Abbreviations

BMI: body mass index; CVR-P: cardiovascular risk parameters; CVD: cardiovascular disease; FFQ: food frequency questionnaire; GLMs: general linear models; HDL-c: HDL cholesterol; LDL-c: LDL cholesterol; MedDiet: Mediterranean diet;

ABSTRACT

Background Study of dietary patterns is gaining interest. Although the health benefits of yogurt and lignans have been investigated separately, as far as we know, their associative effect has not been previously studied.

Objective To examine the association between yogurt and lignans using biomarkers of cardiovascular disease risk in an elderly population.

Design A cross-sectional analysis of the association between baseline dietary information and cardiovascular risk parameters using food frequency questionnaires (FFQ).

Participants A total of 7169 Spanish participants of the PREDIMED study (elderly men and women at high cardiovascular risk) enrolled from June 2003 to June 2009.

Main outcome measures Cardiovascular risk parameters (CVR-P) including cholesterol, triglycerides, glucose, body mass index, weight, waist circumference, and blood pressure.

Statistical Analysis General linear models (GLM) were used to assess the relationship between categorical exposure variables (yogurt, total dairy, lignans, and yogurt plus lignans) and CVR-P.

Results Yogurt and lignans appear to have beneficial effects on human health separately, but consumption of both was associated with greater improvements in some cardiovascular health parameters. In particular, participants with higher consumption of both yogurt and lignans showed lower levels of total cholesterol (estimated beta-coefficients (β)=-6.18, P=0.001) and LDL cholesterol (β=-4.92, P=0.005). In contrast participants with less consumption of yogurt and lignans showed higher levels of body mass index (β=0.28, P=0.007) and weight (β=1.20, P=0.008).

Conclusions: A high consumption of lignans and yogurt is associated with a better profile of CVR-P in an elderly Mediterranean population. Further research is warranted to explore the mechanisms and consequences of this potential effect.

INTRODUCTION

Polyphenols such as lignans, [1] which are able to reach the colon to be metabolized by microbiota, may have additional health benefits due to their metabolites. Some polyphenols have even been considered as prebiotics, because of their ability to alter the microbiota profile and/or levels. [2] The main lignan polyphenols are pinoresinol, matairesinol, secoisolariciresinol, 1-acetoxypinoresinol, lariciresinol, syringaresinol and isolariciresinol (**Fig.1**). Beneficial health effects such as cancer prevention and cardiovascular diseases (CVD) have been related to lignan intake.[3] Flaxseed and other seeds have high lignan concentrations, as do some fruits and vegetables, and beverages like wine, coffee and tea. [4]

Probiotics are live microorganisms that confer health benefits on the host when administered in adequate amounts [5]. Most of the probiotics currently consumed by humans come from fermented dairy products such as yogurt (produced using cultures of *Streptococcus thermophilus and Lactobacillus bulgaricus*) [6]. The benefits attributed to probiotics include the prevention/management of diarrhea, enhancement of the immune response and improved lactose digestion and absorption.[7]

Since nutrients and foods are consumed in combination, nutritional epidemiology recognizes the importance of studying the effect of dietary patterns on health [8]. Food synergy is defined as additive or more than additive influences of foods and food constituents on health, and it is a concept that links dietary patterns and foods with disease prevention [9].

Previous studies in the PREDIMED (*Prevención con Dieta Mediterránea*) framework have shown an association between yogurt consumption and a decrease in the incidence of metabolic syndrome and type 2 diabetes [10,11]. However, the associative effects of yogurt and lignan consumption have not been studied to date. The aim of this work is to assess the health benefits of lignans and yogurt consumption on cardiovascular risk parameters (CVR-P) such as lipid profile, glycemic profile, body mass index and blood pressure in this well-characterized elderly population.

