users and participants with an intermediate education level. Accounting for selection bias via inverse probability weighting did not substantially modify our findings (data not shown). Models with additional adjustment for a propensity score are presented in **Supplemental Table S3**. Here, the investigated associations were attenuated but remained statistically significant. **Discussion** The present results show, for the first time, a strong negative association between the consumption frequency of organic foods and BMI change over time, as well as a marked reduction of the risk of overweight and obesity. In stratified analyses, significant associations were observed in almost all investigated subgroups, except for dietary supplement users and participants with an intermediate level of education. Importantly, both participants with a low level of physical activity and participants with a low education level presented a significantly lower risk of obesity with increasing organic food consumption. It is noteworthy that the nutritional quality of the diet, estimated by using an a priori dietary index reflecting adherence to the French nutritional guidelines (32).

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appears to be a key effect modifier. Indeed, the strongest associations were observed among 258 participants presenting a high nutritional quality of the diet. 259 Consumption frequency of organic foods and the risk of obesity or overweight 260 We prospectively observed a markedly lower risk of obesity among subjects with a high 261 consumption frequency of organic foods. Previous investigations of data from the NutriNet-262 Santé cohort have revealed that regular consumers of organic foods presented a healthier diet 263 and healthier lifestyle characteristics (related to physical activity and tobacco use) as 264 compared to irregular consumers or non-consumers. Moreover, regular consumers of organic 265 foods in the NutriNet-Santé study presented specificities with respect to chronic disease 266 history (23,37). After accounting for these potential confounders, the findings of the present 267 268 study were partially attenuated but the association remained strong and highly significant, with a reduction in the risk of obesity of 37% after a 3·1 y follow-up. 269 A similar association was observed for overweight, although the strength of the association 270 was smaller. 271 Comparison of our results with the findings of other studies 272 No previous longitudinal study has investigated the association between organic food 273 consumption frequency and weight change or the risk of overweight and obesity, but a 274 275 potential beneficial link between body weight and organic food consumption or purchase has been documented in several cross-sectional studies (23,24,38). For instance, a previous 276 investigation of NutriNet-Santé data (23) has shown that regular organic food consumers 277 showed a markedly lower probability of overweight (excluding obesity) and obesity 278 compared to non-consumers (-36% and -62% in men and -42% and -48% in women, 279 respectively). In addition, in the German National Nutrition Survey II (24), as compared to 280 non-buyers of organic food, buyers of organic food presented lower proportions of 281 overweight (35.5% versus 39.2%) and obesity (17.9% versus 22.5%). Our findings are also 282

concordant with a small Italian clinical study (including 100 healthy males and 50 males suffering from chronic kidney disease, CDK) that reported a statistically significant reduction in weight among CDK patients after introducing an organic diet for a 2-week period $(85.17\pm13.97 \text{ kg at baseline versus } 79.52\pm10.41 \text{ kg after the 2-week intervention, p}<0.05)^{(39)}$. Overall, the currently available cross-sectional or longitudinal surveys consistently reported an association between higher organic food consumption and a lower BMI. The association with a lower increase in BMI over time that we observed in the present study is of particular interest as it supports a possible role of the organic-based diet in weight management among all subjects, beyond the risk of overweight or obesity among initially normal weight (or underweight) individuals. Modulating effect of the nutritional quality of the diet There is growing evidence supporting the observation that consumers of organic food present a nutritionally healthier diet as well as other beneficial lifestyles such as lower alcohol consumption, no smoking and a higher physical activity level (23,24,40,41). Thus, we hypothesized that the link between consumption of organic foods and body weight might be modulated by the overall nutritional quality of the diet. Indeed, we found that the strongest reduction in obesity risk (related to a higher consumption frequency of organic foods) was observed among participants with a healthier diet. Conversely, among participants with a less healthy diet (susceptible to promote weight gain), the association between consumption frequency of organic food and obesity risk was of smaller magnitude. It is well known that unhealthy eating habits play a key role in the etiology of obesity (3). Therefore, the mode of production of the foods consumed may be of secondary importance in these subjects. It is also possible that their dietary patterns, which are low in fruit and vegetables, lead to less

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contaminated diets.

