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Emmanuelle Kesse-Guyot, Mathilde Touvier, Adina Henegar, Sébastien Czernichow, Pilar Galan, et al.. Higher adherence to French dietary guidelines and chronic diseases in the prospective SU.VI.MAX cohort: Diet quality and chronic diseases. European Journal of Clinical Nutrition, 2011, 65 (8), pp.887 - 894. 10.1038/ejcn.2011.61. hal-00640218

# HAL Id: hal-00640218 https://hal.science/hal-00640218

Submitted on 11 Nov 2011

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1	Higher adherence to French dietary guidelines and chronic diseases in the prospective
2	SU.VI.MAX cohort
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19	Running head: Diet quality and chronic diseases
20	Word count: Text 3 040 Abstract 195

22 Abstract

23 Background/Objectives: Nutritional recommendations are widely disseminated, but

24 assessment of their predictive value for risk of chronic diseases and mortality is essential for

ensuring their validity. We evaluated, in a large population-based study, the association

26 between the French Programme National Nutrition Santé (PNNS) Guideline Score (GS)

27 (maximum score of 15 points), an a priori-based score, and the incidences of cancer,

28 cardiovascular disease (CVD) and overall mortality.

29 Subjects/Methods: Subjects included in the present analysis (n=5 823) were participants in

30 the Supplémentation en Vitamines et Minéraux AntioXydants study (SU.VI.MAX), with

31 available data for estimating the PNNS-GS. Hazards ratios (HR) and 95% confidence

32 intervals (95% CI) for outcomes (cancer, CVD and death) were estimated across quartiles of

33 PNNS-GS using Cox proportional hazards models.

34 **Results:** A total of 734 major events were recorded during an average 11.6-year follow-up

35 (maximum 13 years): 423 cancers, 193 ischemic diseases and 118 deaths. In the fully-

36 adjusted model, a significant reduction in CVD risk between the first and fourth PNNS-GS

37 quartiles (HR=0.65, 95% CI= 0.41, 1.00, P for trend=0.04) was observed. No significant

38 overall association with risk of cancer or death was detected.

39 Conclusions: These observations support the role of nutritional guidelines in prevention of40 CVD.

41 Keywords: nutritional guidelines, dietary index, cancer, mortality, cardiovascular diseases

#### 43 Introduction

In the past few decades, associations between nutritional factors and chronic diseases, especially cardiovascular diseases (CVD) and cancer, have been widely investigated. A posteriori and a priori methods which take into account overall diet have emerged to overcome the limitations of the nutrient or single food approach based on correlations and interactions between dietary pattern components (Moeller *et al.*, 2007). Although a posteriori methods enable to empirically deriving dietary patterns, a priori scores are often based on nutritional guidelines or diet quality (Moeller *et al.*, 2007).

51 A major issue lies in assessing the predictive value of adherence to nutritional guidelines for

52 primary prevention of chronic disease risk, since guidelines are theoretically designed for this

53 purpose. Some studies have investigated the potential effect of adherence to dietary

54 guidelines, including or not physical activity, on the incidence of chronic diseases, cancer,

55 CVD and overall mortality, as recently reviewed (Waijers *et al.*, 2007).

56 Initial and subsequent a priori scores based on Dietary Guidelines for Americans (DGA),

57 were shown to be only weakly or not at all associated with CVD and cancer occurrence

58 (Waijers *et al.*, 2007). This may be partly due to variations in construction of dietary scores

and disparities in sample size and follow-up duration for some studies. Despite the absence of

60 a significant association with chronic disease risk, better adherence to dietary scores has been

61 consistently associated with lower mortality (Kaluza *et al.*, 2009; Kant *et al.*, 2009).

We had previously developed a score (FSIPO) based on the nine public health goals of the French Nutrition and Health Program (Estaquio *et al.*, 2008). In the SU.VI.MAX cohort, this score was associated with a significant 36% reduction in the risk of chronic diseases and death among men, but no significant association was observed among women. Such arguments concerning nutritional guidelines should be more convincing and comprehensive, mainly in terms of public health messages. 69 based on the individual French national nutritional guidelines (Estaquio *et al.*, 2009), aimed to

70 describe the level of dietary adherence to these guidelines.

71 The purpose of the present work was to evaluate the prospective associations between PNNS-

GS quartiles and risk of chronic diseases and mortality during a maximum 13-year follow-up.