PARTICIPANTS AND METHODS

Study design

A cross-sectional study was performed with baseline data from the PREDIMED cohort. A detailed description of the study has been published before [12,13]. Baseline data collection took place in Spain from June 2003 to June 2009. Briefly, the PREDIMED study was a large prospective, multicenter, randomized and controlled trial that aimed to assess the effect of the traditional Mediterranean diet (MedDiet) on the primary prevention of clinical cardiovascular events in elderly participants at high risk, and took place from October 2003 to December 2010. The 7447 eligible participants were randomized to one of the following intervention groups: MedDiet supplemented with extra virgin olive oil, MedDiet supplemented with nuts, or a control diet (low-fat diet) group. The trial was stopped after a median follow-up of 4.8 years due to the benefits of the MedDiets on the prevention of major cardiovascular events (myocardial infarction, stroke, or cardiovascular death) compared to the low-fat group [14].

This study was conducted according to the guidelines of the Declaration of Helsinki and all procedures involving human participants/patients were approved by the Institutional Review Boards of the participating centers (Clinical Trial Registration: ISRCTN of London, England: 35739639). Written informed consent was obtained from all participants.

Population characteristics, cardiovascular risk parameters, anthropometric measures and diet

From the 7447 participants, 275 were excluded since they did not complete the food frequency questionnaire (FFQ) at baseline and 3 participants whose HDL-cholesterol (HDL-c) values were missing. Finally, the number of participants included was 7169.

To assess the diet and lifestyle characteristics of the population, participants filled out the following validated questionnaires: a 137-item semi-quantitative FFQ [15], a 14-point score questionnaire on adherence to the traditional MedDiet [16], and the Spanish version of the Minnesota Leisure Time Physical Activity Questionnaire [17]. Participants also filled out a general questionnaire to provide information about lifestyle habits, concurrent diseases and medication use.

Body weight and height were measured with minimum clothing and no shoes, using calibrated scales and wall-mounted stadiometers, respectively. Blood pressure was measured in a sitting position, using a semiautomatic sphygmomanometer (Omron HEM-705CP, Hoofddorp, The Netherlands), in triplicate with a 5-min interval between each measurement, and the mean of these values was recorded, following the procedures recommended by the European Hypertension Society [18]. Biochemical analysis was performed in local laboratories. Glucose was measured by the glucose-oxidase method, cholesterol by esterase-oxidase-peroxidase, Triglycerides (TGs) by glycerol-phosphate oxidase-peroxidase, and HDL-c by direct measurement. All local laboratories satisfied external quality control requirements. When TGs were <300 mg/dL, LDL-cholesterol (LDL-c) was calculated with the Friedewald formula[19]. A concordance study of nine laboratories was conducted. From each study, a mean of 200 samples were analysed for total cholesterol, HDL-c, and TGs. The Medical Research Institute of del Mar laboratory, which used ABX-Horiba commercial kits in a PENTRA-400 autoanalyzer (ABX-Horiba), was used as a reference. One center was unable to provide samples for the concordance study. The concordance analysis of lipid measurements showed, respectively, a r^2 and a confidence interval (95%) between 0.85 and 0.97, and 0.85 (0.77, 0.90) and 0.97 (0.95, 0.98) for total cholesterol; between 0.82 and 0.92, and 0.81 (0.78, 0.83) and 0.92 (0.89, 0.95) for HDL-c; between 0.81 and 0.99, and 0.81 (0.73, 0.87) and 0.99 (0.99, 0.99) for triglycerides; and between 0.82 and 0.96, and 0.82 (0.74, 0.88) and 0.99 (0.99, 0.99) for glucose.

Categories of lignan and yogurt consumption

Total energy and nutrient intake were calculated using Spanish food composition tables [20]. Lignan intake was calculated by multiplying the content of lignans in a particular food item (mg/g) by the daily consumption of this food item (g/day). Data about the lignan content in foods were obtained from the Phenol-Explorer database[21]. Values of lignan intake were divided into low or high, the median being the cut-point, or into tertiles, depending on the analysis.