Several hypotheses can be proposed to explain the differences in the risk of obesity between organic food consumers and non-consumers who present a healthy diet. Because we adjusted and then stratified for the global nutritional quality of the diet (using the mPNNS-GS score) in our models, it is not probable that our results were biased by the fact that organic food consumers present healthier diets. Other possible explanations include differences in organic food and conventional food with respect to various nutritional compounds. First, the results of a number of studies argue for a higher concentration of polyunsaturated fatty acids (especially n-3 fatty acids) in organic dairy and meat products; and of antioxidants (especially vitamin C and phenolic compounds) in organic plant foods (11-13). While observed differences in nutrient content can vary by about 10-68% at the food level (not accounted for in our study), it is possible that the overall variations of nutrient intake in an organic diet is sufficient to affect weight management (42,43). However, this remains to be further evaluated. Another hypothesis is related to the fact that individuals with a higher adherence to the French nutritional guidelines tend to consume more plant-based foods. It is well known that plant foods are frequently contaminated by various pesticide residues (about 45% of the tested samples in Europe) (44) because they are heavily sprayed with pesticides during conventional agricultural production and storage. This hypothesis is in line with findings of human surveys that have related obesity and type 2 diabetes to pesticide exposure (7,9,10,45,46). Thus, unlike the consumption of pesticide-free or only slightly contaminated plant products (11,14,15), a high consumption of conventionally grown plant foods may be related to adverse health effects related to higher pesticide exposure. Indeed, replacing conventional food by organic food has repeatedly been shown to drastically reduce the level of organophosphate residues in human urines (16-20). A specific example of a potential adverse health effect of contaminated fruit and vegetables is that high consumers of conventional or contaminated fruits and vegetables presented a particularly low semen quality

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(47,48). This reinforces the concept that different dietary profiles (with various degrees of intake of contaminated food) lead to different levels of exposure to "obesogen" chemicals (9), but this hypothesis needs to be investigated in future biomonitoring-based studies that compare organic and conventional diets with various dietary profiles. Potential mechanistic pathways explaining the association between organic food consumption and body weight Our findings may be interpreted in light of the reduced exposure to pesticides among organic food consumers. Pesticides (prohibited in organic farming when they are synthetic) often present endocrine-disrupting properties that cause developmental and reproductive abnormalities via the modification of signaling processes (46). Besides, new scientific research argues for a role of pesticides in metabolic disruption, (22) leading to obesity and type 2 diabetes ⁽⁹⁾. Mechanistic pathways depend on the type of pesticides. Previous studies have shown an alteration of glucose and lipid metabolism by organochlorines ⁽⁴⁹⁾. Moreover, organochlorines have been shown to affect the control of adipogenesis through an alteration of glucose transport and glycolysis, an alteration of mitochondrial activity, and of fatty acid oxidation ⁽⁴⁹⁾. Organophosphates have been shown to alter carbohydrate and lipid metabolism by disrupting glucose homeostasis (49). In addition, some pesticides have been shown to affect the regulation of eating behavior and the differentiation of adipocytes ⁽⁵⁰⁾. Further studies are necessary to better evaluate metabolic disruption and the "obesogen" capacity of endocrine-disrupting chemicals contained in conventional foods. Strengths and limitations The main limitation of our study is that it is based on self-reported weight and height data. However, these data have been shown to have a good concordance with data from clinical assessments in a validation study (26). This validation study showed high intraclass correlation coefficients, ranging from 0.94 for height to 0.99 for weight, and the concordance for BMI