#### 73 Materials and methods

#### 74 *Population*

68

75 The design and rationale of the SU.VI.MAX study (Supplémentation en Vitamines et
76 Minéraux Antioxydants) have been extensively detailed previously (Hercberg *et al.*, 1998).

77 The SU.VI.MAX study was initially designed as a randomized, double-blind, placebo-78 controlled, primary prevention trial to test the potential efficacy of daily supplementation with 79 antioxidant vitamins and minerals at nutritional doses on the incidence of cancers, 80 cardiovascular diseases and overall mortality. Eligible subjects, 7 713 women aged 35-60 81 years and 5 028 men aged 45–60 years at baseline, were included in 1994-1995 and initially 82 followed up for 7.5 y. After stopping supplementation, the follow-up was extended to 13 83 years. The SU.VI.MAX study was approved by the Ethical Committee for Studies with 84 Human Subjects of the Paris-Cochin Hospital (CCPPRB n°706) and the "Commission 85 Nationale Informatique et Liberté" (CNIL n°334641), which ensures that medical information 86 be kept confidential and anonymous.

87 *Data assessment* 

Sociodemographic data and lifestyle, including gender, date of birth and tobacco status, were
collected using a self-administrated questionnaire at baseline.

Subjects were asked to provide a 24-h record every 2 months for a total of 6 records per year
covering all days of the week and all seasons. To facilitate coding food portions, participants
were assisted by an instruction manual which included validated photographs of more than

93 250 typical foods represented in three different portion sizes. Subjects could also choose from 94 two intermediate or two extreme portions, for a total of seven different possible portion sizes 95 (Le Moullec et al., 1996). As previously detailed (Touvier et al., 2010), dietary records that 96 reported  $\leq 100 \text{ kcal/d or} \geq 6000 \text{ kcal/d were excluded and further subjects who had } \geq 2/3 \text{ of their}$ 97 records that reported  $\leq 800$  kcal/d in men and  $\leq 500$  kcal/d in women were excluded. Dietary 98 nutrient intakes were calculated using a food composition table which included more than 900 99 foods (Hercberg S (coordinator), 2005). Specific information on weekly consumption of 100 seafood was collected by a self-administrated questionnaire at baseline. In addition, alcohol 101 intake (grams of alcohol per day) was estimated using a short validated semi-quantitative 102 dietary questionnaire (Lasfargues et al., 1990). 103 A French validated self-administered version of the Modifiable Activity Questionnaire 104 (MAO) was used in 1998 to assess physical activity (Vuillemin *et al.*, 2000). Type, frequency

and duration of activity, each performed at least 10 times for 10 minutes each session during leisure time over the past 12 months, were collected. Using published compendiums (Ainsworth *et al.*, 2000), metabolic equivalent tasks (MET) were assigned to each leisure activity reported and summary scores were computed, including the average MET-h per week of physical activity. For subjects with missing data for the MAQ, we used data from other sources and imputations as previously reported (Estaquio *et al.*, 2009).

111 At the first clinical examination during the follow-up (1995-1996), weight was measured

112 using an electronic scale (Seca, Germany), with subjects wearing indoor clothes and no shoes.

113 Height was measured under the same conditions with a wall-mounted stadiometer.

114 *Cases ascertainment* 

115 Information about health was self-reported via a monthly questionnaire. Other sources of

116 information regarding outcome included yearly visits. In case of no contact with a participant

117 for a long period, or failure to show up for the yearly visit, an investigation was launched to

