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Association between organic food consumption and Metabolic Syndrome: cross-sectional results from the NutriNet-Santé study

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Abstract

Purpose: Metabolic Syndrome (MetS), a multicomponent condition, is a cardiovascular disease predictor. Although exposure to agricultural pesticides has been suggested as a potential contributor to the rising rates of obesity, type 2 diabetes and other features of metabolic disorders, no studies have focused on the association between consumption of organic food (produced without synthetic pesticides) and MetS. We aimed to investigate the cross-sectional association between organic food consumption and MetS in French adults to determine whether it would be worth conducting further studies, particularly large prospective and randomised trials.

Methods: A total of 8,174 participants from the NutriNet-Santé study who attended a clinical visit and completed an organic food frequency questionnaire were included in this cross-sectional analysis. We evaluated the association between the proportion of organic food in the diet (overall and by food group) and MetS using Poisson regression models while adjusting for potential confounders.

Results: Higher organic food consumption was negatively associated with the prevalence of MetS: adjusted prevalence ratio was 0.69 (95%CI: 0.61, 0.78), when comparing the 3rd tertile of proportion of organic food in the diet with the first one (p-value <0.0001). Higher consumption of organic plant-based foods was also related to a lower probability of having MetS. In addition, when stratifying by lifestyle factors (nutritional quality of the diet, smoking status, physical activity), a significant negative association was detected in each subgroup (p-values <0.05), except among smokers.

Conclusions: Our results showed that a higher organic food consumption was associated with a lower probability of having MetS. Additional prospective studies and randomised trials are required to ascertain the relationship between organic food consumption and metabolic disorders.

Keywords: metabolic syndrome, metabolic traits, organic food consumption, dietary pattern

Abbreviations: BMI, Body Mass Index; CI, Confidence Intervals; CNIL, National Commission on Informatics and Liberty; DBP, Diastolic Blood Pressure; EFSA, European Food Safety Authority; ENNS, French National Nutrition and Health Survey; HDL, High Density Protein; IRB, Institutional Review Board of the French Institute for Health and Medical Research; INSEE, French National Institute of Statistics and Economic Studies; IPAQ, International Physical

Activity Questionnaire; LDL, Low Density Protein; MetS, Metabolic Syndrome; mPNNS-GS, modified Programme National Nutrition Guideline Score; Org-FFQ, organic Food Frequency Questionnaire; Persistent Organic Pollutants, POP; PUFA, Polyunsaturated Fatty Acids; PR, Prevalence Ratios; SBP, Systolic Blood Pressure

1 **Introduction**

2 Metabolic Syndrome (MetS), a collection of metabolic abnormalities, is a clinical condition used
3 to identify individuals at increased risk of cardiovascular mortality early in the disease process
4 [1–4]. Features of MetS combine dyslipidaemia, elevated blood pressure and glycaemia, and
5 abdominal obesity [5]. The prevalence of MetS reached 25% of the population in Europe [6], in
6 line with the rising rate of obesity and type-2 diabetes. In France, where the MetS appeared to be
7 lower than in most industrialised countries, MetS prevalence would be comprised between 14.1%
8 and 21.1% depending on definitions used, according to the French National Nutrition and Health
9 Survey (ENNS) carried out in 2006-2007 [7].

10

11 Although the aetiology of MetS is complex, some major environmental risk factors are well-
12 known, and include diet [8–12], physical activity [13] or tobacco smoking [14]. While the role of
13 dietary patterns (e.g. vegetarian or Mediterranean diets [10–12, 15]) on the risk of onset of MetS
14 has been thoroughly investigated, no studies have taken into consideration the mode of food
15 production (i.e. organic or conventional farming practices) in the association between diet and
16 metabolic status.

17

18 Consumers are increasingly concerned about what they eat and about the potential harmful
19 effects of pesticide residues on their health [16–18], and as a result, more and more are turning to
20 organic food [19], since the use of synthetic pesticides and chemical fertilisers is prohibited by
21 organic farming regulations [20]. The latest European Food safety Authority (EFSA) report on
22 pesticide residues in food [21] indicates a lower dietary exposure to pesticides via organic foods
23 than via conventional crop-based foods. In addition, a cross-over Australian study showed a
24 drastic (about 90%) reduction in urinary organophosphate exposure in adults after a change
25 toward a 80% organic food-based diet [22], in line with several studies previously conducted
26 among children [23–25]. Existing systematic reviews and meta-analyses comparing organically
27 and conventionally produced foods also pointed differences in nutritional composition amongst
28 which higher content in polyphenol compounds [26–29], antioxidants [26, 30–33] and vitamins
29 [26–28, 30] in organic crops as well as the beneficial fatty acid profiles in organic dairy products
30 [27, 31, 32]. They also found lower concentrations of nitrate [26, 27, 30, 33] and lower levels of
31 iodine and selenium in organic milk [32]. Significantly lower concentrations of cadmium in

32 organic food have also been reported [26] while no differences have been observed for other
33 toxic metals [28]. Although these findings overall argue for a more favourable nutritional
34 composition of organic products compared to conventional alternatives, the clinical relevance of
35 these differences, however, remains uncertain.

36
37 The study of the impact of organic food consumption on metabolic status is of high interest as
38 several epidemiological studies have suggested a link between pesticide exposure and metabolic
39 disorders [34–37]. In addition to well-established contributors to cardio-metabolic diseases (such
40 as lack of physical activity and energy overconsumption), newly identified potential risk factors
41 include endocrine disrupting pesticides such as organochlorides, organophosphates, carbamates
42 and pyrethroids [38, 39]. Besides, various nutritional factors - for which differences have been
43 observed between organic and conventional products - have been linked to a decreased risk for
44 some cardiovascular outcomes (such as omega-3 polyunsaturated fatty acids (PUFA) [40, 41],
45 polyphenols [42], several metal pollutants and more specifically cadmium [43] and more
46 controversially nitrate and nitrite [44, 45]).