The FFQ included questions concerning consumption of dairy products. In the validation study, the intra-class correlation coefficient between dairy product consumption from the FFQ and repeated food records was 0.84 [22]. Responses to individual dairy items of the FFQ were converted to average daily consumption (g/day) and categorized into total yogurt (including full-fat and low-fat) and total dairy without yogurt (including all types of milk, cheeses, custard, whipped cream and ice cream). The consumptions were then divided into the following categories: 0 yogurts/day, from 0 to <1 yogurts/day and ≥1 yogurts/day, or tertiles, depending on the analysis. Total dairy consumption was divided in tertiles.

Lignan, dairy and other nutrient intake were adjusted for total energy intake since it is associated with disease risk and is usually proportional to nutrient intake.

Statistical analysis

Descriptive analyses were conducted to compare baseline characteristics across categories of yogurt consumption at baseline. Values are presented as mean±SD for continuous variables and frequencies (and percentages) for categorical variables. For continuous variables, differences between groups were examined using an ANOVA test. For categorical data, chi square tests were used.

General Linear Models (GLMs) were used to assess the relationship between categorical exposure variables (lignans, yogurt, total dairy and yogurt plus lignans) and cholesterol, triglycerides, blood pressure, glucose and weight. In multivariable models, adjusted for recruitment center, sex, age, smoking, soft drinks, carbohydrates, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, n-3 fatty acids, family history of heart disease, diabetes, hypertension, dairy, fiber and energy intake. A test for linear trend was performed with the use of the resulting variable as a continuous one.

Given the prebiotic of lignans, it is plausible that yogurt consumption may have differential effects on CVR-P depending on the intake of these polyphenolic compounds. Therefore, to test for statistical interactions between lignans and yogurt on different CVR-P, stratified analyses were performed and interaction p-values were calculated.

All statistical analyses were conducted using SAS software [23], version 9 (SAS Institute, Inc., Cary, NC).All t- tests were 2-sided and *p*-values below 0.05 were considered significant.

RESULTS

The baseline characteristics of the study participants are summarized in **Table 1**. Around 23% of the population did not consume any yogurt (1631 participants), 54% consumed <1 yogurt per day (3840 participants) and 24% consumed ≥1 yogurt per day (1698 participants). The distribution of sex, smoking, level of education, energy expenditure at leisure time, age, participants with hypertension and cholesterol was significantly different between groups. In contrast, participants with diabetes were equally distributed among the three yogurt groups. Participants with the highest yogurt intake also had the highest intake of carbohydrates, protein and fiber, but the lowest cholesterol intake levels. Non-consumers had higher blood pressure, glucose and triglycerides but a lower body mass index (BMI) and HDL-c levels. There were no significant differences between yogurt consumption and Mediterranean Diet adherence (MedDiet Score).

Lignans and food sources

Individual lignan intake and their chemical structures, as well as the main lignan food sources ingested by the PREDIMED cohort, are represented in **Figure 1**. The most consumed was pinoresinol (0.31±0.25 mg/day), followed by 1-acetoxypinoresinol (0.25±0.12 mg/day), lariciresinol (0.12±0.06 mg/day), syringaresinol (0.07±0.09 mg/day), secoisolariciresinol (0.06±0.06 mg/day), isolariciresinol (0.03±0.07mg/day), medioresinol (0.01±0.01 mg/day) and matairesinol (0.004±0.002 mg/day). The main lignan food sources were olive oil (over 60%), wheat products (about 15%), tomato and derivatives (8%), red wine (5%), asparagus (4%), kiwis (3%) and others fruits and vegetables. **Supplemental Table 1** shows the main food sources of each individual lignan.

Lignan intake and CVR-P

Table 2 shows the relationship between lignan intake and CVR-P. Participants with the highest (>0.67 mg/day) and medium (0.46-0.67 mg/day) intakes of lignan had significantly lower glucose levels in plasma (β=-6.08, P<0.001 and β=-4.16, P=0.002, respectively) compared to those with the lowest lignan intake (P-trend=0.02). No significant associations were observed for other CVR-P across the lignan groups.