- 118 determine the reasons. In case of a suspected event, investigations were conducted to obtain
- 119 relevant medical data (clinical, biochemical, histological and radiological reports) from
- 120 participants, physicians and/or hospitals. All events were then reviewed and validated by an
- 121 independent expert committee, unaware of the supplementation group assignment. Causes of
- 122 death were confirmed using information provided by physicians or family members. Vital
- 123 status of all subjects and causes of death were verified using the national death registry.
- 124 Health events were classified using the International Classification of Diseases, 10th
- 125 Revision, Clinical Modification (ICD-10-CM) (WHO, 2003). Major outcomes included
- 126 cardiovascular events (ICD-10-CM codes I20-I24) and cancer of any kind (ICD-10-CM codes
- 127 C00-C97, D00-D09, D37-D48), except for basal cell carcinoma of the skin (ICD-10-CM
- 128 codes C44 and M809-M811) and all-cause mortality. First, we considered as outcome the
- 129 occurrence of a major chronic disease event defined as a combination of CVD, cancer or
- 130 death, whichever came first. Secondly, we also studied each health event separately. Subjects
- 131 contributed person-time up to the date of the health outcome (n=635), the date of the last
- 132 completed questionnaire or contact (n=1 145) or September 1<sup>st</sup> 2007 (n=4 043), whichever
- 133 occurred first. CVD was not accounted for in cancer analysis, and vice-versa.
- 134 *PNNS-GS computation*
- 135 PNNS-GS computation, including food grouping, serving sizes, scoring, cut-off and penalties,
- 136 was previously described in detail (Estaquio *et al.*, 2009). Briefly, the score included 13
- 137 components for a total of 15 points maximum. Eight components referred to food groups,
- 138 including recommended servings, and four components were related to overall limitation. The
- 139 final component dealt with adherence to the physical activity recommendation. Scoring and
- 140 cut-off values are presented in table 1. Each component's subscore were summed for a
- 141 theoretical maximum total of 15 points.

- 142 A penalty for overconsumption was assigned to individuals with energy intakes higher than
- 143 needs. Schofield's basal metabolic rate was estimated using age, height and weight. Basal

144 metabolic rate and physical activity level were used to estimate energy expenditures

- 145 (Schofield, 1985). If energy intake was greater than 5% compared to calculated energy needs,
- 146 an identical fraction was deducted from the score (Estaquio *et al.*, 2009).
- 147 *Inclusion criteria*
- 148 In the present analysis, we selected men and women aged 45-60 y at baseline who provided at
- 149 least three 24-h records during the first 2 years of follow-up and other data needed for PNNS-
- 150 GS computation, and who had no missing co-variables for the present analyses (Fig. 1).
- 151 We excluded subjects who developed health outcomes during the first two years of follow-up.
- 152 Statistical analysis
- 153 Means of food and nutrient intake were calculated from at least three 24-h dietary records
- 154 during the first two years of follow-up. Body mass index (BMI) was calculated as the ratio of
- 155 weight to squared height  $(kg/m^2)$ .
- 156 Descriptive results are reported as mean  $\pm$  standard deviation or percent across quartiles of
- 157 PNNS-GS. Reported P-values referred to the Kruskal-Wallis test or chi<sup>2</sup> test as appropriate.
- 158 Hazard ratio (HR) of disease risk or death and 95% confidence intervals (CI) across quartiles
- 159 of PNNS-GS (using the 1<sup>st</sup> quartile as reference) were estimated using Cox proportional
- 160 hazards models (Cox, 1972).
- 161 Graphic methods (log-log (survival) versus log-time plots) were used to check for
- 162 proportional hazards assumptions for this study. An interaction between PNNS-GS quartiles
- and gender, intervention group, tobacco status and BMI (<25, 35-30, >30 kg/m<sup>2</sup>) on the risk
- 164 of chronic diseases or mortality was tested.
- Models were controlled for age (continuous), smoking status (never, former, current), education level (primary school, secondary school, high school or equivalent), total energy

- 167 intake from diet (continuous), BMI (continuous) and daily supplementation (placebo or168 intervention group) to account for the study design.
- 169 Analyses among smokers and former smokers were further adjusted on frequency (1-5, 6-10,
- 170 10-15, 16-20, 21-30, >30 cigarettes per day) and duration of tobacco use (1-5, 6-10, 11-15,
- 171 16-20, 21-30, >30 years). Among former smokers, time since quitting was also accounted for
- 172 **1-5**, 6-10, 11-15, 16-20, 21-30, >30 years).
- 173 Significance tests were 2-sided, with a type I error set at <0.05. All analyses were performed
- 174 using SAS software (SAS Institute, version 9).
- 175 Results
- 176 The present analyses included 5 823 subjects (2 437 men and 3 386 women) from the 12 741
- 177 subjects initially participating in the SU.VI.MAX study (Fig. 1).
- 178 At baseline, men and women were aged  $51.9 \pm 4.7$  and  $47.0 \pm 6.5$  years, respectively.
- 179 During the follow-up period (mean=11.6 years, corresponding to 66 168 person-years), 734
- 180 major chronic disease endpoints were recorded among 635 subjects: 423 cancers (201 in men
- and 222 in women), 193 cardiovascular diseases (154 in men and 39 in women) and 118
- 182 deaths (70 in men and 48 in women).
- 183 Characteristics of the population are presented across PNNS-GS quartiles (Table 2). Subjects
- 184 were more often women, older, higher educated and non-smokers with increasing PNNS-GS
- 185 quartiles. Additionally, they showed lower energy intake, higher energy from proteins and
- 186 carbohydrates and lower energy from lipids with increasing PNNS-GS quartile overall.
- 187 After adjustment for age and gender (Table 3), a decrease in risk of CVD across the quartiles
- 188 of PNNS-GS was observed. In the fully adjusted multivariate model, the hazard risk for CVD
- 189 of participants in the upper quartile of PNNS-GS compared to those in the lower was 0.65
- 190 (95%CI=0.42, 1.00, P for trend=0.04). Other outcomes were not associated with the PNNS-
- 191 GS quartiles.

