The Journal of Nutrition
**Nutritional Epidemiology**

# A Healthy Dietary Pattern at Midlife, Combined with a Regulated Energy Intake, Is Related to Increased Odds for Healthy Aging[1–3]

Karen E Assmann,[4]* Camille Lassale,[4] Valentina A Andreeva,[4] Claude Jeandel,[5] Serge Hercberg,[4,6] Pilar Galan,[4] and Emmanuelle Kesse-Guyot[4]

[4]University of Paris 13, Nutritional Epidemiology Research Team (EREN), Centre of Research in Epidemiology and Statistics Sorbonne Paris Cité, National Institute of Health and Medical Research (INSERM) U1153, National Institute for Agricultural Research (INRA) U1125, National Conservatory of Arts and Crafts (CNAM), Community of Universities and Establishments (COMUE) Sorbonne Paris Cité, Bobigny, France; [5]Department of Geriatrics, Centre Balmès, CHU Montpellier, Université Montpellier I, Montpellier, France; and [6]Department of Public Health, Hôpital Avicenne, Bobigny, France

## Abstract

**Background:** Few studies have investigated the long-term impact of overall dietary patterns (DPs) on healthy aging (HA), and current findings are inconsistent.

**Objective:** Our study's objective was to investigate the association between empirically derived DPs in midlife and HA after 13 y of follow-up.

**Methods:** Baseline dietary data from repeated 24-h dietary records (on average, 10 records per participant) of a subsample of the SU.VI.MAX (SUpplémentation en Vitamines et Minéraux AntioXydants) study allowed extraction of 2 DPs with the use of principal components analysis on 37 food groups. HA was assessed in 2007–2009 among 2796 participants of the SU.VI.MAX study aged 45–60 y at baseline (1994–1995), who were initially free of diabetes, cardiovascular disease, and cancer. HA was defined as not developing any major chronic disease, good physical and cognitive functioning, no limitations in instrumental activities of daily living, no depressive symptoms, no health-related limitations in social life, good overall self-perceived health, and no function-limiting pain. The association between DPs (in tertiles) and HA was evaluated by using multivariable logistic regression, and a potential interaction with energy intake was investigated.

**Results:** A ''Western'' and a ''healthy'' DP were identified. After adjustment for a large number of potential confounders, there was no significant association between the Western DP and HA. Moreover, the healthy pattern was not associated with HA among subjects with high (i.e., greater than or equal to the median) energy intake. Among subjects with low (i.e., less than the median) energy intake, on the other hand, higher scores on the healthy DP were related to higher odds of HA (OR for tertile 3 vs. tertile 1: 1.49; 95% CI: 1.11, 2.00; *P*-trend = 0.01).

**Conclusion:** Adherence to a healthy diet in midlife that provides micronutrients, fiber, and antioxidants while regulating energy intake may help to promote HA. *J Nutr* 2015;145:2139–45.

**Keywords:** dietary patterns, healthy aging, midlife exposure, nutrition, energy intake

## Introduction

In the context of a steady increase in life expectancy, maintaining health and well-being in aging populations has become a major public health challenge. It is predicted that the proportion of elderly persons (≥60 y) in the global population will reach 32% in 2050 (1); hence, it is urgent to identify modifiable environmental factors that could help preserve good overall health status during aging.

The concept of "successful aging" or "healthy aging" (HA)[7] is largely based on a multidimensional model proposed by Rowe and

[1] Supported by the French National Research Agency (no. ANR-05-PNRA-010), the French Ministry of Health, Médéric, Sodexo, Ipsen, MGEN, and Pierre Fabre. Mederic and MGEN are French health insurance organizations, which are complementary to the National Health Insurance System. Ipsen and Pierre Fabre are private pharmaceutical companies. Sodexo, a food catering company, supported the study by organizing meetings between researchers and study participants. KEA was supported by a doctoral fellowship from the Ecole Doctorale Galilée, University of Paris 13, Sorbonne Paris Cité.

[2] Author disclosures: KE Assmann, C Lassale, VA Andreeva, C Jeandel, S Hercberg, P Galan, and E Kesse-Guyot, no conflicts of interest. The funding organizations did not have any involvement in the design/conduct of the research, in data analysis/interpretation, or in writing/approval of the manuscript.

* To whom correspondence should be addressed. E-mail: k.assmann@eren.smbh.univ-paris13.fr.

[3] Supplemental Table 1 is available from the ''Online Supporting Material'' link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.

[7] Abbreviations used: AHEI, Alternative Healthy Eating Index; DP, dietary pattern; FOXO, class O forkhead box transcription factor; HA, healthy aging; PCA, principal components analysis; SU.VI.MAX, SUpplémentation en VItamines et Minéraux AntioXydants.



Manuscript received February 5, 2015. Initial review completed April 2, 2015. Revision accepted July 6, 2015.
First published online August 5, 2015; doi:10.3945/jn.115.210740.

Kahn (2), which encompasses the combination of a low risk of disease and disease-related disability, high levels of mental and physical health, and active engagement with life. Over the past decades, many different operationalized definitions of HA/successful aging have been developed, thus inciting an ongoing debate related to the heterogeneity of the HA concept. Indeed, there are important variations in the choice of components included into HA definitions as well as in the nature of their measurement. Currently, no agreed-upon standard definition exists (3).

Among the most important modifiable factors that may have an impact on HA, diet is prominent (4). Although focusing on individual components of the diet is important to understand the effects of specific aspects of nutrition on health, foods and nutrients are eaten in a variety of combinations, leading to interactive, cumulative, or confounding effects (5).Thus, the scientific literature has emphasized the need to examine diet by holistic approaches on the basis of both a priori techniques (dietary scores constructed to reflect nutritional recommendations or specific dietary concepts) and a posteriori techniques [empirically derived dietary patterns (DPs)]. Although the scientific literature on the association between DPs and specific health conditions (especially cancer, diabetes, and cardiovascular disorders or diseases) has substantially increased over the past decades (4, 6–10), research focusing on HA is scant (11–13).