47
48 Nonetheless, to our knowledge, the link between a diet largely based on organic foods (namely
49 with a potential low pesticide exposure and potentially a more favourable nutritional profile) and
50 metabolic status has never been explored. Studies evaluating the associations between obesity
51 and organic food consumption are scarce ; only three studies (two of which were conducted in the
52 NutriNet-Santé cohort) have shown that regular organic food consumption was negatively related
53 to obesity [46–48].

54
55 Hence, the objective of the present study was to examine the specific relationship between
56 organic food consumption (overall and by food groups) and the presence of MetS using a cross-
57 sectional design, among a large sample of adults residing in France from the NutriNet-Santé
58 study. Through this exploratory analysis, we aimed to provide some evidence in the field of
59 organic food consumption and metabolic disorders to determine whether this particular domain
60 merits further investigation.

61

62

63 **Methods**

64 *Study population and design*

65 This study is based on the NutriNet-Santé study data, an ongoing observational web-based cohort
66 study launched in May 2009. Its overall aim is to investigate the relationships between nutrition
67 and health as well as the determinants of dietary behaviours and nutritional status. The NutriNet-
68 Santé study's rationale, design, and methodology have been described elsewhere [49]. In brief,
69 upon enrolment in the NutriNet-Santé study and each year thereafter, participants are asked to
70 provide information on sociodemographic and various lifestyle factors, health status, physical
71 activity, anthropometric factors, and diet. The NutriNet-Santé study is conducted in accordance
72 with the Declaration of Helsinki, and all procedures were approved by the Institutional Review
73 Board of the French Institute for Health and Medical Research (IRB Inserm number
74 0000388FWA00005831) and the National Commission on Informatics and Liberty (CNIL
75 numbers 908450 and 909216). Electronic informed consent was obtained from each participant
76 (EudraCT no.2013-000929-31).

77
78 Additionally, in 2011-2014, the NutriNet-Santé participants were invited, on a voluntary basis, to
79 attend a visit for biological sampling and clinical examination in one of the local centres
80 throughout France. Electronic and paper written informed consents were obtained from all
81 participants attending the visit. All procedures were approved by the 'Consultation Committee for
82 the Protection of Participants in Biomedical Research' (C09-42 on May 5th 2010) and the CNIL
83 (n° 1460707).

84 85 *Data collection*

86 Dietary data

87 Food and organic food consumption were assessed through a validated self-administered semi-
88 quantitative food frequency questionnaire [50], to which additional questions about frequencies
89 of consumption of organic foods were added (Org-FFQ). The Org-FFQ has been described in
90 details elsewhere [51]. Briefly, the Org-FFQ included 264 food and beverage items, coupled for
91 the most part with specified serving sizes. The questionnaire also included photographs for some
92 specific categories that are not usually consumed in predetermined portion. For each food item,
93 participants were asked to provide their consumption frequency over the past year (through a

94 drop-down list including yearly, monthly, weekly or daily units) as well as the quantities
95 consumed. In addition, the frequency of organic food consumption was assessed using the
96 following statement: ‘How often was the product of organic origin?’. Answers modalities were
97 assessed by a 5 frequency-categories scale with modalities from ‘never’ to ‘always’ (never,
98 rarely, half of time, often and always).

99
100 Modalities of frequencies of organic food consumption were translated into quantitative data by
101 attributing a weight of 0, 0.25, 0.5, 0.75 and 1 to the respective following categories: ‘never’,
102 ‘rarely’, ‘half the time’, ‘often’ and ‘always’. Thus, we calculated the proportion of organic food
103 in the whole diet by dividing the total organic food consumption (in grams per day) out of the
104 total consumption without water (in grams per day). We also calculated the proportion of organic
105 food in 16 main food groups among consumers. Nutrient intakes were assessed using a generic
106 food composition database (independent of the food production - organic or conventional),
107 specifically developed for the items of the Org-FFQ, which was based on the NutriNet-Santé
108 original food composition table that includes more than 3000 items [52].

109
110 In addition, we computed the mPNNS-GS (modified Programme National Nutrition Santé
111 Guideline Score), a diet quality score based on adherence to the French dietary guidelines
112 excluding the physical activity component [53].

113 Information on anteriority of organic food consumption (referring to the number of years for
114 which participants have been consuming organic products) was collected via a questionnaire
115 pertaining to attitudes towards organic food administered in July 2014.

116
117 Covariates

118 At baseline and during follow-up phases, self-administered questionnaires were used to collect
119 information on sociodemographic factors and lifestyle, and medication use, including sex, age,
120 education (highest degree achieved), marital status, number of children, smoking habits, income,
121 place of residence, physical activity (as assessed by the International Physical Activity
122 Questionnaire (IPAQ) [54, 55]), and antidiabetic, antihypertensive and lipid-lowering
123 medications. Monthly income per household unit was calculated using INSEE (French National
124 Institute of Statistics and Economic Studies) calculation [56].

125 Clinical data assessment

126 During the clinical examination, anthropometrics and blood pressure were measured by trained
127 personnel using standardised protocols. Systolic and diastolic blood pressures (SBP and DBP
128 respectively) were measured 3 times at 1-minute intervals in a seated position after lying down
129 for 5 minutes using an automatic validated device (HEM-7015IT; OMRON, Rosny-sous-Bois,
130 France). Mean values were calculated for the analyses. The clinical examination also comprised
131 measures of weight, height, and waist circumference. Weight was measured once using an
132 electronic scale (BC-418MA; TANITA, Tokyo, Japan) with participants only wearing underwear
133 and barefoot. Height was measured once with a wall-mounted measuring rod. Body mass index
134 (BMI in kg/m^2) was calculated. Waist circumference was measured as the circumference midway
135 between the lower ribs and iliac crests.