- 192 No significant interactions were found between gender or supplementation group and PNNS-
- 193 GS on the risk of chronic diseases or death (P>0.30).

194 However, a significant interaction (P=0.03) was observed between tobacco status and PNNS-195 GS quartiles on the risk of cancer. All other interactions were non-significant. Analyses were 196 therefore separately performed in never-smokers, former smokers and current smokers. No 197 association of PNNS-GS with the risk of cancer was observed among never-smokers (HR Q4 198 versus Q1=0.84, 95%CI =0.55, 1.30) or former smokers (HR Q4 versus Q1=1.19, 199 95%CI=0.74, 1.91). However, in the subgroup of smokers, a higher toward risk of cancer was 200 observed in subjects in the fourth PNNS-GS quartile compared to the first (HR=2.50, 201 CI95%=1.10, 5.68, P for trend=0.02).

202 **Discussion** 

In our study, a 35% reduction in the risk of cardiovascular diseases was observed among subjects showing better compliance with French nutritional guidelines. A non-statistically significant trend towards an increase in risk of cancer was observed among smokers only, with a statistically significant interaction between PNNS-GS and smoking status. No relationship was observed in terms of overall mortality and cancer incidence.

208 We should mention several strengths and limitations of our study. First, the generalization of 209 our findings is subject to caution. Indeed, our subjects were volunteers participating in a 210 nutritional intervention study (Hercberg et al., 2004) who generally had a higher education 211 level and occupational status, along with a healthier diet, than the general population. 212 Furthermore, selection may have led to an overselected sample, as subjects displaying 213 complete data for PNNS-GS computation may have been particularly compliant and health-214 conscious. Such a limitation might have led to homogeneity in our population. However, we 215 had previously reported variability in PNNS-GS in the SU.VI.MAX study (Estaquio et al., 216 2009). Second, the absence of an association between PNNS-GS and cancer risk and 217 mortality may have been partly due to a lack of power due to the small sample size, the rather 218 young age of the population or too short a follow-up period, which did not enable detecting an 219 association with such long times process as cancer development or death. Other possible 220 explanations are related to the inclusion process of motivated subjects, who may present 221 overall "healthy" behavior in addition to the cohort effect, leading to a lower incidence of 222 death and/or cancer. Finally, information on frequency, duration and time since stopping of 223 smoking were ordinal, a possible residual confounding from smoking cannot entirely been 224 removed especially in the highest categories.

225 Development of an a priori score for assessing diet via a holistic approach is of crucial 226 importance for taking into account dietary factors when examining the relationship between 227 nutrition and health. Nutritional guideline-based scores are also useful tools for monitoring 228 compliance with nutritional guidelines and evaluating dietary guidelines for disease 229 prevention. Nonetheless, development of a priori indices present some limitations which were 230 recently extensively discussed (Moeller et al., 2007; Waijers et al., 2007). Briefly, not all 231 components of the diet are accounted for, and scoring, cut-off criteria and selection of 232 components are subjective decisions. In addition, the a priori method did not account for the 233 full range of consumption, as components are dichotomized or ordinal. However, as shown in 234 the literature, several of them have proven to be predictive of later disease and mortality, 235 underlying the validity of nutritional recommendations currently disseminated in populations. 236 Despite the fact that it is only rarely accounted for in the literature (Estaquio *et al.*, 2008; 237 Harnack et al., 2002), physical activity may be of particular interest, as a healthy diet and 238 physical activity may act synergistically to enhance chronic disease prevention. However, 239 findings remained stable by removing physical activity of the PNNS-GS (data not shown). 240 When assessed in the same population, the FSIPO was shown to be associated with a 36% 241 lower risk of "major chronic diseases" (including cancer, CVD and death) among men only.