The objective of our study was to examine the prospective association between midlife DPs and HA evaluated 13 y later in a large cohort. We hypothesized that it was important to consider both the quality and the overall quantity of the diet in tandem. Indeed, a beneficial impact of a specific DP on health could be counterbalanced by increased energy intake. Thus, we also investigated a potential modulating effect of energy intake on the relation between DPs and HA.

## Methods

*Study design and participants.* The French SU.VI.MAX (SUppIémentation en Vitamines et Minéraux AntioXydants) study (1994–2002) was initially a randomized, double-blind, placebo-controlled primary prevention trial with a planned follow-up of 8 y (trial registration at www.clinicaltrials.gov under NCT00272428). It was designed to test the potential effect of antioxidant supplementation on the incidence of cancer, ischemic heart disease, and overall mortality (14, 15). At the end of the trial phase, participants were invited to undergo an additional 2-y follow-up. From the initial sample, 6850 participants were included on a voluntary basis in the SU.VI.MAX 2 observational study (2007–2009), aimed at investigating the impact of nutrition on the quality of aging (16). During SU.VI.MAX 2, clinical and neuropsychological examinations were carried out and questionnaires were completed by participants.

The SU.VI.MAX and SU.VI.MAX 2 studies were conducted according to the guidelines laid down in the Declaration of Helsinki of 1975 as revised in 1983 and were approved by the Ethics Committee for Studies with Human Participants of Paris-Cochin Hospital (CCPPRB 706 and 2364, respectively) and the Commission National Informatique et Liberté (CNIL 334641 and 907094, respectively). Written informed consent was obtained from all participants.

From the 6850 participants in the SU.VI.MAX.2 study, we selected those who were older than 45 y at baseline with available dietary data (i.e., ≥3 valid 24-h dietary records at baseline) and without prevalent diabetes, cardiovascular disease, or cancer at baseline or missing data on ≥1 variables needed for the computation of HA status. Finally, participants with at least 1 missing covariable value were removed, leaving a final sample of 2796 men and women (**Figure 1**).

*Definition of HA.* On the basis of the concept developed by Rowe and Kahn (2) and of suggestions to expand this concept by accounting for individuals' own perceptions (3) and mental health (17), we defined HA as follows: not developing cancer, cardiovascular disease, or diabetes during follow-up; good physical and cognitive functioning; no limitations in instrumental activities of daily living; no depressive symptoms; no health-related limitations in social life; good overall self-perceived health; and no function-limiting pain (**Table 1**). A detailed description of this definition has been published elsewhere (18).

The ascertainment of cancer and cardiovascular disease events during the follow-up was extensively described previously (15, 19). Briefly, cardiovascular disease and cancer of any kind, except for basal cell carcinoma of the skin, were defined by using the 10th International WHO Classification of Diseases (20). Diabetes was defined as fasting blood glucose ≥1.26 g/L, antidiabetic medication use, or self-declared diabetes at the end of follow-up. The remaining HA criteria were assessed by using data from the SU.VI.MAX 2 examination (2007–2009). Good physical functioning was defined as having ≥11 of 12 points (21–23) on the Short Physical Performance Battery (24). Good cognitive function was defined as ≥27 points (25) on the Mini-Mental State Examination (26), ≥19 of 48 points on the delayed cued-recall score of the 48-item cued recall test (27), and ≥5.5 points on the number-letter switching task of the Delis-Kaplan Trail Making Test (28, 29). The absence of limitations in instrumental activities of daily living was defined by using the 8-item Lawton scale (30), and the absence of depressive symptoms was defined as <16 of 60 points on the Center for Epidemiologic Studies–Depression scale (31, 32). Three final criteria were assessed by using information from the Medical Outcome Study Short Form 36 (33): no health-related limitations in social life (items on the intensity and frequency of social life limitations), good overall self-perceived health (item on general health), and no function-limiting pain (items on the intensity and frequency of pain-related limitations).

*Dietary data and DP extraction.* During the SU.VI.MAX study, participants were invited to complete a 24-h dietary record every 2 mo for a total of 6 records/y. Data were collected through computerized questionnaires by using Minitel, a small terminal used in France as an adjunct to the telephone. When coding food portions, participants used an instruction manual that included validated photographs of >250 foods represented in 3 different portion sizes. Participants could also choose from 2 intermediate or 2 extreme portions, for a total of 7 possible portion sizes (34). As previously reported (16), dietary records

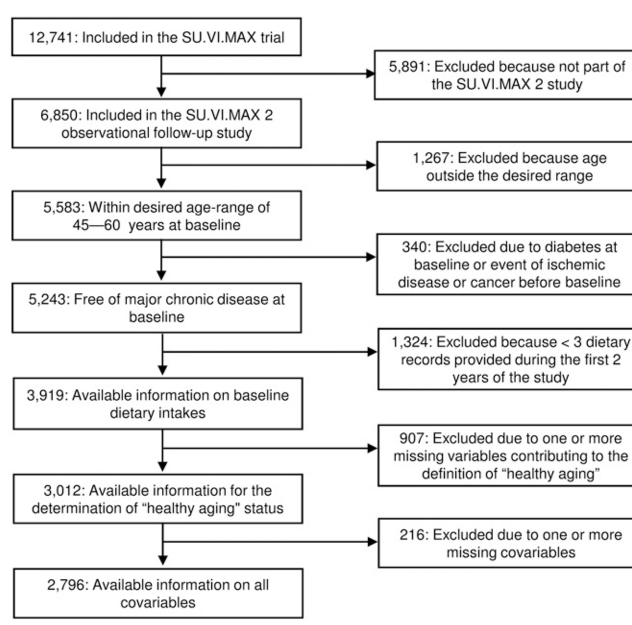


**FIGURE 1** Selection of participants of the SU.VI.MAX and SU.VI.MAX 2 studies (France, 1994–2009) for the present analyses. SU.VI.MAX, SUpplémentation en VItamines et Minéraux AntioXydants.