136

137 Biological data assessment

138 During the visit, blood samples were collected after at least a 6h-fast period and centralised and
139 analysed at a single laboratory (IRSA, Tours, France). Total serum cholesterol (cholesterol
140 oxidase C8000, Abbott), HDL-cholesterol (High Density Protein – cholesterol) (direct accelerator
141 C8000, Abbott), serum triglycerides (glycerol kinase C8000, Abbott) and fasting blood glucose
142 were measured (hexokinase on C 8000 automat, Abbott, Suresnes, France). LDL-cholesterol
143 (Low Density Protein – cholesterol) was calculated using the Friedwald formula [57].

144

145 Definition of MetS

146 Individuals defined as presenting MetS were those having any three of the following five criteria
147 according to the 2009 interim consensus statement [5]:

- 148 - abdominal obesity (waist circumference ≥ 94 cm for men and ≥ 80 cm for women),
- 149 - elevated blood pressure (SBP/DBP $\geq 130/85$ mmHg or antihypertensive medication),
- 150 - elevated triglyceridemia (≥ 150 mg/dL or fibrate medication),
- 151 - low HDL-cholesterolemia (< 40 mg/dL for men or < 50 mg/dL for women),
- 152 - elevated glycaemia (fasting glycaemia > 100 mg/dL or antidiabetic medication).

153

154 *Statistical analysis*

155 Among respondents to the Org-FFQ (n=33,384), we selected those who attended the medical
156 visit (n=9,373), with valid anthropometric and biological data (n=8,354), with available
157 covariates, which led to a final sample of 8,174 individuals (2,602 men and 5,572 women).

158
159 Participant characteristics (sociodemographic and dietary traits) were compared across tertiles of
160 proportion of organic food in the diet using ANCOVA with linear contrast (continuous variables)
161 and Cochran-Mantel-Haenszel trend test (categorical variables). Values are reported as means
162 with standard deviations (SD) or percent as appropriate. Based on the source population
163 (respondents to the Org-FFQ), excluded and included participants were compared using Mann-
164 Whitney U tests and Chi²-tests.

165
166 A total of 16.7% of subjects met the criteria for MetS (23.8% in men and 13.4% in women) in the
167 study sample. Since the occurrence of the dependent variable exceeded 10%, odds ratios from
168 standard logistic regressions could not be considered as appropriate proxies for relative risks [58].
169 We therefore used an alternative method recommended by Zou et al. [59] based on Poisson
170 regression models with robust errors to evaluate the association between tertiles of proportion of
171 organic food in the diet, as well as tertiles of proportion of organic food in 16 food groups, and
172 having MetS (binary dependent variable). The lower tertile of proportion of organic food in the
173 diet was considered as reference category. We reported Prevalence Ratios (PR) and 95%
174 Confidence Interval (95% CI) as well as P-values from linear contrast.

175
176 A first model was crude (model 1). A second model (main model, model 2) was adjusted for age,
177 sex, educational level, monthly income, physical activity, smoking habits, season of blood
178 sampling, time lag between organic food questionnaire completion and clinical visit, occupational
179 status, location, energy intake and overall dietary quality (reflected by the mPNNS-GS as a
180 continuous variable). A supplementary model (model 3) was further controlled for BMI to
181 determine the association of organic food consumption with MetS beyond adiposity. An
182 additional model (model 4) was also performed by adding to the main model the anteriority of
183 organic food consumption (as a categorical variable: non-organic food consumption, organic food
184 consumption for less than 5 years, organic food consumption for more than 5 years). The models

185 pertaining to the association between the proportion of organic food in several food groups and
186 MetS were additionally adjusted for the corresponding food group consumption.

187
188 Furthermore, in an attempt to distinguish the role of organic food from that of potential correlated
189 lifestyles, we investigated the association between the proportion of organic food in the diet (as a
190 continuous variable) and having MetS stratified by various behavioural factors: overall nutritional
191 quality of the diet (using tertiles of mPNNS-GS), smoking habits and physical activity.

192
193 ANCOVA models were also performed to evaluate the relationship between the proportion of
194 organic food in the diet and various metabolic traits (fasting blood glucose, waist circumference,
195 SBP, DBP, serum triglycerides and HDL-cholesterol) among sub-samples who were not taking
196 any related medications for the specific outcome. To improve normality, anthropometric
197 variables and biomarkers were logarithmically transformed before analysis and adjusted
198 geometric means (95%CI) across tertiles of proportion of organic food in the diet are provided.
199 Same confounding covariates as those previously described for MetS in model 2 were used.

200
201 All tests of significance were two-sided, and the type I error was set at 5%. All analyses were
202 performed using SAS software (version 9.4, SAS Institute, Inc.).

203 204 **Results**

205 Participants included in our study were older (58.16 ± 12.34 y vs. 53.20 ± 14.07 y), more often
206 men (32% vs. 25%) and had more frequently a monthly income higher than 2700 € per household
207 unit (32% vs. 39%) than respondents to the Org-FFQ excluded from the analysis (data not
208 tabulated).

209 210 *Characteristics of the participants*

211 Main characteristics of the study sample across tertiles of proportion of organic food in the diet
212 are presented in **Table 1**. Low organic food consumers (tertile 1) consumed no or very little
213 organic food while, in tertile 3, organic food made up, on average, 0.62 (0.18) of the diet.
214 Compared to low organic food consumers, high organic food consumers were less often men,
215 younger and more often highly educated. No statistically significant difference was observed

216 concerning monthly income per household unit across tertiles of proportion of organic food in the
217 diet. High organic food consumers also lived less frequently in a population-dense urban unit
218 (>200 000 inhabitants) than low organic food consumers. They were also more often never
219 smokers and more frequently presented a high physical activity. Higher organic food
220 consumption was also associated with a higher overall nutritional quality of the diet, lower
221 alcohol consumption and a lower body mass index.