242 Therefore, use of FSIPO or PNNS-GS may lead to different conclusions, probably due to their 243 varying conceptions. First, both FSIPO and PNNS-GS shared some characteristics (fruits and 244 vegetables, physical activity, alcohol), but differed regarding scoring criteria and definitions 245 of indicators. For example, for fruit and vegetables, public health objectives considered that a 246 "low consumer" ate <3.5 servings/day", while the nutritional advice used as a reference in the 247 PNNS-GS defined it as "at least 5 servings/ day". In addition, fruits and vegetables weighed 248 higher in the FSIPO than in the PNNS-GS. Second, since the FSIPO was developed with a 249 view toward public health objectives, cardiovascular risk factors such as hypertension, 250 hypercholesterolemia and body mass were accounted for. Although no statistically significant 251 interaction between gender and PNNS-GS was observed on the risk chronic diseases, we 252 nonetheless performed these analyses in men and women separately (data not shown). 253 Regarding composite variable, no association was found with PNNS-GS whatever the gender. 254 This finding strengthens the above-cited hypothesis. Thus, we hypothesize that the association 255 between chronic diseases and FSIPO was mainly influenced by a stronger reduction in risk of 256 CVD.

Few studies have reported a significant predictive value for nutritional guideline-based scores in the risk of overall mortality (Huijbregts *et al.*, 1997; Kaluza *et al.*, 2009; Seymour *et al.*, 2003). In our study, the absence of an association may have been due to too short a follow-up (mean=11.6 y) among middle-aged subjects.

In agreement with our results, other studies detected an association between adherence to nutritional guidelines (for Americans), assessed using the original HEI, and risk of CVD. Among subjects with a high level of HEI, a significant reduction in CVD risk of 28% in men (McCullough *et al.*, 2000a) and of 14% in women (McCullough *et al.*, 2000b) was observed, but no association was observed for cancer risk in either gender. Subsequent analysis based on an alternate version of the HEI was more accurate than the original HEI at predicting CVD risk but again, no association was observed with cancer risk (McCullough *et al.*, 2002;
McCullough *et al.*, 2006).

269 Like most of the studies, we did not found an association with risk of overall cancers (Kaluza 270 et al., 2009; McCullough et al., 2000a; McCullough et al., 2000b; McCullough et al., 2006; 271 Seymour et al., 2003). In contrast, one study on a large cohort (Reedy et al., 2008) observed 272 lower risk of colorectal cancer among men with higher scores (HEI, alternate HEI, RFS), but 273 this was true for women only with higher HEI-2005. Another study carried out among 274 postmenopausal women showed a significant protective effect of an increased Dietary 275 Guidelines Index Score upon cancer risk (Harnack *et al.*, 2002), particularly for cancers of the 276 colon, bronchus and lung, breast and uterus.

277 The lack of an association between dietary scores and cancer risk in many studies may be 278 partly related to the fact that cancers are studied overall due to the lack of power when 279 considering site-specific cancers, whereas some nutritional factors may be protective for some 280 sites only. Finally, since certain factors seemed to play particular important role in cancer 281 prevention (American Institute for Cancer Research / World Cancer Research Fund, 2007), 282 the components of scores related to these factors should be carefully considered. Indeed, some 283 food groups such as alcohol, processed meat, fruit and vegetables may weigh more strongly in 284 terms of with cancer risk.

An increase in risk was observed among the small subgroup of smokers with the highest PNNS-GS compared to the lowest. Usually, smoking has been frequently associated with a cluster of unhealthy behavior (Kesse-Guyot *et al.*, 2009; McNaughton *et al.*, 2007). No study reported an interaction between the nutritional score and smoking in terms of risk of cancer. Nevertheless, vegetable and fruit consumption was recently related to an increase in risk of colorectal cancer among smokers, while a protective effect was observed among never and former smokers (van Duijnhoven *et al.*, 2009). One observational study (Touvier *et al.*, 2005) and a recent meta-analysis of randomized clinical trials (Druesne-Pecollo *et al.*, 2009) reported association between beta-carotene supplementation and several types of cancers among smokers. Mechanisms based on in vitro studies might explain the harmful effects of beta-carotene in smokers. Beta-carotene may act as a pro-oxidant at high doses, affecting cell proliferation or apoptosis in cells exposed to smoke condensate, or it may increase DNA oxidative damage (Druesne-Pecollo *et al.*, 2009).