**TABLE 1** Criteria used to define ''healthy aging'': SU.VI.MAX and SU.VI.MAX 2 studies (France, 1994–2009)[1]

| Criteria[2] | Corresponding Rowe and Kahn criterion[3] | Definition |
|---|---|---|
| Good physical functioning | Maintenance of high physical and cognitive function | SPPB ≥11/12 |
| Good cognitive functioning | Maintenance of high physical and cognitive function | MMSE ≥27, RI-48 ≥19/48, and DK-TMT ≥5.5 |
| No limitations in IADL | Avoiding disease and disability | <1 limitation |
| No depressive symptoms | — | CES-D <16/60 |
| No health-related limitations in social life | Sustained engagement in social and productive activities | SF-36 responses: 1–2 for item 6 and 3–5 for item 10 |
| Good overall self-perceived health | — | SF-36 responses: 1–3 for item 1 |
| No function-limiting pain | Avoiding disease and disability | SF-36 responses: 1–3 for item 7 and 1–2 for item 8 |
| No incident major chronic disease | Avoiding disease and disability | No incident diabetes, cancer, or cardiovascular disease during follow-up |

[1] Adapted from another article in which the SU.VI.MAX definition of ''healthy aging'' was originally published (18). CES-D, Center for Epidemiologic Studies–Depression Scale; DK-TMT, Delis-Kaplan version of the Trail Making Test; IADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination; RI-48, 48-item cued recall test; SF-36, Medical Outcome Study Short Form 36; SPPB, Short Physical Performance Battery; SU.VI.MAX, SUpplémentation en VItamines et Minéraux AntioXydants.
[2] All criteria were assessed at follow-up (2007–2009), except for the incidence of major chronic disease, which was assessed over the follow-up period (1994–2009). All subjects were free of major chronic disease at study inclusion.
[3] See reference 2.

that reported <100 or >6000 kcal/d were excluded; furthermore, men reporting <800 kcal/d and women reporting <500 kcal/d across at least one-third of their dietary records were also excluded. These cutoffs are commonly used for analyses of SU.VI.MAX data (35).

*Covariates.* Data on sex, age, education (primary, secondary, or university level), occupational category (homemakers, manual workers, intermediate professions, managerial staff, or an intellectual profession), smoking status (never smoked or former or current smoker), and physical activity (infrequent, <1 h walking/d, ≥1 h walking/d) were collected at baseline through self-administered questionnaires.

*Statistical analysis.* For the present analyses, we used all 24-h dietary records collected during the first 2 y of the SU.VI.MAX study as a measure of habitual dietary intake at baseline. Thus, all days of the week and all seasons were covered, and individual and seasonal variability was accounted for. A mean ± SD of 10.1 ± 3.1 dietary records were available per subject at baseline. Nutrient intakes and the intakes of >950 different foods were based on the reported mean intakes across all selected 24-h records. To prepare food intake data for principal components analysis (PCA), the different food items were aggregated into 37 food groups. PCA was then performed by using SAS Proc Factor (version 9.3; SAS Institute) to derive DPs on the basis of the original food group variables (consumption in g/d). These patterns are independent linear combinations of the predefined 37 food groups, maximizing the explained variance. Next, factors were rotated by orthogonal transformation by using the Varimax option. The number of DPs retained was determined according to Cattel's scree plots (plots of the total variance explained by each pattern) and the interpretability of the factors. DPs were labeled on the basis of the types of foods exhibiting the strongest correlations and having the highest factor loadings. Food groups with absolute factor-loading coefficients >0.3 were considered to be strongly associated with a pattern. For each participant, the individual pattern score was calculated by summing the intake of the 37 food groups, weighted by their factor loading. A comparison of participant characteristics between those included in our analysis and those who were excluded [considering all SU.VI.MAX participants older than 45 y and with available dietary data at baseline ($n$ = 6370) as the "source population"] was also performed.

For purposes of partly correcting for selection bias, all analyses were carried out by using inverse probability weighting (36, 37). For each subject of the "source population," the probability to be included in the present analysis was estimated by using a multivariable logistic regression model (dependent variable: "included: yes/no"; independent variables: baseline characteristics such as sociodemographic, lifestyle, and health variables). The data were analyzed by using the inverse of the probability to be included (multiplied by the sampling proportion $n_{\text{included}}/ n_{\text{total}}$) as the respective weight.

Baseline characteristics are presented by HA status as percentages or means ± SDs, and differences were tested by using chi-square and Wilcoxon's rank-sum tests. Logistic regression models were performed to estimate the association between the retained DPs (as tertiles) and subsequent HA. Values are presented as ORs (95% CIs), with $P$ values for (log)-linear trend. These $P$ values were calculated by modeling the tertile variable as an ordinal variable (i.e., without placing it into the class statement of SAS Proc Logistic).

Tests for a potential effect modification by energy intake were performed by including interaction terms into our models. Interactions between the different DPs were also tested. In sensitivity analyses, a simplified DP as described by Schulze et al. (38) was estimated and further tested with respect to subsequent HA. For this purpose, food group consumption displaying a correlation coefficient |>0.3| with the DP was retained and standardized (mean = 0, SD = 1) before being summed. All analyses were conducted with SAS (version 9.3), with a significance level of 0.05.

## Results

A total of 2796 participants were included in the present analysis. The sample's mean baseline age was 51.9 ± 4.5 y and mean follow-up time was 13.3 ± 0.7 y.