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classification was 93% (sensibility=88% and specificity=99%). Second, the generalizability of our findings is limited since participants were volunteers involved in a long-term cohort focused on nutrition and health. The individuals included in our study sample are thus likely to be particularly health conscious. A final limitation pertains to the difficulty to disentangle the role of overall dietary patterns from the role of organic food consumption, despite of the extensive adjustment and stratification made. Since the design of our study is observational, residual confounding cannot be ruled out. In particular, it is likely that unmeasured or only indirectly measured factors, including genetic factors, ethnicity, environmental (e.g. food or built environment) or psychological factors (e.g. occupational stress) may modify the association between organic food consumption and obesity. Our study also presents important strengths. First, the rich and accurately collected data permitted to account for a broad range of potential confounders, including lifestyles and health outcomes. Moreover, the very large sample size of our study enabled us to conduct statistically powerful stratified analyses. Another important strength is the prospective design of our analysis that implies a high level of evidence. Finally, the availability of accurate dietary data allowed us to adjust for the nutritional quality of the diet, using a validated dietary index.

Conclusion

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This study, based on data collected in a very large prospective cohort, is the first to support a prospective relation between consumption frequency of organic foods and body weight change, as well as a strong negative association with the risk of overweight and obesity. The overall nutritional quality of the diet may exert a modulating effect in these relationships, with a stronger effect observed among those presenting a healthy plant-based diet. Further studies, especially studies based on quantitative organic consumption data taking into account a diversity of dietary profiles (plant based, western etc.), are needed to confirm these results. If

confirmed, these findings are of major interest from a public health point of view, as they 382 reinforce the need to fine-tune nutritional guidelines by accounting for the mode of food 383 production. 384 Acknowledgment 385 The authors Nathalie Arnault, Stephen Besseau, Laurent Bourhis, Julien Allègre, Than Duong Van, 386 Younes Esseddik, Cédric Agaesse, Claudia Chahine, Paul Flanzy, Mac Rakotondrazafy and Fabien 387 388 Szabo for their technical contribution to the NutriNet-Santé study. 389 Financial support The NutriNet-Santé study is supported by the French Ministry of Health (DGS), the French 390 Institute for Health Surveillance (InVS), the National Institute for Prevention and Health 391 Education (INPES), the Foundation for Medical Research (FRM), the National Institute for 392 Health and Medical Research (INSERM), the National Institute for Agricultural Research 393 (INRA), the National Conservatory of Arts and Crafts (CNAM), and the University of Paris 394 13. 395 **Conflict of Interest** 396 397 None of the authors declares any conflict of interest. 398 Authorship 399 EKG: conducted the literature review and drafted the manuscript; EKG: performed analyses; EKG, JB, KEA, PG, SH and DL: were involved in the interpretation of results and critically 400 reviewed the manuscript; and SH, PG and EKG: were responsible for the development of the 401 design and the protocol of the study. All authors read and approved the final manuscript. 402

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Table 2 Components of the organic score, across organic score quartiles, Nutrinet-Santé study, N=62,224*