298 In conclusion, better adherence to French nutritional guidelines was associated with a lower

299 incidence of CVD after a maximum 13-year follow-up period in middle-aged adults. These

300 findings partially argue for the benefits of nutritional guidelines, and similar investigations

- 301 should be reproduced in other varied populations. Complementary investigations in high-risk
- 302 subgroups are also needed.
- 303

## 304 Ackowledgment

- 305 This work was granted by the ANR (n°ANR-05-PNRA-010), DGS (Ministry of Health) and
- 306 was supported by Médéric, Ipsen, Sodexo, MGEN and Pierre Fabre. Conflict of interest: none
- 307 declared.
- 308

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403 Table 1 Components and scoring for calculation of the PNNS-GS, according to PNNS

## 404 recommendation scores

I	<b>Recommendation</b>	Scoring criteria	<mark>Score</mark>
Fruits and	≥5 servings/d	0 to <3.5 servings/d	0
vegetables		3.5 to <5 servings/d	<mark>0.5</mark>
		5 to <7.5 servings/d	1
		≥7.5 servings/d	2
Bread, cereals,	At each meal according to	0 to <1 servings/d	0
potatoes and	appetite	1 to <3 servings/d	<mark>0.5</mark>
legumes		3 to <6 servings/d	1
		≥6 servings/d	<mark>0.5</mark>
Whole grain food	Preferentially choose whole	0 to <0.33 servings/ $d^1$	0
	grains and whole grain	0.33 to $<0.66$ servings/d <sup>1</sup>	<mark>0.5</mark>
	breads	≥0.66 servings/d <sup>1</sup>	1
Milk and dairy	3 servings/d	0 to <1 servings/d	0
<mark>products (yogurt,</mark>	(individuals aged≥ 55 years:	1 to $<2.5$ servings/d	<mark>0.5</mark>
<mark>cheese, etc.)</mark>	3-4 servings/d)	2.5 to 3.5 servings/d (participants aged $\geq$ 55y: 2.5 to 4.5	1
		servings/d)	
		>3.5 (participants aged ≥55y: >4.5 servings/d)	0
Meat and poultry,	1-2 servings/d	0 servings/d	<mark>0</mark>
seafood and eggs		>0 to <1 servings/d	<mark>0.5</mark>
		1 to 2 servings/d	1
		>2 servings/d	<mark>0</mark>
Seafood	≥2 servings/wk	<2 servings/wk	0
		≥2 servings/wk	1
Total added fats <sup>2</sup>	Limit consumption	Lipids from animal and vegetable added fats >16%EI <sup>3</sup> /d	0
		Lipids from animal and vegetable added fats ≤16%EI <sup>3</sup> /d	1
Vegetable added	Favor fats of vegetable	No consumption of vegetable oil or ratio vegetable oil/total	<mark>0</mark>
<mark>fats</mark>	origin	added fats ≤0.5	
		No consumption of added fats or ratio vegetable oil/total added	1
		fats >0.5	
Sweetened foods <sup>2</sup>	Limit consumption	Added sugars from sweetened foods $\geq 15\% \text{ EI}^3/\text{d}$	<mark>-0.5</mark>

		Added sugars from sweetened foods $[10 - 15[\% EI^3/d]$	<mark>0</mark>
		Added sugars from sweetened foods $\leq 10\% \text{ EI}^3/\text{d}$	1
Water and soda <sup>4</sup>	Drink water as desired;	< 1 L of water and > 250 mL of soda/d	<mark>0</mark>
	Limit sweetened beverages	$\geq$ 1 L of water and $\geq$ 250 mL of soda/d	<mark>0.50</mark>
	to ≤1 one glass/d	$\leq$ 1 L of water and $\leq$ 250 mL of soda/d	<mark>0.75</mark>
		$\geq$ 1 L of water and $\leq$ 250 mL of soda/d	1
Alcohol <sup>5</sup>	≤2 glasses of wine/d for	>20 g ethanol/d for women and >30 g ethanol/d for men	<mark>0</mark>
	women and ≤3 glasses of	Ethanol $\leq 20$ g/d for women and $\leq 30$ g/d for men	<mark>0.8</mark>
	wine/d for men	Abstainers and irregular consumers (<1 glass of wine/wk)	1
Salt	Limit consumption	>12 g/d	<mark>-0.5</mark>
		>10 to 12 g/d	<mark>0</mark>
		>8 to 10 g/d	<mark>0.5</mark>
		<mark>≥6 to 8 g/d</mark>	1
		<u>≤ 6 g/d</u>	1.5
Physical activity	At least the equivalent of 30	0 to <30 min/d	<mark>0</mark>
	min of brisk walking/d	30 to <60 min/d	1
		≥ 60 min/d	<mark>1.5</mark>