Compared with excluded subjects, those included in the present study were significantly older, better educated, more often nonsmokers, and more physically active and exhibited a healthier diet. Moreover, they were less likely to have hyperglycemia and dyslipidemia (data not shown). Baseline characteristics according to HA status are presented in **Table 2**.

Participants who exhibited HA [$n$ = 1096 (39.2%)] were more often men, better educated, and more physically active and less often manual workers compared with the other subjects [$n$ = 1727 (61.8%)]. They also had a lower energy intake from protein and a lower BMI.

*DPs.* Two DPs were identified by PCA (**Supplemental Table 1**), which accounted for 15% of the initial variance. The first pattern was positively correlated with intakes of alcoholic beverages, meat and poultry, processed meat, refined grains, cheese, potatoes, and salted snacks and was thus labeled a "Western" pattern. The second DP was positively correlated with the consumption of vegetables, vegetable fat, fruit, whole grains, fish, sweetening products, soup, and fresh dairy products and was thus labeled a "healthy" pattern.

*Overall association between DPs and HA.* Results for the overall association between DPs and HA are presented in **Table 3**. After accounting for a variety of confounders, there was no significant association between the Western DP and HA.

**TABLE 2** Baseline characteristics of participants according to subsequent healthy aging status: SU.VI.MAX and SU.VI.MAX 2 studies (France, 1994–2009)[1]

| Baseline characteristics | Without healthy aging ($n$ = 1727) | With healthy aging ($n$ = 1096) | $P$[2] |
|---|---|---|---|
| Age, y | 52.3 ± 4.6 | 51.3 ± 4.3 | <0.0001 |
| Men, % | 50.3 | 56.3 | 0.002 |
| Intervention group, % | 51.4 | 55.7 | 0.03 |
| Educational level, % | | | |
| Primary | 23.7 | 16.3 | <0.0001 |
| Secondary | 40.1 | 38.5 | |
| University level or equivalent | 36.2 | 45.2 | |
| Occupational status, % | | | <0.0001 |
| Homemaker/inactive | 8.9 | 6.4 | |
| Manual worker | 6.6 | 4.0 | |
| Intermediate profession | 56.4 | 52.7 | |
| Managerial staff/intellectual profession | 28.1 | 37.0 | |
| Living arrangement, % living alone | 14.0 | 11.8 | 0.09 |
| Smoking habits, % | | | 0.23 |
| Never smoker | 51.2 | 51.4 | |
| Former smoker | 37.3 | 39.2 | |
| Current smoker | 11.4 | 9.4 | |
| Physical activity level, % | | | |
| Irregular or no physical activity | 24.7 | 19.1 | 0.001 |
| <1 h/d | 30.3 | 30.8 | |
| ≥1 h/d | 44.9 | 50.1 | |
| Energy intake, kcal/d | 2185 ± 625 | 2208 ± 585 | 0.24 |
| Alcohol intake, g/d | 20.1 ± 21.1 | 19.9 ± 19.0 | 0.13 |
| Carbohydrates,[3] % | 42.0 ± 6.2 | 42.3 ± 5.9 | 0.40 |
| Lipids,[3] % | 40.1 ± 5.3 | 40.0 ± 4.9 | 0.86 |
| Protein,[3] % | 17.9 ± 2.8 | 17.7 ± 2.6 | 0.02 |
| Number of 24-h records | 10.0 ± 3.2 | 10.3 ± 3.0 | 0.02 |
| BMI, kg/m$^2$ | 24.3 ± 3.4 | 23.9 ± 3.0 | 0.02 |

[1] Values are means ± SDs unless otherwise indicated. SU.VI.MAX, SUpplémentation en VItamines et Minéraux AntioXydants.
[2] Wilcoxon's rank-sum test (continuous variables) or chi-square test (categorical variables).
[3] Percentage of alcohol-free energy intake.

Moreover, there was a positive association between the healthy DP and HA that was close to reaching significance ($P$ = 0.08) but was not linear. In addition, an interaction between the healthy pattern and energy intake was observed ($P$-interaction < 0.01). However, there was no significant interaction between the Western DP and energy intake.

*Subgroup analyses.* Results of the stratified analyses of the association between the healthy DP and HA according to energy intake are presented in **Table 4**. Among participants with higher energy intakes, the healthy DP was not related to the probability of HA. In contrast, among participants with lower energy intakes, a positive association between the healthy pattern and HA was observed, even after accounting for potential confounders. No interaction between the Western and the healthy DPs on HA was detected ($P$ > 0.2).

*Sensitivity analysis.* To examine the robustness of the observed findings, we reanalyzed our data using simplified DPs. Our findings are presented in **Table 5**. In general, the results were concordant with those of the main analyses: whereas there were no overall significant associations between the DPs and HA, there was a significant positive relation between the healthy DP and HA among individuals with caloric intakes the were less than the median ($P$ = 0.01). Among participants with energy consumption that was greater than or equal to the median, no significant results were observed.

## Discussion

*Summary of findings.* In this large cohort of French adults, there was no significant overall association between adherence to a "healthy" DP and HA after adjustment for important

**TABLE 3** Association between dietary pattern and healthy aging: SU.VI.MAX and SU.VI.MAX 2 studies[1]

| Dietary pattern | Tertile[2] 1 ($n$ = 932) | 2 ($n$ = 932) | 3 ($n$ = 932) | $P$-trend |
|---|---|---|---|---|
| Western | | | | |
| Model 1 | 1.00 | 1.09 (0.88, 1.35) | 0.71 (0.53, 0.95) | 0.03 |
| Model 2 | 1.00 | 1.15 (0.93, 1.43) | 0.80 (0.60, 1.07) | 0.17 |
| Healthy | | | | |
| Model 1 | 1.00 | 1.51 (1.24, 1.83) | 1.33 (1.07, 1.65) | 0.01 |
| Model 2 | 1.00 | 1.42 (1.17, 1.73) | 1.19 (0.95, 1.49) | 0.08 |