	Q1	Q2	Q3	Q4	\mathbf{P}^{\dagger}
Fruits	0.06 (0.25)	0.57 (0.52)	0.95 (0.41)	1.49 (0.53)	<0.0001
Vegetables	0.07 (0.27)	0.59 (0.55)	0.97 (0.48)	1.51 (0.54)	< 0.0001
Rice, pasta, other cereals	0.06 (0.23)	0.42 (0.51)	0.90 (0.50)	1.62 (0.52)	< 0.0001
Breads	0.05 (0.22)	0.36 (0.51)	0.82 (0.53)	1.44 (0.59)	<0.0001
Flour	0.04 (0.20)	0.23 (0.45)	0.67 (0.62)	1.47 (0.65)	< 0.0001
Vegetable oils	0.04 (0.22)	0.27 (0.51)	0.74 (0.65)	1.58 (0.58)	<0.0001
Dairy products	0.05 (0.23)	0.40 (0.54)	0.86 (0.58)	1.42 (0.65)	<0.0001
Meats & seafoods	0.02 (0.14)	0.19 (0.41)	0.50 (0.54)	0.92 (0.66)	<0.0001
Eggs	0.13 (0.36)	0.70 (0.70)	1.19 (0.70)	1.72 (0.54)	<0.0001
Soja products	0.06 (0.24)	0.20 (0.44)	0.40 (0.59)	0.88 (0.76)	<0.0001
Sweet products	0.03 (0.19)	0.33 (0.48)	0.76 (0.50)	1.38 (0.58)	<0.0001
Tea, coffee, herbal tea	0.04 (0.19)	0.27 (0.47)	0.66 (0.59)	1.33 (0.67)	<0.0001
Wines	0.03 (0.17)	0.14 (0.35)	0.29 (0.47)	0.65 (0.64)	<0.0001
Ready-to-use dishes	0.01 (0.08)	0.06 (0.24)	0.19 (0.39)	0.39 (0.54)	<0.0001
Dietary supplements	0.03 (0.18)	0.13 (0.36)	0.25 (0.49)	0.56 (0.68)	<0.0001
Other dietary items	0.01 (0.12)	0.09 (0.30)	0.24 (0.45)	0.80 (0.80)	<0.0001

Q ; Quartile

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^{*}Values are means (SD) of sub-score given that non-consumption, occasional, regular consumption are coded 0, 1, 2, respectively.

^{538 &}lt;sup>†</sup>P for linear trend

Table 3 Association between organic score in quartile and BMI change over time,

Nutrinet-Santé study, 2009-2015, N=62,224*

model	Q1	Q2	Q3	Q4	P for
					trend
Model 1 [†]	0·00 (ref)	0.01 (-0.13, 0.15)	-0.06 (-0.20, 0.08)	-0.34 (-0.49, -0.20)	<0.0001
Model 2 [‡]	0·00 (ref)	0.03 (-0.11, 0.17)	0.01 (-0.13, 0.16)	-0.15 (-0.31, -0.00)	0.05
Model 3 [§]	0·00 (ref)	0.03 (-0.12, 0.17)	0.01 (-0.14, 0.15)	-0.16 (-0.32, -0.01)	0.04

Q; Quartile

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- *Values are mean differences (95% confident intervals). A negative value (-0·xx) indicates that the observed increase (expressed as a percentage of the initial anthropometric marker) was lower of 0·xx in the respective quartile than in quartile 1 (ref).
- [†]Model 1 is adjusted for age and gender.
- [‡]Model 2 is model 1 further adjusted for month and year of inclusion, duration of follow-up,
 occupation, marital status, education, monthly income per unit, dietary supplement use,
 mPNNS-GS, PCA-extracted dietary patterns scores, energy intake, physical activity and
 tobacco status.
- 550 §Model 3 is model 2 further adjusted for the history of chronic diseases.

Table 4 Prospective association between quartiles of the organic score and overweight or obesity risk, Nutrinet-Santé study, 2009-2015.

	Model	Q1	Q2	Q3	Q4	P for
						trend
Overweight	(N=3,259/40,042)					
	Model 1 [†]	1.00	0.94 (0.86- 1.04)	0.83 (0.75-0.91)	0.62 (0.56-0.69)	<:0001
	Model 2 [‡]	1.00	1.00 (0.91, 1.10)	0.93 (0.84, 1.02)	0.75 (0.67, 0.84)	<-0001
	Model 3 [§]	1.00	1.00 (0.91, 1.10)	0.93 (0.84, 1.03)	0.77 (0.68, 0.86)	<-0001
Obesity	(1,337/55,469)					
	Model 1 [†]	1.00	0.87 (0.75, 1.01)	0.79 (0.68, 0.91)	0.52 (0.45, 0.61)	<:0001
	Model 2 [‡]	1.00	0.93 (0.80, 1.08)	0.90 (0.78, 1.04)	0.66 (0.55, 0.78)	<.0001
	Model 3 [§]	1.00	0.94 (0.81, 1.09)	0.92 (0.79, 1.06)	0.69 (0.58, 0.82)	0.0001

*Overweight (including obesity) and obesity analyses were performed among participants who were not overweight or obese at inclusion, respectively. Values are odds ratios (95% confident intervals), using 1st quartile Q1 as the reference.