405 <sup>1</sup> As a proportion of 24-h dietary records during which whole-grain consumption was reported

406 <sup>2</sup> Established according to the French RDA

407 <sup>3</sup> EI: total energy intake without alcohol

408 <sup>4</sup> Water included water, tea, coffee, herbal tea, milk, and diet beverages

409 <sup>5</sup> Pregnant women are advised to abstain from all alcohol consumption during the entire pregnancy

411 Table 2 Baseline characteristic (mean  $\pm$  SD or %) of the population across PNNS-GS

## 412 quartiles, SU.VI.MAX Study, 1994-2007

	Q1	Q2	Q3	Q4	$\mathbf{P}^{1}$
PNNS-GS range	<mark>≤6.52</mark>	<mark>&gt;6.52-≤7.75</mark>	<mark>&gt;7.75-≤9</mark>	<mark>&gt;9</mark>	
Ν	1456	1470	1447	1450	
Male (%)	49.04	42.72	39.32	36.28	<.0001
Age	$48.24 \pm 6.16$	$48.74 \pm 6.16$	$49.09 \pm 6.32$	$50.04 \pm 6.47$	′ <.0001
BMI	$23.98 \pm 3.85$	$24.22 \pm 3.82$	$24.18 \pm 3.66$	23.90 ± 3.39	0.21
Education					
Primary	22.05	20.2	20.53	18.69	0.02
Secondary	38.94	39.8	37.11	39.17	
High	39.01	40.0	42.36	42.14	
Smoking status					
Non-smokers	43.27	47.69	49.76	50.14	<.0001
Former smokers	38.53	37.48	38.91	41.24	
Smokers	18.20	14.83	11.33	8.62	
Intervention group (%)	50.55	51.29	50.73	49.52	0.53
Physical activity <sup>2</sup>					
[0-30[min/d	82.90	66.33	52.45	27.24	<.0001
[30-60[min/d	10.71	17.76	25.16	30.28	
≥60 min/d	6.39	15.92	22.39	42.48	
Energy intake (total) (Kcal/d)	$2\;440.4\;\pm$	2 073.3 ±	$2\ 003.0\ \pm$	$1.922.9 \pm$	<.0001
	646.4	573.7	532.2	520.2	
Energy intake (without	2 259.0 ±	1 944.2 ±	1 893.5 ±	1 831.0 ±	<.0001
alcohol) (Kcal/d)	595.3	525.9	490.8	481.5	

Proteins $(\%)^3$	$17.52 \pm 2.91$	$17.89\pm2.96$	$17.92\pm2.74$	18.19 ± 2.77 <.0001
Carbohydrates $(\%)^3$	$41.27 \pm 6.35$	$41.12 \pm 6.26$	$41.85 \pm 5.91$	42.91 ± 5.82 <.0001
Lipids $(\%)^3$	$41.20 \pm 5.02$	$40.97 \pm 5.11$	$40.21 \pm 5.05$	38.89 ± 5.24 <.0001