[1] Values are ORs (95% CIs) obtained from weighted analyses (inverse probability weighting); $n$ = 2796. Model 1 adjusted for age, sex, follow-up time, energy intake, and number of 24-h records. Model 2 adjusted for variables as in model 1 plus supplementation group, educational level, occupation, physical activity, living arrangement, and smoking status. SU.VI.MAX, SUpplémentation en VItamines et Minéraux AntioXydants.
[2] Tertiles of pattern scores were extracted by principal components analysis. Ranges (medians) of scores for the Western pattern were as follows: tertile 1, −2.9 to −0.5 (−1.0); tertile 2, −0.5 to 0.4 (−0.1); and tertile 3, 0.4–5.1 (1.0). Ranges (medians) for the healthy pattern were as follows: tertile 1, −2.8 to −0.5 (−0.9); tertile 2, −0.5 to 0.3 (−0.1); and tertile 3, 0.3–5.2 (0.9).

**TABLE 4** Association between a healthy dietary pattern and healthy aging, stratified by energy intake: SU.VI.MAX and SU.VI.MAX 2 studies[1]

| | Energy intake less than the sex-specific median[2] | | | | Energy intake greater than or equal to the sex-specific median[2] | | | |
|---|---|---|---|---|---|---|---|---|
| | Tertile 1 ($n$ = 465) | Tertile 2 ($n$ = 466) | Tertile 3 ($n$ = 466) | $P$-trend | Tertile 1 ($n$ = 466) | Tertile 2 ($n$ = 467) | Tertile 3 ($n$ = 466) | $P$-trend |
| Model 1 | 1.00 | 1.24 (0.94, 1.62) | 1.60 (1.20, 2.13) | 0.001 | 1 (—) | 1.13 (0.86, 1.48) | 0.98 (0.73, 1.31) | 0.96 |
| Model 2 | 1.00 | 1.20 (0.91, 1.58) | 1.49 (1.11, 2.00) | 0.01 | 1 (—) | 1.09 (0.83, 1.44) | 0.91 (0.67, 1.23) | 0.59 |

[1] Values are ORs (95% CIs) obtained from weighted analyses (inverse probability weighting); $n$ = 2796. The healthy dietary pattern was extracted by principal components analysis and was modeled as tertiles. Ranges (medians) of scores for participants with low energy intakes were as follows: tertile 1, −2.8 to −0.7 (−1.1); tertile 2, −0.7 to −0.1 (−0.4); and tertile 3, −0.1 to 2.6 (0.4). Ranges (medians) for participants with high energy intakes were as follows: tertile 1, −2.6 to −0.1 (−0.5); tertile 2, −0.1 to 0.7 (0.3); and tertile 3, 0.7–5.2 (1.3). Model 1 adjusted for age, sex, follow-up time, energy intake, and number of 24-h records. Model 2 adjusted for variables as in model 1 plus supplementation group, educational level, occupation, physical activity, living arrangement, and smoking status. SU.VI.MAX, SUpplémentation en VItamines et Minéraux AntioXydants.

[2] Median values of energy intake were 2492 kcal/d in men and 1817 kcal/d in women.

confounders such as tobacco smoking and physical activity. However, in line with our primary hypothesis, energy intake had a modulating effect on this association. Although among individuals with energy intakes that were greater than or equal to the sex-specific median, no significant results were observed, adherence to the healthy DP was associated with ~50% higher odds of HA among participants with energy intakes that were less than the median.

*Comparison with the scientific literature.* A substantial number of observational studies have investigated the association between overall diet and aging-related health outcomes, such as cancer risk, diabetes, cardiovascular disease (4, 6–10), cognition (39, 40), and depression (41, 42). However, there is a dearth of knowledge on the relation between HA and the overall diet, because such studies are rare and findings are mixed (11–13). The 2 available studies that have, like our study, investigated a posteriori DPs in relation to HA were based on the Melbourne Collaborative Cohort (13) and the Whitehall II cohort study (12), respectively. In the first investigation, published by Hodge et al. (13), 4 DPs were extracted by factor analysis and named "vegetables," "fruit," "southern European," and "meat/fatty foods." Only 2 patterns were significantly associated with "successful aging": the "fruit" pattern (positively) and the "meat/fatty foods" pattern (inversely). In the second investigation, published by Akbaraly et al. (12), 2 DPs were extracted by PCA and named "healthy foods" and "Western-type." Only the Western-type pattern was (inversely) associated with "ideal aging."

Akbaraly et al. (12) also examined the role of overall diet by applying an a priori score, the Alternative Healthy Eating Index (AHEI). However, this score was not significantly associated with "ideal aging." In contrast to this, Samieri et al. (11) did identify a positive association between the AHEI and HA in a subsample of the Nurses' Health Study.

Methodologic differences between these 3 studies and our study that may have contributed to the varying results include the differences in definitions of HA (in terms of the included items and



**TABLE 5** Association between simplified dietary patterns and healthy aging: SU.VI.MAX and SU.VI.MAX 2 studies (France, 1994–2009)[1]

| | Tertile | | | |
|---|---|---|---|---|
| | 1 ($n$ = 932) | 2 ($n$ = 932) | 3 ($n$ = 932) | $P$-trend |
| Overall association | | | | |
| Western pattern | | | | |
| Model 1 | 1.00 | 0.89 (0.72, 1.11) | 0.76 (0.57, 1.01) | 0.06 |
| Model 2 | 1.00 | 0.92 (0.74, 1.15) | 0.83 (0.63, 1.11) | 0.22 |
| Healthy pattern | | | | |
| Model 1 | 1.00 | 1.25 (1.03, 1.51) | 1.31 (1.07, 1.62) | 0.01 |
| Model 2 | 1.00 | 1.16 (0.95, 1.41) | 1.18 (0.95, 1.46) | 0.12 |
| Below-median energy intake[2] | | | | |
| Healthy pattern | | | | |
| Model 1 | 1.00 | 1.29 (0.99, 1.70) | 1.61 (1.22, 2.14) | 0.001 |
| Model 2 | 1.00 | 1.17 (0.89, 1.55) | 1.46 (1.09, 1.95) | 0.01 |
| Above-median energy intake[2] | | | | |
| Healthy pattern | | | | |
| Model 1 | 1.00 | 1.11 (0.84, 1.46) | 1.16 (0.87, 1.54) | 0.32 |
| Model 2 | 1.00 | 1.09 (0.82, 1.44) | 1.07 (0.79, 1.45) | 0.63 |