[†]Model 1 is adjusted for age and gender.

[‡]Model 2 is model 1 further adjusted for month and year of inclusion, delay of follow-up, occupation, marital status, education, monthly income per unit, dietary supplement use, mPNNS-GS, PCA-extracted dietary patterns scores, energy intake physical activity and tobacco status.

§Model 3 is model 2 further adjusted for the history of chronic diseases.

562 Supplemental Table S1: Factor loading matrix, NutriNet-Santé study

Variable	Factor1	Factor2
Vegetables	0.65	0.14
Fruit	0.45	0.06
Broth	0.43	0.17
Coffee, tea, tisane	0.43	0.01
Soda	-0·42	0.06
Croissants	-0·37	0.03
Nuts	0.36	0.04
Fat and sweet products	-0·35	0.07
Dried fruits	0.33	-0.03
Snacks	-0.28	0.23
Soya products	0.28	-0.16
Meat and meat products	-0.28	0.39
Seafood	0.27	-0.02
Dairy desserts	-0.25	0.04
Bread and breakfast cereals	0.22	0.54
Cakes and pastries	-0·18	0.15
Alcoholic beverages	-0.18	0.34
Margarine	0.16	0.12
Flour	0.13	0.06
Eggs	0.12	0.02
Animal Fat	0.09	0.41
Dairy products	0.07	-0.09
Cheese	-0.05	0.53
Potatoes	0.05	0.41
Vegetable oils	0.03	0.28
Starchy food	0.03	0.07
Meal substitutes	0.02	-0.16
Sauces	-0.01	0.23
Sweet products	-0.01	0.27
Water and non-sweet bevarages	0.01	0.14
Wine	0.01	0.42

*Absolute values < 0.3 are not displayed in the table.

Supplemental Table S2 Prospective association between quartiles of the organic score and obesity risk, stratified analyses, Nutrinet-Santé study, 2009-2015^{*,†}.

	Q1	Q2	Q3	Q4	P for trend
Education					
< high school diploma	1.00	1.21 (0.91, 1.61)	0.88 (0.65, 1.19)	0.73 (0.52, 1.04)	0.04
High school diploma	1.00	0.80 (0.56, 1.14)	0.97 (0.69, 1.35)	0.82 (0.55, 1.20)	0.48
Post-secondary graduate	1.00	0.95 (0.78, 1.15)	0.92 (0.75, 1.12)	0.69 (0.55, 0.87)	0.003
Physical activity					
<30 min/day brisk walking	1.00	0.68 (0.51, 0.90)	0.76 (0.58, 1.01)	0.53 (0.38, 0.74)	0.001
≥30 min/day brisk walking or equivalent	1.00	0.97 (0.80, 1.18)	0.90 (0.73, 1.10)	0.74 (0.59, 0.92)	0.01
Smoking status					
Never or former smokers	1.00	0.95 (0.81, 1.11)	0.90 (0.76, 1.06)	0.72 (0.59, 0.86)	0.001
Current smokers	1.00	0.74 (0.51, 1.06)	0.95 (0.65, 1.38)	0.55 (0.36, 0.86)	0.04
Dietary supplement users					
yes	1.00	1.16 (0.94, 1.45)	1.05 (0.84, 1.32)	0.79 (0.61, 1.03)	0.11
no	1.00	0.92 (0.75, 1.12)	0.75 (0.60, 0.95)	0.67 (0.52, 0.85)	0.0003

*Obesity analyses were performed among participants who were not obese at inclusion (N=56,806). Values are odds ratios (95% confident intervals), using 1st quartile Q1 as the reference.

reference.