Point for each component

### (theoretical range), mean $\pm$

sd

Fruits and vegetables [0-2]	$0.68\pm0.59$	$0.77\pm0.57$	$0.93\pm0.59$	$1.21 \pm 0.64 < .0001$
Bread, cereals, potatoes and	$0.76\pm0.27$	$0.74\pm0.27$	$0.75\pm0.27$	$0.75 \pm 0.27$ 0.14
legumes [0-1]				
Whole grain food [0-1]	$0.11\pm0.27$	$0.14\pm0.30$	$0.20\pm0.35$	$0.33 \pm 0.42 < .0001$
Milk and dairy products [0-1]	$0.35\pm0.40$	$0.46\pm0.40$	$0.52\pm0.40$	$0.62 \pm 0.41 < .0001$
Meat and poultry, seafood	$0.52\pm0.47$	$0.67\pm0.43$	$0.74\pm0.40$	$0.83 \pm 0.33$ <.0001
and eggs [0-1]				
Seafood [0-1]	$0.20\pm0.40$	$0.28\pm0.45$	$0.42\pm0.49$	$0.65 \pm 0.48 < .0001$
Sweetened foods [0-1]	$0.70\pm0.49$	$0.81\pm0.41$	$0.88\pm0.33$	$0.94 \pm 0.24 < .0001$
Total added fats [0-1]	$0.65\pm0.48$	$0.71\pm0.45$	$0.76\pm0.43$	$0.83 \pm 0.37 < .0001$
Vegetable added fats [0-1]	$0.41\pm0.49$	$0.60\pm0.49$	$0.72\pm0.45$	$0.86 \pm 0.35 < .0001$
Water and soda [0-1]	$0.86\pm0.16$	$0.84\pm0.13$	$0.91\pm0.13$	$0.89 \pm 0.12 < .0001$
Alcohol [0-1]	$0.60\pm0.42$	$0.71\pm0.36$	$0.78\pm0.30$	$0.85 \pm 0.22 < .0001$
Salt [-0.5-1.5]	$-0.10 \pm 0.53$	$0.18\pm0.63$	$0.26\pm0.63$	$0.42 \pm 0.64 < .0001$
Physical activity [0-1.5]	$0.20\pm0.46$	$0.42\pm0.60$	$0.59\pm0.64$	$0.94 \pm 0.61 < .0001$

- 413 <sup>1</sup> P Values based on Kruskal-Wallis test or chi-squared test
- 414 <sup>2</sup> Physical activity: as equivalent of 30 min of brisk walking/d
- 415 <sup>3</sup> Values are percentage of total daily energy intake (without alcohol)

416 Table 3 Hazards ratio (95% CI) of major chronic diseases and PNNS-GS quartiles during the

417 period 1994-2007

	Q1	Q2	Q3	Q4	$\mathbf{P}^1$
Composite variable <sup>2</sup>					
Number of cases	150	161	162	162	
Age and gender-adjusted	1	1.06	1.03	0.97	0.74
HR		(0.84,1.32)	(0.83,1.29)	(0.77,1.21)	
Fully adjusted HR <sup>3</sup>	1	1.05	1.03	0.97	0.77
		(0.84,1.32)	(0.82,1.30)	(0.77,1.24)	
Cancer <sup>4</sup>					
Number of cases	96	101	113	113	
Age and gender-adjusted	1	1.01	1.09	1.01	0.81
HR		(0.76,1.33)	(0.83,1.43)	(0.77,1.34)	
Fully adjusted HR <sup>3</sup>	1	1.05	1.15	1.07	0.54
		(0.79,1.41)	(0.86,1.53)	(0.80,1.44)	
Cardiovascular diseases					
Number of cases	56	53	45	39	
Age and gender-adjusted	1	0.98	0.82	0.68	0.04
HR		(0.68,1.43)	(0.55,1.21)	(0.45,1.03)	
Fully adjusted HR <sup>3</sup>	1	0.93	0.78	0.65	0.04
		(0.63,1.36)	(0.52,1.17)	(0.42,1.00)	
Death					
Number of cases	26	33	27	32	
Age and gender-adjusted	1	1.24	0.99	1.11	0.95
HR		(0.73,2.10)	(0.57,1.74)	(0.64,1.93)	

Fully adjusted HR <sup>3</sup>	1	1.24	0.99	1.11	0.95
		(0.73,2.10)	(0.57,1.74)	(0.64,1.93)	

- 418 <sup>1</sup> Test for trend across quartiles
- 419 <sup>2</sup> Cancer, cardiovascular diseases or death
- 420 <sup>3</sup> Controlled for gender, age (continuous), BMI (continuous), smoking (never, past, current),
- 421 total energy intake (continuous), education (primary school, secondary school, high school or
- 422 equivalent), supplementation group (active versus placebo).
- 423 <sup>4</sup>Cancer included all sites of cancer except basal cell carcinoma of the skin

426 2007.