[1] Values are ORs (95% CIs) obtained from weighted analyses (inverse probability weighting); $n$ = 2796. The dietary patterns were extracted by principal components analysis and were modeled as tertiles. Ranges (medians) of scores for the simplified Western pattern were as follows: tertile 1, −12.6 to −2.8 (−5.0); tertile 2, −2.8 to 1.8 (−0.7); and tertile 3, 1.8–32.1 (5.0). Ranges (medians) for the simplified healthy pattern were as follows: tertile 1, −9.1 to −1.9 (−3.5); tertile 2, −1.9 to 1.0 (−0.5); and tertile 3, 1.0– 22.1 (3.4). Model 1 adjusted for age, sex, follow-up time, energy intake, and number of 24-h records. Model 2 adjusted for variables as in model 1 plus supplementation group, educational level, occupation, physical activity, living arrangement, and smoking status. SU.VI.MAX, SUpplémentation en VItamines et Minéraux AntioXydants.

[2] Less than or greater than or equal to the sex-specific median. Median values were 2493 kcal/d in men and 1817 kcal/d in women.

applied cutoff points). The definitions of Akbaraly et al. (12) (surviving to at least 60 y, absence of chronic conditions, absence of mental health problems, presenting sex- and age-specific performance in cardiometabolic, respiratory, musculoskeletal, and cognitive functioning tests that were greater than or equal to the median) and of Samieri et al. (11) (survival to at least 70 y, absence of major chronic disease, absence of major impairments in cognitive, physical, and mental functioning) appear to be the "strictest" because only 4.0% and 11.0% of subjects were classified as "ideal" or "healthy" agers at follow-up, respectively. In the study by Hodge et al. (13), a much larger proportion of participants (18.6%) were classified as "successful" agers (i.e., surviving to at least age 70 y, having no major chronic disease, not presenting any major limitations in physical functioning, and having good mental health). In our study, the proportion with HA was even higher (39.2%). Next, although the average follow-up periods of the different studies were approximately comparable (ranging from 12 to 16 y), there were large differences in mean baseline ages (ranging from 51.3 y in the study by Akbaraly et al. to ~64 y in the study by Hodge et al.). These age differences, combined with sex differences (the analysis by Samieri et al. included only women) and important cultural differences given the different study locations (our study: France; Hodge et al.: Australia; Akbaraly et al.: United Kingdom; Samieri et al.: United States), likely explain the variation in eating habits across studies, yielding differences in extracted DPs and AHEI distributions.

Overall, despite certain inconsistencies in study findings, each of the available studies showed a significant association between at least 1 DP or a priori score and HA. Thus, our study and other available investigations tend to suggest a relation between overall diet and HA.

The specificity of our results concerning the "healthy" DP for individuals with energy intakes that were less than the median suggests that high energy intakes may "counterbalance" beneficial effects of "healthy" DPs. Indeed, a recently published study in a Mediterranean population (43) showed an inverse association between a high energy intake (defined as being in the highest tertile; i.e., consumption of ≥1700 kcal/d) and "successful aging." While the dietary data in our study were based on repeated 24-h records, Tyrovolas et al. (43) used a semiquantitative FFQ, which may explain the apparent differences in energy intakes (in our study, the highest tertile of daily energy intake was 2436 kcal; data not shown). Moreover, compared with our HA model, the concept used by Tyrovolas et al. was based on a different set of variables (educational level, financial resources, physical activity level, BMI, psychological health, participation in social activities, cardiovascular disease risk factors, and dietary habits). Yet overall, the results by Tyrovolas et al. support our hypothesis that an adapted energy intake has an important role in HA.

Furthermore, caloric restriction has been much discussed as a potentially beneficial factor for increased longevity and a lowered probability of age-related chronic disease (44). The discussed underlying biological mechanisms include enhanced genomic stability and chromatin remodeling, as well as improved chaperone-mediated protein homeostasis. Key signaling pathways include the inhibition of Protein kinase B, which activates class O forkhead box transcription factors (FOXOs), which have been shown to upregulate DNA repair, autophagy, antioxidant activity, stress resistance, and cell proliferation (44). The applicability of caloric restriction (and notably severe caloric restriction) to humans, however, is controversial—notably because covering all nutrient needs while lowering energy intake may be an unrealistic aim for the general population (44). In this context, our results stress the need for both a regulated (i.e., not necessarily a drastically reduced) energy intake and high dietary quality, because only the combination of a less-than-median energy intake and adherence to a healthy DP was associated with a higher probability for HA.

*Limitations and strengths.* Some limitations of our study should be noted. First, there is wide diversity in the definitions of HA in the literature. However, by grounding our concept on the Rowe and Kahn model, with an additional focus on subjective criteria as recently suggested (3, 17), we strove to obtain a rather "classical," yet progressive definition. Second, most variables used in the definition of HA were not available at baseline. However, the fact that participants were middle-aged at baseline, and initially free of chronic diseases and sufficiently healthy to be included in a long-term nutritional trial, suggests that there was a low proportion of participants who would have been classified as "non–healthfully aging" at baseline. Finally, the SU.VI.MAX cohort consists of volunteers who were willing to participate in a long-term intervention trial and a subsequent follow-up examination, which may limit the external validity of our findings.