†Models are adjusted for age, gender, month and year of inclusion, delay of follow-up,

occupation, marital status, education, monthly income per unit, dietary supplement use,

mPNNS-GS, PCA-extracted dietary patterns scores, energy intake physical activity, tobacco

status and for the history of chronic diseases.

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Supplemental Table S3 Prospective association between quartiles of the organic score

and obesity risk, sensitive analysis, Nutrinet-Santé study, 2009-2015.

Model	Q1	Q2	Q3	Q4	P for trend
Model 1 [†]	1.00	0.87 (0.81, 0.94)	0.79 (0.73, 0.85)	0.52 (0.48, 0.57)	<.0001
Model 2 [‡]	1.00	0.93 (0.87, 1.01)	0.91 (0.84, 0.98)	0.67 (0.61, 0.72)	<.0001
Model 3 [§]	1.00	0.95 (0.88, 1.02)	0.92 (0.86, 0.99)	0.70 (0.64, 0.76)	<.0001

- 575 *Obesity analyses were performed among participants who were not obese at inclusion
- 576 (N=56,806). Values are odds ratios (95% confident intervals), using 1st quartile Q1 as the reference.
- [†]Model 1 is adjusted for age and gender and propensity score.
- [‡]Model 2 is model 1 further adjusted for month and year of inclusion, delay of follow-up,
- occupation, marital status, education, monthly income per unit, dietary supplement use,
- 581 mPNNS-GS, PCA-extracted dietary patterns scores, energy intake physical activity and
- tobacco status.

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583 §Model 3 is model 2 further adjusted for the history of chronic diseases.

Figure 1. Participants of the NutriNet-Santé selected for the present analyses, 2009–2015

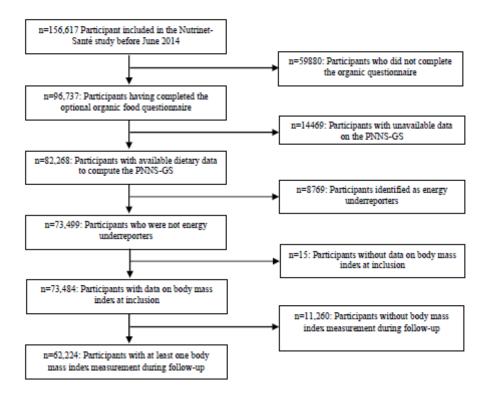


Figure 2. Prospective association between organic score in quartile and risk of obesity

stratified according the nutritional quality of the diet, Nutrinet-Santé, 2009-2015*

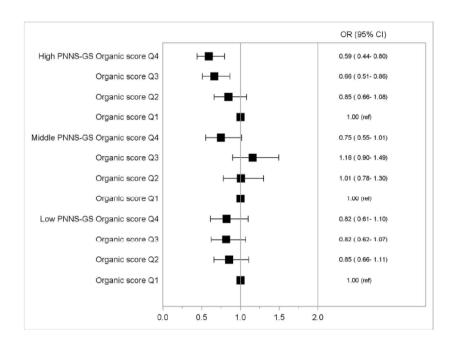


Figure 2. Prospective association between organic score in quartile and risk of obesity stratified according the nutritional quality of the diet, Nutrinet-Santé, 2009-2015*
*Values are odds ratios (95% confident intervals) using the 1st quartile (Q1) as the reference, adjusted for

income per unit, dietary supplement use, mPNNS-GS, PCA-extracted dietary patterns scores energy intake, physical activity, tobacco status and history of chronic diseases.

*Values are odds ratios (95% confident intervals) using the 1st quartile (Q1) as the reference, adjusted for age, gender, month and year of inclusion, delay of follow-up, occupation, marital status, education, monthly income per unit, dietary supplement use, mPNNS-GS, PCA-extracted dietary patterns scores energy intake, physical activity, tobacco status and history of chronic diseases.