222

223 *Association between the proportion of organic food in the diet and MetS*

224 **Table 2** shows the association between tertiles of proportion of organic food in the diet and
225 MetS. In the main model (model 2), higher organic food consumption was associated with a
226 lower probability of having MetS ($PR_{\text{tertile3 vs. tertile 1}}=0.69$, 95%CI=0.61-0.78; p for linear contrast
227 <0.0001). The association was attenuated but persisted even after controlling for BMI ($PR_{\text{tertile3 vs.}}$
228 $\text{tertile1}=0.86$, 95%CI=0.76-0.98; p for linear contrast =0.02) (model 3) or for the anteriority of
229 organic food consumption ($PR_{\text{tertile3 vs. tertile1}}=0.69$, 95%CI=0.59-0.80; p for linear contrast
230 <0.0001) (model 4).

231

232 *Association between the proportion of organic food according to food groups and MetS*

233 **Table 3** shows a marked negative association between an increased consumption of products
234 from organic origin for plant food groups (including fruit and vegetables, starchy foods, whole-
235 grain products and oil; all p for linear contrast ≤ 0.0005) as well as sweetened foods and non-
236 alcoholic beverages (p for linear contrast <0.0001) and MetS. Similar results were observed, but
237 to a lesser extent, for eggs, dairy products and fast food. In contrast, no significant association
238 was found in the cases of seafood and meat, poultry and processed meat (p>0.05).

239

240 *Association between the proportion of organic food in the diet and metabolic components*

241 In the fully adjusted model, among subgroups of individuals who were not taking any related
242 medication for the specific outcome, higher organic food consumption was significantly
243 associated with lower fasting blood glucose, waist circumference, SBP and DBP, and
244 triglycerides (all p for linear contrast <0.05), but not with HDL-cholesterol (**Table 4**).

245

246 *Association between the proportion of organic food in the diet and MetS according to overall*
247 *dietary quality, smoking status and physical activity*

248 Stratified analyses are illustrated in **Figure 1**. After stratifying by tertiles of the mPNNS-GS
249 (reflecting overall dietary quality), higher organic food consumption (modelled as a continuous
250 variable) was negatively associated with MetS, regardless the level of dietary quality, when
251 adjusting for sociodemographic and lifestyle variables. Similar results were obtained when
252 stratifying by other lifestyle factors including smoking status and physical activity level, except
253 among current smokers.

254

255 **Discussion**

256 In this cross-sectional study, we observed that a higher organic food consumption (i.e. a
257 proportion of organic food in the diet >38%, corresponding to the 3rd tertile) was associated with
258 a lower probability of having MetS as well as lower levels of glycaemia, blood pressure,
259 triglycerides, and waist circumference after adjustment for the major known confounding factors.
260 No significant association was observed with the HDL-cholesterol. The negative association was
261 observed, in particular, when the proportion of plant food from organic sources increased, and
262 persisted among different subgroups of the study sample.

263 To the best of our knowledge, no studies had previously investigated the specific association
264 between organic food consumption and metabolic disorders, and MetS in particular.

265 Some data is however available regarding anthropometric traits of organic food consumers. A
266 study conducted in Germany showed that buyers of organic food exhibited lower body weight
267 compared to non-buyers [47]. However, the primary aim of that study was descriptive and did not
268 take into account potential confounding factors. Hence, lower body weights among frequent
269 buyers of organic foods could be attributable to healthier lifestyles rather than to differences in
270 consumption of organic and conventional foods. Previous cross-sectional findings from the
271 NutriNet-Santé have also highlighted a negative association between regular organic food
272 consumption and BMI in fully adjusted models [46]. More recently, in a prospective study
273 carried out in the same cohort [48], we showed, after controlling for major confounders, that an
274 increase of self-reported organic food frequency was associated with a significantly lower risk of
275 overweight and obesity.

276 In the present work, associations between high organic food consumption and the prevalence of
277 MetS remained significant even after carefully adjusting for a wide range of confounders
278 (including overall dietary quality, physical activity, sex, and BMI).

279
280 A potential hypothesis explaining, at least in part, our findings may be the reduced dietary
281 exposure of high organic food consumers to synthetic pesticides. Indeed, as European Union
282 legislation allows only a very limited number of natural pesticides to be used in organic food
283 production, the occurrence of synthetic pesticide residues in organic crops is much lower than in
284 conventional crops [21, 26]. In the last report of the EFSA, 15.5% of organic foods contained
285 pesticide residues (0.8% above the Maximum Residue Level) vs. 44.4% of conventional products
286 (2.7% above the Maximum Residue Level) [21]. It can thus be hypothesised that individuals who
287 consume a high level of organic food in their diet would reduce their overall dietary exposure to
288 pesticides, as highlighted in studies conducted in adults [22, 60] or in children [23, 24].

289
290 Several epidemiological studies have suggested a link between pesticide exposure, obesity and
291 metabolic disorders. Our findings may be interpreted in light of some studies which showed, for
292 instance, a positive association between an increased risk for abnormal glucose regulation and
293 exposure to pyrethroids [61]. The findings from the Agricultural Health cohort study, conducted
294 in 30,000 farmers in the US, suggested that long-term occupational exposure, in particular
295 organochlorine and organophosphate insecticide exposure, could be associated with increased
296 risk of developing diabetes [62]. However, epidemiological studies about the impact of exposure
297 to organophosphorus compounds (widely used in agriculture) in the general population, on
298 metabolic status are lacking.