Total yogurt, full-fat yogurt, low-fat yogurt or dairy intake and CVR-P

The associations between the intake of yogurt, full-fat yogurt, low-fat yogurt or other dairy and CVR-P are presented in **Table 2**. Participants who ate yogurt (any kind) had significantly lower total cholesterol levels (β=-2.92, P=0.02 for <1 yogurt/day, and β=-3.33, P=0.03 for ≥1 yogurt/day, P-trend=0.03) compared to non-consumers. Those with the highest intake (≥1 yogurt/day) also had lower triglyceride levels (β=-6.94, P=0.02) compared to non-consumers. In addition, in both groups, yogurt consumption was associated with higher weight (β=0.90, P=0.004 and β=0.88, P=0.02 for 1 yogurt/day and ≥1 yogurt/day, respectively, P-trend=0.007).

A low intake of full-fat yogurt was associated with higher weight and higher diastolic blood pressure (β=0.78, P=0.01 and β=0.81, P=0.02 respectively). An intake of ≥1 yogurt/day of full-fat yogurt was correlated with a decrease in triglyceride levels (β=-9.33, P=0.03). However, there were no significant differences in the other CVR-P. Regarding low-fat yogurt, consumers of 1 yogurt/day had lower total cholesterol (β=-4.40, P<0.001), HDL-c (β=-1.05, P=0.01), LDL-c (β=-3.80, P<0.001) and diastolic blood pressure (β=-0.076, P=0.02) but higher weight (β=0.64, P=0.03) compared to non-consumers.

Finally, association between total dairy intake and CVR-P was examined. A total dairy intake of more than 500 g/day was associated with lower total cholesterol (β=-4.36, P=0.002), and diastolic blood pressure (β=-0.78, P=0.04), and a higher glucose level in plasma (β=7.89, P<0.001). Total dairy intake of 200-500g/day was associated with lower total cholesterol (β=-4.30, P<0.001), HDL-c (β=-0.87, P=0.04), LDL-c (β=-2.34, P=0.03), and a higher glucose level (β=2.64, P=0.04). Significant linear associations were found for total dairy and total cholesterol (P-trend<0.001), HDL-c (P-trend=0.005), LDL-c (P-trend=0.048), glucose (P-trend<0.001), systolic blood pressure (P-trend=0.025), and diastolic blood pressure (P-trend=0.02).

Joint analysis of lignans and yogurt consumption

Table 3 shows the results of the GLMs used to assess the association between yogurt consumption and different CVR-P stratified by lignan intake. Participants with the highest consumption of lignans (>0.6 mg/day) and total yogurt had significantly lower levels of total cholesterol (β=-6.18, P=0.001, P-interaction=0.01) and LDL-c (β=-4.92, P=0.005, P-interaction=0.05), and triglycerides levels (β=-7.98, P=0.049, P-interaction=0.21), however, P for interaction was not significant in this last parameter. . Participants with higher consumption of yogurt but lower intake of lignans (<0.6 mg/day) had significantly higher BMI (β=0.51, P=0.006) and weight (β=1.35, P=0.01), but there were no differences in participants within the high lignan intake group (β=-0.04, P=0.81, P-interaction=0.41 and β=0.391, P=0.45, P-interaction=0.42, respectively).

DISCUSSION

In the present cross-sectional study, the ameliorative effect of lignans, yogurts and the joint consumption of lignans and probiotics on CVR-P in humans was explored. In studies dealing with yogurt and lignan consumption separately, beneficial effects on human health have been reported, but in this study their joint consumption had a stronger impact on CVR-P, and was associated with lower cholesterol, LDL-c and a tendency to lower triglyceride levels. To our knowledge, this is the first time it has been proposed that polyphenols and yogurt can improve CVR-P, especially the lipid profile.