Our study also exhibits some important strengths, including its longitudinal design, a wide range of indicators of a healthy/unhealthy aging process, as well as high-quality data on diet and potential confounders. In addition, selection bias, which constitutes an important methodologic challenge when focusing on the epidemiology of aging, was accounted for by using an innovative statistical method (inverse probability weighting).

In conclusion, our findings suggest that there may be an overall impact of midlife DPs on HA, beyond an impact on individual health outcomes. According to our results, dietary habits corresponding to a healthy DP—with concomitant controlled total energy intake—may be beneficial. In this context, it is urgent to better characterize diet-related lifestyles that efficiently promote HA and thus help reduce the social, health care, and economic burdens related to aging.

**Acknowledgments**

We thank Younes Esseddik, Gwenaël Monot, Paul Flanzy, Mohand Aït Oufella, Yasmina Chelghoum, and Than Duong Van (computer scientists); Rachida Mehroug (logistics assistant); and Nathalie Arnault, Véronique Gourlet, Fabien Szabo, Laurent Bourhis, and Stephen Besseau (statisticians) for their technical contribution to the SU.VI.MAX study. We also thank Stéphane Raffard, who was responsible for standardization of the cognitive evaluation, and Frédérique Ferrat, who coordinated the logistic aspects of the neuropsychological evaluation. SH, PG, and EK-G designed the research (development of the concept, design, and protocol of the SU.VI.MAX/SU.VI.MAX 2 studies and coordination of data collection); KEA performed the statistical analysis and wrote the manuscript; EK-G provided methodologic guidance; and KEA, CL, VAA, CJ, SH, PG, and EK-G were involved in interpreting the results and editing the manuscript for important intellectual content. All authors read and approved the final version of the manuscript.

## References

1. United Nations, Department of Economic and Social Affairs, Population Division [Internet]. World population prospects: the 2012 revision, highlights and advance tables. New York: United Nations; 2013 [cited 2015 Jul 23]. Available from: http://esa.un.org/wpp/documentation/pdf/WPP2012_HIGHLIGHTS.pdf.
2. Rowe JW, Kahn RL. Successful aging. Gerontologist 1997;37:433–40.
3. Cosco TD, Prina AM, Perales J, Stephan BC, Brayne C. Operational definitions of successful aging: a systematic review. Int Psychogeriatr 2014;26:373–81.