299
300 Among potential mechanisms, it has been reported that exposure to endocrine disruptors such as
301 various currently used pesticides, i.e. organophosphates and pyrethroids would impact glucose
302 homeostasis and fat metabolism [38, 63]. Organophosphorus compounds would disrupt
303 carbohydrate homeostasis, resulting in elevated serum glucose levels [64]. Among disrupting
304 effects of the organophosphates, mechanistic pathways may involve oxidative damage and
305 inflammatory cytokines, possibly leading to compensatory responses accompanied with reduced
306 insulin signalling in insulin sensitive organs [63].

307 This seems in agreement with our findings concerning biomarkers related to glucose and fat
308 metabolism, namely glycaemia and triglyceride levels. As regards blood pressure, to our
309 knowledge, no studies have investigated the specific association between exposure to widely used
310 pesticides and blood pressure. Thus experimental and epidemiological data focusing on effects of
311 organophosphate, pyrethroid or carbamate exposure and their synergistic association to
312 hypertension risks are necessary. We did not find a significant higher level of HDL-cholesterol in
313 individuals with higher organic food consumption after controlling for main confounding factors,
314 in line with the few available data regarding dietary pesticide exposure and this specific
315 biomarker.

316 Moreover, in addition to the potential effects of dietary pesticide exposure, mainly through
317 conventional plant-food consumption, on cardiometabolic disorders, our results can also be
318 interpreted in light of findings of a study carried out in rats which found overall better health and
319 physiological parameters among animals fed with an organic diet, of which higher concentrations
320 of polyphenols, plasma glucose, leptin or insulin-like growth factor 1 [65].

321 In addition, our analyses interestingly showed a negative association between higher
322 consumption of plant-based foods from organic origin and MetS while no association was
323 detected in the case of meat, poultry and processed meat.

324 These results can be considered in the light of the EFSA report [21] which showed that about half
325 plant food samples were contaminated by pesticide residues and that Maximum Residue Levels
326 were frequently exceeded for some plant-based products (e.g. strawberries, lettuce, apples or
327 oats) while this was not the case for animal-based foods like pork meat or cow milk. Thus,
328 conventional foods from plant origin would be the major contributors to current dietary pesticide
329 exposure, unlike animal-based foods.

330 Interestingly, we found significant negative associations between MetS prevalence and increasing
331 consumption of dairy products and eggs. These findings can be interpreted in light of studies
332 reporting more favourable fatty acid compositions in organic dairy products [31, 32]. Indeed,
333 recent meta-analyses have indicated that organic milk [32], and potentially organic meat [66],
334 contained a higher amount of omega-3 fatty acids, which are main components of a beneficial
335 diet for the cardiovascular system, compared to conventional products. Switch from conventional
336 to organic dairy and meat products could therefore lead to higher amounts of omega-3 fatty acids
337 and in turn positively affect cardiometabolic status. However, it is difficult to conclude to the

338 nutritional significance of these differences on health, as these increases remain probably modest
339 and their effects unknown.

340
341 It should be borne in mind that high organic food consumers are high consumers of fruit,
342 vegetables and whole-grain products [47, 53]. Plant-based diets have also been associated with
343 reduced risk of having MetS [10, 15]. In order to take into account the healthier dietary patterns
344 of high organic food consumers, as well as other potentially healthy lifestyle factors that play a
345 role in the development of MetS, we conducted stratified analyses, allowing to partially
346 overcome the ‘nutritional’ role of dietary patterns. Except in smokers, a higher proportion of
347 organic food in the diet was negatively related to MetS, whatever the subgroups considered. In
348 particular, the association was observed across all subgroups. Among smokers, no association
349 was observed between organic food consumption and MetS. One explanation might be that the
350 tobacco risk factor prevails, and in turn, in this ‘high risk subgroup’, the consumption of organic
351 food could play a minor role. Another explanation might be the relatively small size of that
352 specific subgroup. The non-significant result may therefore be related to limited statistical power.

353
354 *Limitations and strengths*

355 A major limitation of this study includes its cross-sectional design, restricting causal inference.
356 Although we adjusted for a large number of confounding factors including variables related to
357 healthy lifestyles, we cannot omit the residual confounding due to the specific profiles of high
358 organic food consumers (36,37). In addition, the NutriNet-Santé participants are more interested
359 in nutrition and health topics than the general population. Specifically, the participants of the
360 NutriNet-Santé study exhibit specific sociodemographic profiles [67] and healthier dietary habits
361 [68] than the general population. Besides, organic food consumption was assessed using a self-
362 administered food frequency questionnaire which is prone to measurement error. This has also
363 probably led to an overestimation of the consumption in particular for organic food [51]. Finally,
364 we did not have data regarding genetic factors that can play a role in the onset of MetS. Caution
365 is therefore needed when generalising the results.

366
367 Important strengths should also be acknowledged. We used accurate biological measures
368 (performed in a single laboratory) and clinical data (assessed by trained technicians using

369 standardised procedures). The use of the Org-FFQ permitted to obtain detailed data on food
370 consumption, including information on the usual proportion coming from organic sources of
371 several food groups, within the overall diet. The use of a wide range of covariables, including
372 sociodemographic and lifestyle variables, enabled us to precisely characterise the individuals of
373 our study. Furthermore, the large size of the sample enabled us to conduct stratified analyses with
374 a sufficient statistical power, and to have a wide diversity of profiles.

375
376 *Conclusion*
377 In conclusion, our results provide the first insights into the undocumented research field of
378 metabolic health and organic food consumption. Our findings show that the highest the
379 consumption of organic food, the lowest the probability of having MetS. The associations that
380 were observed merit future investigation, and bolster the argument for the conduction of well-
381 designed randomised controlled trials. Besides, further prospective research based on accurate
382 data with regard to the nature of foods consumed is also needed to confirm these findings and
383 assess the long-term effects of organic food consumption on metabolic disorders. In a context of
384 tremendous growth of organic food consumption and where cardiovascular diseases remain the
385 first cause of mortality worldwide, these findings could be of major interest to drive the design of
386 future public health policies.