Some polyphenols can be metabolized and absorbed through the gut barrier but usually they reach the colon, where they can be metabolized by the microbiota and absorbed [24]. Lignans are metabolized by the intestinal microbiota to enterodiol and enterolactone [1,25]. There is some evidence indicating that lignan-rich foods are protective against cardiovascular disease and some cancers, including breast, colon, and prostate cancer [3,26,27]. In this study, higher intake of lignans was associated with a decrease on glucose levels. In addition, stratified analyses on sex showed less glucose levels for both men and women (data not shown). Pinoresinol was the major lignan ingested, principally (96%) from olive oil. In a study of plant lignans by During et al. [28], pinoresinol showed the strongest anti-inflammatory effect in the human intestine. In a cross-sectional study including 242 males and females in northern Italy, matairesinol was associated with lower vascular inflammation and endothelial dysfunction [29]. In a prospective cohort study with 570 men [30], 4 lignans (lariciresinol, pinoresinol, secoisolariciresinol, and matairesinol) were investigated and the intake of matairesinol was inversely associated with mortality due to a reduction in cardiovascular disease and cancer. In this population, matairesinol was the least consumed lignan, and the main food sources of lignans were olive oil, wheat, tomato, red wine, asparagus and kiwis (**Supplemental Table 1**).

The gut microbiota can also be influenced by the diet, which has a direct impact on the gut environment, including transit time and pH [31]. The prebiotic effect of polyphenols has been studied previously [2], and it is suggested they could affect the relative viability of beneficial bacterial groups like *Firmicute*s and *Bacteroides* [32–34]. The polyphenol-microbiota interaction is evident [35,36], but more holistic approaches involving the use of high-throughput “omics” tools are needed to shed light on its physiological relevance for humans.

Yogurt, as a probiotic, has benefits for consumer health. Its functional properties have been confirmed by studies on the metabolic activity of yogurt bacteria in the human intestine [6,37–39]. As a functional food, yogurt has been associated with benefits for cardiovascular and gastrointestinal health, weight management, and type 2 diabetes, among others [40,41]. In this study, total yogurt and low-fat yogurt intake were correlated with higher weight, but when yogurt was consumed in a high lignan diet no weight increase was observed. Obesity is a CVR-P and is related with increased levels of triglycerides, LDL-c, and cholesterol, and decreased levels of HDL-c. In accordance with Cormier et al. [42], yogurt consumption was associated with lower levels of cholesterol and triglycerides. Stratified analyses on sex showed some differences between men and women, more than one yogurt per day was associated with lower levels of cholesterol and triglycerides in men, but higher BMI and weight in women. Full-fat yogurt was correlated with higher LDL-c and lower triglycerides, and low-fat yogurt was correlated with lower total cholesterol, HDL-c and LDL-c, but with no impact on triglycerides. It has been proposed that the potential underlying mechanisms for weight loss or the prevention of weight gain could be stimulatory effects on the growth of beneficial intestinal bacteria [43]. An alternative mechanism of action is that yogurt consumption induces higher satiety and therefore appetite reduction [40]. The latter effect could also involve microbiota, with microbial manipulation of eating behavior via the nervous system and the gut-brain axis [44,45]. A study by H. Zapata et al. [46] concludes that manipulating the intestinal microbiota may be beneficial for maintaining health in older adults.

A high consumption of lignans and yogurt was associated with lower levels of total cholesterol, LDL-c and triglycerides, while HDL-c did not decrease, indicating an improved lipid profile. Yogurt consumption did not affect serum glucose levels, but these were significantly higher when total dairy was considered. On the one hand, it seems that microbiota associated with yogurt intake metabolizes lignans more efficiently and, on the other, lignans help to modulate gut microbiota by increasing the beneficial strains.

Studying the role of diet in chronic conditions such as cardiovascular diseases is complex, as “we don’t eat nutrients, we eat foods”[47]. Therefore, focusing on the synergy between foods and bioactive compounds could be a useful approach. Limiting analysis to individual nutrients may fail to take into account many potential interactions between dietary components, and requires a large sample size and adjustment for other nutrients[48,49].