4. Kiefte-de Jong JC, Mathers JC, Franco OH. Nutrition and healthy ageing: the key ingredients. Proc Nutr Soc 2014;73:249–59.
5. Jacobs DR Jr., Gross MD, Tapsell LC. Food synergy: an operational concept for understanding nutrition. Am J Clin Nutr 2009;89 Suppl:1543S–8S.
6. Waijers PM, Feskens EJ, Ocke MC. A critical review of predefined diet quality scores. Br J Nutr 2007;97:219–31.
7. Kontogianni MD, Panagiotakos DB. Dietary patterns and stroke: a systematic review and re-meta-analysis. Maturitas 2014;79:41–7.
8. Sofi F, Abbate R, Gensini GF, Casini A. Accruing evidence on benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis. Am J Clin Nutr 2010;92:1189–96.
9. Kant AK. Dietary patterns: biomarkers and chronic disease risk. Appl Physiol Nutr Metab 2010;35:199–206.
10. Kourlaba G, Panagiotakos DB. Dietary quality indices and human health: a review. Maturitas 2009;62:1–8.
11. Samieri C, Sun Q, Townsend MK, Chiuve SE, Okereke OI, Willett WC, Stampfer M, Grodstein F. The association between dietary patterns at midlife and health in aging: an observational study. Ann Intern Med 2013;159:584–91.
12. Akbaraly T, Sabia S, Hagger-Johnson G, Tabak AG, Shipley MJ, Jokela M, Brunner EJ, Hamer M, Batty GD, Singh-Manoux A, et al. Does overall diet in midlife predict future aging phenotypes? A cohort study. Am J Med 2013;126:411–9.
13. Hodge AM, O'Dea K, English DR, Giles GG, Flicker L. Dietary patterns as predictors of successful ageing. J Nutr Health Aging 2014;18:221–7.
14. Hercberg S, Galan P, Preziosi P, Roussel AM, Arnaud J, Richard MJ, Malvy D, Paul-Dauphin A, Briancon S, Favier A. Background and rationale behind the SU.VI.MAX study, a prevention trial using nutritional doses of a combination of antioxidant vitamins and minerals to reduce cardiovascular diseases and cancers. Int J Vitam Nutr Res 1998;68:3–20.
15. Hercberg S, Galan P, Preziosi P, Bertrais S, Mennen L, Malvy D, Roussel AM, Favier A, Briancon S. The SU.VI.MAX study: a randomized, placebo-controlled trial of the health effects of antioxidant vitamins and minerals. Arch Intern Med 2004;164:2335–42.
16. Kesse-Guyot E, Amieva H, Castetbon K, Henegar A, Ferry M, Jeandel C, Hercberg S, Galan P. Adherence to nutritional recommendations and subsequent cognitive performance: findings from the prospective Supplementation with Antioxidant Vitamins and Minerals 2 (SU.VI.MAX 2) study. Am J Clin Nutr 2011;93:200–10.
17. Depp C, Vahia IV, Jeste D. Successful aging: focus on cognitive and emotional health. Annu Rev Clin Psychol 2010;6:527–50.
18. Assmann KE, Andreeva VA, Jeandel C, Hercberg S, Galan P, Kesse-Guyot E. Healthy aging five years after a period of daily supplementation with antioxidant nutrients: a post hoc analysis of the French randomised trial SU.VI.MAX. Am J Epidemiol 2015. In press.
19. Hercberg S, Kesse-Guyot E, Druesne-Pecollo N, Touvier M, Favier A, Latino-Martel P, Briancon S, Galan P. Incidence of cancers, ischemic cardiovascular diseases and mortality during 5-year follow-up after stopping antioxidant vitamins and minerals supplements: a post-intervention follow-up in the SU.VI.MAX study. Int J Cancer 2010;127:1875–81.
20. WHO. International classification of diseases. 10th revision, clinical modification. Geneva (Switzerland): WHO; 2003.
21. Hugenschmidt CE, Burdette JH, Morgan AR, Williamson JD, Kritchevsky SB, Laurienti PJ. Graph theory analysis of functional brain networks and mobility disability in older adults. J Gerontol A Biol Sci Med Sci 2014;69:1399–406.
22. Cavallari M, Moscufo N, Skudlarski P, Meier D, Panzer VP, Pearlson GD, White WB, Wolfson L, Guttmann CR. Mobility impairment is associated with reduced microstructural integrity of the inferior and superior cerebellar peduncles in elderly with no clinical signs of cerebellar dysfunction. Neuroimage Clin 2013;2:332–40.
23. Wakefield DB, Moscufo N, Guttmann CR, Kuchel GA, Kaplan RF, Pearlson G, Wolfson L. White matter hyperintensities predict functional decline in voiding, mobility, and cognition in older adults. J Am Geriatr Soc 2010;58:275–81.
24. Guralnik JM, Simonsick EM, Ferrucci L, Glynn RJ, Berkman LF, Blazer DG, Scherr PA, Wallace RB. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85–94.
25. Pendlebury ST, Cuthbertson FC, Welch SJ, Mehta Z, Rothwell PM. Underestimation of cognitive impairment by Mini-Mental State Examination versus the Montreal Cognitive Assessment in patients with transient ischemic attack and stroke: a population-based study. Stroke 2010;41:1290–3.
26. Folstein MF, Robins LN, Helzer JE. The Mini-Mental State Examination. Arch Gen Psychiatry 1983;40:812.
27. Adam S, Van der Linden M, Ivanoiu A, Juillerat AC, Bechet S, Salmon E. Optimization of encoding specificity for the diagnosis of early AD: the RI-48 task. J Clin Exp Neuropsychol 2007;29:477–87.
28. Delis DC, Kaplan E, Kramer JH. Delis-Kaplan Executive Function System (D-KEFS) examiner's manual. 1st ed. San Antonio (TX): The Psychological Corporation; 2001.
29. Delis DC, Kaplan E, Kramer JH. Delis-Kaplan Executive Function System (D-KEFS) technical manual. 1st ed. San Antonio (TX): The Psychological Corporation; 2001.
30. Graf C. The Lawton instrumental activities of daily living (IADL) scale. Medsurg Nurs 2008;17:343–4.
31. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.
32. Morin AJ, Moullec G, Maiano C, Layet L, Just JL, Ninot G. Psychometric properties of the Center for Epidemiologic Studies Depression Scale (CES-D) in French clinical and nonclinical adults. Rev Epidemiol Sante Publique 2011;59:327–40.
33. Leplège A, Ecosse E, Verdier A, Perneger TV. The French SF-36 Health Survey: translation, cultural adaptation and preliminary psychometric evaluation. J Clin Epidemiol 1998;51:1013–23.
34. Le Moullec N, Deheeger M, Preziosi P, Montero P, Valeix P, Rolland-Cachera MF, Potier de Courcy G, Christides JP, Galan P, Hercberg S. Validation du manuel photos utilisé pour l'enquête alimentaire de l'étude SU.VI.MAX. [Validation of the photo manual used for the dietary assessment of the SU.VI.MAX study.] Cah Nutr Diet 1996;31:158–64 (in French).
35. Lassale C, Fezeu L, Andreeva VA, Hercberg S, Kengne AP, Czernichow S, Kesse-Guyot E. Association between dietary scores and 13-year weight change and obesity risk in a French prospective cohort. Int J Obes (Lond) 2012;36:1455–62.
36. Cole SR, Hernan MA. Constructing inverse probability weights for marginal structural models. Am J Epidemiol 2008;168:656–64.
37. Seaman SR, White IR. Review of inverse probability weighting for dealing with missing data. Stat Methods Med Res 2013;22:278–95.
38. Schulze MB, Hoffmann K, Kroke A, Boeing H. An approach to construct simplified measures of dietary patterns from exploratory factor analysis. Br J Nutr 2003;89:409–19.
39. van de Rest O, Berendsen AA, Haveman-Nies A, de Groot LC. Dietary patterns, cognitive decline, and dementia: a systematic review. Adv Nutr 2015;6:154–68.
40. Allès B, Samieri C, Feart C, Jutand MA, Laurin D, Barberger-Gateau P. Dietary patterns: a novel approach to examine the link between nutrition and cognitive function in older individuals. Nutr Res Rev 2012;25:207–22.
41. Lai JS, Hiles S, Bisquera A, Hure AJ, McEvoy M, Attia J. A systematic review and meta-analysis of dietary patterns and depression in community-dwelling adults. Am J Clin Nutr 2014;99:181–97.
42. Rahe C, Unrath M, Berger K. Dietary patterns and the risk of depression in adults: a systematic review of observational studies. Eur J Nutr 2014;53:997–1013.
43. Tyrovolas S, Haro JM, Mariolis A, Piscopo S, Valacchi G, Makri K, Zeimbekis A, Tyrovola D, Bountziouka V, Gotsis E, et al. The role of energy balance in successful aging among elderly individuals: the multinational MEDIS study. J Aging Health 2015. In press.
44. Fontana L, Partridge L. Promoting health and longevity through diet: from model organisms to humans. Cell 2015;161:106–18.