Contribution statement

SH, PG, DL and EKG conceived and designed research; JB performed the statistical analysis and wrote the article; JB, HL, SA, CJ, BA, SH, MT, DL, PG and EKG were involved in revising the work critically for important intellectual content; JB had primary responsibility for final content. All authors read and approved the final manuscript.

Conflicts of interest

None of the authors declare any conflicts of interest.

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Table 1. Main characteristics of the sample across tertiles of proportion of organic food in the diet, n=8,174, NutriNet-Santé study^a

Characteristics	Tertile 1 (n=2,724)	Tertile 2 (n=2,725)	Tertile 3 (n=2,725)	P trend ^b
Proportion of organic food in the whole diet (ratio)	0.04 (0.04)	0.24 (0.07)	0.62 (0.18)	<0.0001
Men (%)	38.99	30.53	25.98	<0.0001
Age (y)	59.03 (12.84)	57.96 (12.41)	57.50 (11.71)	<0.0001
Educational level (%)				<0.0001
<i>Primary</i>	25.48	23.05	20.99	
<i>High school diploma</i>	14.72	14.09	13.69	
<i>University level or equivalent</i>	59.80	62.86	65.32	
Occupational status (%)				<0.0001
<i>Retired</i>	56.06	51.01	47.05	
<i>Employees</i>	9.14	9.69	9.69	
<i>Intermediate profession</i>	10.61	12.48	12.4	
<i>Managerial staff</i>	15.16	19.60	20.37	
<i>Never employed</i>	7.60	6.24	8.55	
<i>Self employed</i>	1.43	0.99	1.94	
Monthly income per household unit (%)				0.49
<i>Refuse to declare</i>	4.70	4.18	5.21	
<i>900-1200 €</i>	8.26	6.72	7.78	
<i>1200-1800 €</i>	20.15	19.63	20.15	
<i>1800-2700 €</i>	27.90	28.77	29.43	
<i>>2700 €</i>	38.99	40.70	37.43	
Location (%)				<0.0001
<i>Rural community</i>	16.45	18.79	21.98	
<i>Urban unit with a population smaller than 20 000 inhabitants</i>	13.99	14.13	16.11	
<i>Urban unit with a population between 20 000 and 200 000 inhabitants</i>	15.16	16.59	16.00	
<i>Urban unit with a population higher than 200 000 inhabitants</i>	54.41	50.50	45.91	
Smoking habits (%)				0.03
<i>Never smoker</i>	46.26	47.63	50.61	
<i>Former smoker</i>	44.35	43.89	43.08	
<i>Current smoker</i>	9.40	8.48	6.31	
Physical activity level (%)				<0.0001
<i>Low</i>	20.30	17.03	14.72	
<i>Moderate</i>	40.42	42.06	39.60	
<i>High</i>	39.28	40.92	45.69	
Time lag between dietary data collection and visit (months)	23.90 (11.38)	22.99 (11.39)	22.17 (11.36)	<0.0001
mPNNs-GS (/13.5)	8.35 (1.79)	8.65 (1.71)	8.86 (1.78)	<0.0001
Alcohol consumption (g/d)	127.77 (173.76)	121.85 (159.03)	98.07 (121.78)	<0.0001

Energy intake (kcal/d)	2032.06 (644.43)	2021.03 (609.60)	2027.76 (617.92)	0.80
Carbohydrates ^c	39.40 (7.50)	39.27 (7.40)	39.45 (7.43)	0.81
Lipids ^c	40.70 (6.88)	41.20 (6.92)	42.38 (7.27)	<0.0001
Proteins ^c	19.51 (3.58)	19.13 (3.45)	17.80 (3.48)	<0.0001
BMI (kg/m ²)	25.14 (4.52)	24.69 (4.34)	23.87 (3.99)	<0.0001

Abbreviations: BMI, Body Mass Index.

^a Values are means (SD) or percent, as appropriate.

^b Linear contrast test from ANCOVA (continuous variables) or Mantel-Haenszel Chi² trend-test (categorical variables).

^c As a percentage of alcohol-free energy intake.

Table 2. Association between tertiles of proportion of organic food in the diet and MetS, n=8,174, NutriNet-Santé study^a

	Proportion of organic food in the whole diet (ratio)			P for linear contrast
	Tertile 1 [0.00-0.12[Tertile 2 [0.12-0.38[Tertile 3 [0.38-1.00]	
N	2,724	2,725	2,725	
Cases N (%)	565 (20.7)	469 (17.2)	329 (12.1)	
<i>Model 1</i>	1 (ref)	0.83 (0.74, 0.93)	0.58 (0.51, 0.66)	<0.0001
<i>Model 2</i>	1 (ref)	0.91 (0.82, 1.02)	0.69 (0.61, 0.78)	<0.0001
<i>Model 3</i>	1 (ref)	0.98 (0.88, 1.09)	0.86 (0.76, 0.98)	0.02
<i>Model 4^b</i>	1 (ref)	0.94 (0.83, 1.06)	0.69 (0.59, 0.80)	<0.0001

Abbreviations: MetS, Metabolic Syndrome; ref, reference.

^a Values are prevalence ratios, PR (95%CI) for the relation between the proportion of organic food as a categorical variable (tertiles) and Metabolic Syndrome modelled as a binary variable.

Model 1 is unadjusted. Model 2 is adjusted for age, sex, educational level, monthly income, physical activity, smoking habits, season of blood sampling, time lag between organic food questionnaire completion and clinical visit, occupational status, location, energy intake and overall dietary quality (estimated by the mPNNs-GS as a continuous variable). Model 3 is Model 2 further adjusted for BMI. Model 4 is Model 2 further adjusted for the anteriority of organic food consumption.