Table 1 Baseline characteristics of the sample across organic score quartiles, Nutrinet-Santé study, 2009-2014, N=62,224*

	Q1	Q2	Q3	Q4	P [†]
N	15,245	16,249	15,807	14,923	
Organic score max=32	0.73 (0.82)	4.96 (1.41)	10·36 (1·68)	19·15 (4·21)	<0.0001
Female (%)	73.45	77-94	78.71	81.63	<0.0001
Age (years)	44.16 (15.34)	44.36 (14.83)	45.62 (14.29)	46·72 (13·29)	<0.0001
Follow-up duration (days)	1140·34 (504·64)	1157·01 (500·06)	1144.88 (501.80)	1118·12 (499·69)	<0.0001
Education (%)					<0.0001
Unidentified	0.68	0.66	0.58	0.82	
< high school diploma	23.68	20.09	17·21	15.22	
High school diploma	19·12	17.01	15.44	13.99	
Post-secondary graduate	56-52	62·24	66.76	69.97	
Monthly income per unit household unit in € (%)					<0.0001
Missing	12.06	11.50	10.62	9.35	
900-1200	19-48	16.13	13.26	12.36	
1200-1800	26.76	25.15	22.67	23.09	
1800-2700	21.66	23.72	24.89	26·20	
>2700	20.05	23.50	28.56	29.00	

Occupational categories (%)					<0.0001
Non employed	5.60	5.35	5.18	5.84	
Retired	21.66	20.35	21.40	20.31	
Employee/Manual worker	23.22	19.82	16.67	14.29	
Intermediate profession	16.20	17-44	17.42	18.53	
Managerial staff	17-82	21-47	25.48	28.26	
Never employed	13.93	13.92	12.17	10.43	
Craftsman, shopkeeper, business owner,	1.58	1.66	1.68	2.34	
farmer					
Dietary supplement use (%)	35.52	45.55	51.58	62·13	<0.0001
Cohabiting (%)	80.89	81.88	83.22	86.32	<0.0001
Tobacco status (%)					<0.0001
Former smoker	33.05	33.09	35.51	37.69	
Current smoker	15.29	15.31	14.46	13.12	
Never smoker	51.66	51.60	50.03	49·19	
Physical activity (%)					<0.0001
Missing	15.12	14.36	12.85	11.96	
Low	15.12	14.36	12.85	11.96	
Medium	27.65	27.92	30.04	31.9	

High	33.67	37·15	38.33	39.5	
Energy intake (kcal/d)	1942-90 (514-75)	1914·76 (487·92)	1908·50 (491·42)	1894·24 (474·50)	<0.0001
% Carbohydrates	42.59 (6.89)	42.93 (6.81)	43.05 (6.94)	43.43 (7.11)	<0.0001
% Lipids	39·22 (6·61)	38.95 (6.46)	38.96 (6.58)	39·45 (6·72)	0.0017
% Proteins	17.87 (3.95)	17.80 (3.92)	17.67 (4.01)	16.81 (3.92)	<0.0001
Alcohol consumption (g/d)	8.65 (14.11)	8.27 (13.16)	8.22 (12.23)	7.63 (11.20)	<0.0001
mPNNS-GS	7.60 (1.62)	7.87 (1.62)	8.15 (1.60)	8.44 (1.58)	<0.0001
Body mass index (kg/m²) at baseline	24.50 (4.87)	23.96 (4.56)	23.71 (4.31)	23.00 (3.90)	<0.0001
Obesity [‡] (%) at baseline	11.79	9-42	7-96	5.58	<0.0001
Body mass index (kg/m²) at follow-up	24.72 (4.92)	24·17 (4·62)	23.91 (4.40)	23·13 (4·00)	<0.0001
Obesity [‡] (%) at follow-up	12.62	10.04	8.78	6.06	< 0.0001

529 Abbreviations: Q; Quartile

^{*}All variables were assessed at baseline, except when listed as "at follow-up"

[†]P for linear contrast

532 [‡]Body mass index ≥30 kg/m²