^b As the questionnaire from which the question was extracted was optional, sample size was 6,911.

Table 3. Association between tertiles of proportion of organic food according to food groups and MetS, NutriNet-Santé study^a

	N ^b	Proportion of organic food of the food group (ratio)			P for linear contrast
		Tertile 1	Tertile 2	Tertile 3	
Fruit and vegetables (including juices and soups)	8,169	1 (ref)	0.95 (0.85, 1.06)	0.78 (0.69, 0.89)	<0.0001
Starchy foods	8,170	1 (ref)	1.00 (0.90, 1.11)	0.69 (0.61, 0.79)	<0.0001
Whole-grain products	6,850	1 (ref)	0.99 (0.87, 1.12)	0.78 (0.68, 0.90)	0.0005
Oil	8,093	1 (ref)	0.97 (0.87, 1.09)	0.74 (0.65, 0.84)	<0.0001
Seafood	7,963	1 (ref)	0.89 (0.77, 1.03)	1.02 (0.92, 1.13)	0.75
Meat, poultry, processed meat	7,939	1 (ref)	1.06 (0.95, 1.19)	0.98 (0.87, 1.11)	0.76
Eggs	7,907	1 (ref)	0.92 (0.82, 1.04)	0.83 (0.73, 0.93)	0.002
Dairy products	8,025	1 (ref)	0.93 (0.83, 1.04)	0.84 (0.75, 0.95)	0.004
Butter, margarine	7,583	1 (ref)	0.95 (0.85, 1.07)	0.82 (0.72, 0.92)	0.0006
Sweetened foods	8,166	1 (ref)	0.91 (0.82, 1.02)	0.69 (0.61, 0.78)	<0.0001
Alcoholic beverages	7,680	1 (ref)	0.89 (0.78, 1.01)	0.88 (0.78, 0.99)	0.03
Non-alcoholic beverages	8,174	1 (ref)	0.93 (0.83, 1.03)	0.67 (0.59, 0.76)	<0.0001
Fast food	7,934	1 (ref)	0.94 (0.83, 1.08)	0.87 (0.78, 0.97)	0.01
Extra food (including snacks, chips, salted biscuits, dressing and sauces)	8,133	1 (ref)	0.97 (0.86, 1.08)	0.76 (0.67, 0.86)	<0.0001
Other fats (including mayonnaise, fresh cream, vegetal fresh cream)	7,613	1 (ref)	1.10 (0.98, 1.24)	0.89 (0.79, 1.00)	0.05
Dairy and meat substitutes (including soy-based products) ^c	3,275	N\A	1 (ref)	0.75 (0.62; 0.91)	N\A
Plant-based products (fruit and vegetables, starchy foods, whole-grain products, oil, dairy- and meat substitutes)	8,174	1 (ref)	0.96 (0.86, 1.07)	0.76 (0.67, 0.86)	<0.0001

Abbreviations: MetS, Metabolic Syndrome; ref, reference.

^a Values are prevalence ratios, PR (95%CI) for the relation between the proportion of organic food in the food group, as a categorical variable (tertiles) and Metabolic Syndrome modelled as a binary variable, adjusted for age, sex, educational level, monthly income, physical activity, smoking habits, season of blood sampling, time lag between organic food questionnaire completion and clinical visit, occupational status, location, energy intake, overall dietary quality (estimated by the mPNNS-GS as a continuous variable) and food group intake, among consumers of the food group.

^b Number of consumers of the food group.

^c Groups were defined using the median value as the number of non-consumers of the food group was particularly high.

Table 4. Association between tertiles of proportion of organic food in the diet and metabolic traits, NutriNet-Santé study^a

	N	Proportion of organic food in the whole diet (ratio)			P for linear contrast
		Tertile 1	Tertile 2	Tertile 3	
Fasting blood glucose (g/L)					
<i>Model 1</i>	8,174	0.91 (0.91; 0.92)	0.90 (0.90; 0.91)	0.89 (0.89; 0.90)	<0.0001
<i>Model 2</i>	7,941	0.91 (0.90; 0.91)	0.91 (0.90; 0.91)	0.90 (0.90; 0.91)	0.01
Waist circumference (cm)					
<i>Model 1</i>	8,174	84.91 (84.44; 85.37)	83.23 (82.79; 83.68)	80.88 (80.48; 81.29)	<0.0001
<i>Model 2</i>	8,174	86.57 (85.93; 87.21)	85.99 (85.35; 86.64)	84.1 (83.47; 84.73)	<0.0001
SBP (mmHg)					
<i>Model 1</i>	8,174	129.03 (128.40; 129.67)	126.99 (126.36; 127.62)	125.54 (124.93; 126.14)	<0.0001
<i>Model 2</i>	6,170	127 (126.1; 127.9)	126.1 (125.2; 127.1)	125.4 (124.4; 126.3)	0.0002
DBP (mmHg)					
<i>Model 1</i>	8,174	76.89 (76.53; 77.25)	75.97 (75.61; 76.32)	75.68 (75.32; 76.04)	<0.0001
<i>Model 2</i>	6,170	77.16 (76.56; 77.78)	76.45 (75.84; 77.07)	76.10 (75.50; 76.72)	0.0002
Serum triglycerides (g/L)					
<i>Model 1</i>	8,174	0.92 (0.90; 0.93)	0.89 (0.88; 0.91)	0.85 (0.83; 0.86)	<0.0001
<i>Model 2</i>	7,693	0.92 (0.89; 0.94)	0.91 (0.89; 0.94)	0.87 (0.85; 0.89)	<0.0001
HDL-cholesterol (g/L)					
<i>Model 1</i>	8,174	0.60 (0.60; 0.61)	0.62 (0.61; 0.62)	0.63 (0.62; 0.63)	<0.0001
<i>Model 2</i>	6,846	0.59 (0.59; 0.60)	0.59 (0.59; 0.60)	0.60 (0.59; 0.61)	0.25

Abbreviations: BMI, Body Mass Index; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; HDL, High Density Protein, LDL, Low Density Protein.

^a Values are adjusted geometric means (95%CI) for the relation between the proportion of organic food as a categorical variable (tertiles) and metabolic traits. P-value referred to log-transformed variables.

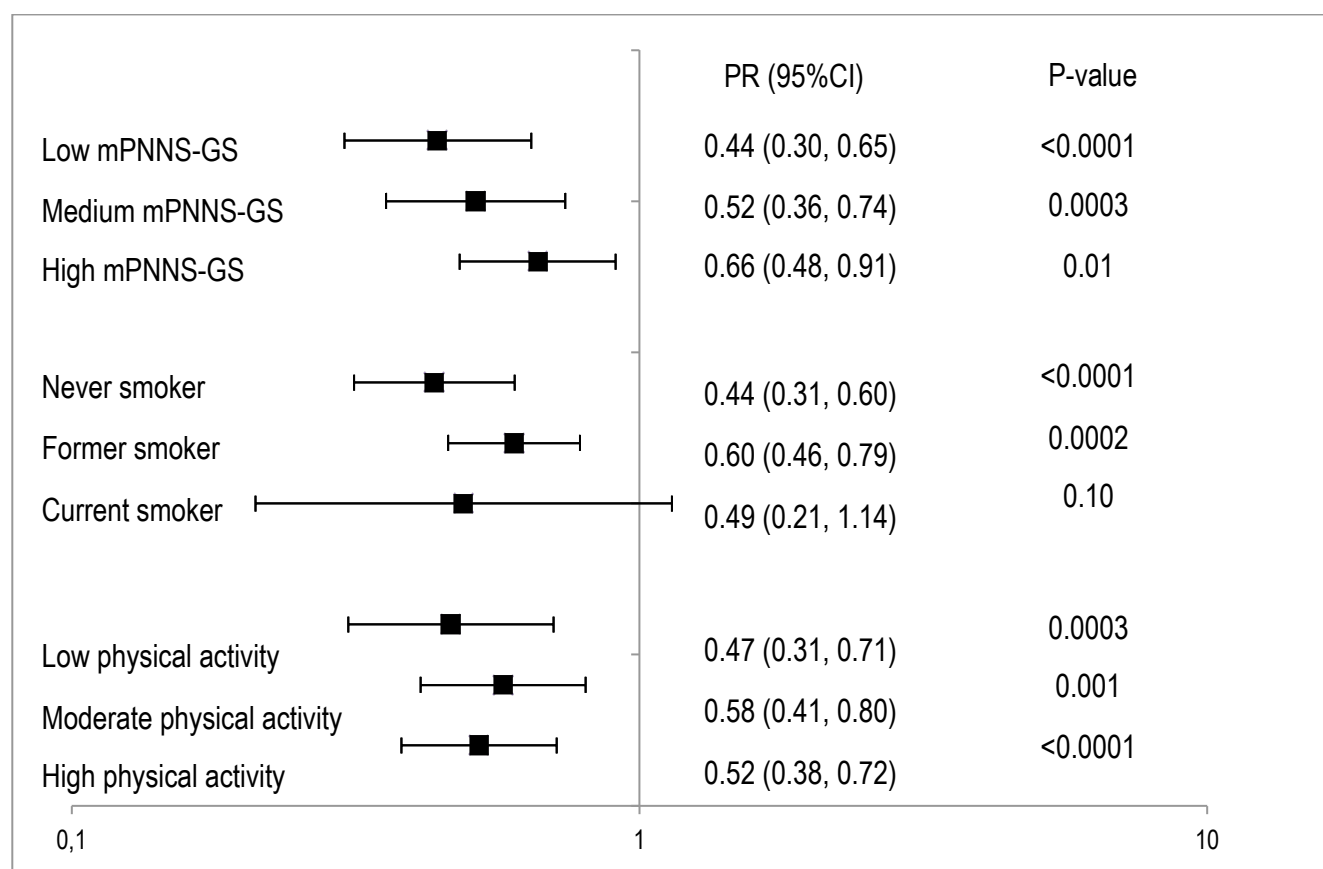
Model 1 is unadjusted. Model 2 is performed among sub-samples who are not taking any related medications for the specific outcome and is adjusted for age, sex, educational level, monthly income, physical activity, smoking habits, season of blood sampling, time lag between organic food questionnaire completion and clinical visit, occupational status, location, energy intake and overall dietary quality (estimated by the mPNNS-GS as a continuous variable).

Figure 1. Association between the proportion of organic food in the diet (as a continuous variable) and MetS across subgroups, n=8,174, NutriNet-Santé study

Abbreviations: CI, Confidence Interval; mPNNS-GS, modified Programme Nationale Nutrition Santé Guideline Score; PR, Prevalence Ratios.

^a Model adjusted for age, sex, educational level, monthly income, season of blood sampling, time lag between organic food questionnaire completion and clinical visit, occupational status, location, energy intake and overall dietary quality (estimated by the mPNNS-GS as a continuous variable) and all other variables presented in the Figure.

Figure 1. Association between the proportion of organic food in the diet (as a continuous variable) and MetS across subgroups, n=8,174, NutriNet-Santé study^a



Abbreviations: CI, Confidence Interval; mPNNS-GS, modified Programme Nationale Nutrition Santé Guideline Score; PR, Prevalence Ratios.

^aModel adjusted for age, sex, educational level, monthly income, season of blood sampling, time lag between organic food questionnaire completion and clinical visit, occupational status, location, energy intake and overall dietary quality (reflected by the mPNNS-GS as a continuous variable) and all other variables presented in the Figure.