This study has taken a challenging approach by focusing on the potential health benefits of lignans, yogurt and their joint consumption; nevertheless, some limitations should be noted. Firstly, the data obtained was from an elderly population at high cardiovascular risk, which may limit the generalization of the results. Secondly, lignan intake was calculated with FFQs and Phenol-Explorer, which is the most comprehensive polyphenol database available, but information about some foods is still limited. It should also be considered that polyphenol content in foods can differ according to the cooking, maturity at harvesting, environmental factors or storage conditions [1,50]. It is important to be aware the fact that some confounding variables as lifestyle or stress among others could be ignored since they were not recorded in the questionnaires. Finally, as this is an observational study, it is unable to establish a cause-effect relationship; therefore a clinical trial would be crucial to confirm the hypothesis.

CONCLUSIONS

These findings suggest that an associative effect of lignans and yogurt may ameliorate CVR-P in humans. Therefore, daily low-fat yogurt consumption in a healthy, well-balanced diet with a high content of lignan-rich foods, such as flaxseed or extra virgin olive oil, may be recommended to enhance the beneficial effects of these two foods obtained when ingested separately, at least in elderly populations. Further clinical trials in this direction are needed, focusing on the differences in lignan metabolites between yogurt consumers and non-consumers. The modification of microbiota communities with the intake of yogurt and lignans and their impact on health should also be studied.

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Supplemental table 1. Mean intake of lignan compounds and their food sources of 7169 elderly Spanish participants at high cardiovascular risk from the PREDIMED study.

Lignan	**Intake (mg/day)**	**SD**[a]	**Food sources**
Pinoresinol	0.31	0.25	Olive oil (96%), asparagus (0.7%), refined wheat (0.6%), whole-grain wheat (0.6%)
1-Acetoxypinoresinol	0.25	0.12	Olive oil (100%)
Lariciresinol	0.12	0.06	Wheat (67%), whole-grain wheat (11%), tomato (6.5%), asparagus (4%)
Secoisolariciresinol	0.06	0.06	Kiwi (37%), asparagus (31%), red wine (19%), whole-grain wheat (6%)
Syringaresinol	0.07	0.09	Whole-grain wheat (81%), asparagus (10%), kiwis (3%), red wine (3%)
Isolariciresinol	0.03	0.07	Red wine (100%)
Medioresinol	0.01	0.01	Whole-grain wheat (53%), tomato (21%), kiwi (15%), asparagus (8%)
Matairesinol	0.004	0.002	Red wine (74%), asparagus (8%), tea (6%), whole-grain wheat (6%)

[a] Standard Desviation

Table 1. Baseline characteristics of 7169 elderly Spanish participants at high cardiovascular risk from the PREDIMED cohort according to categories of yogurt consumption assessed by food frequency questionnaire adjusted for energy.

	Non consumers	**< 1 yogurt/day**	**≥1 yogurt/day**	
Characteristics	**n (%)**	**n (%)**	**n (%)**	***P value***[a]
No. of participants (n=7169)	1631 (22.7)	3840(53.6)	1698 (23.7)	
Sex, women	663 (40.6)	2201 (57.3)	1216 (71.6)	<.001
Smoking				<.001
Never	784 (48.0)	2382 (62.0)	1217 (71.7)	
Current	393 (24.1)	622 (16.2)	187 (11.0)	
Former	454 (27.8)	836 (21.8)	294 (17.3)	
Education				0.01
University	68 (4.2)	148 (3.8)	55 (3.2)	
Secondary	309 (18.9)	754 (19.6)	271 (15.9)	
Elementary	1254 (76.9)	2938 (76.5)	1372 (80.8)	
Arterial Hypertension[b]	1310 (80.3)	3197 (83.3)	1420 (83.6)	0.01
Diabetes[c]	813 (49.8)	1808 (47.08)	848 (49.9)	0.06
Hypercholesterolemia[d]	1134 (69.5)	2804 (73.0)	1247 (73.4)	0.01
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	***P value***[e]
Age (years)	67.3 ± 6.2	66.8 ± 6.1	67.5 ± 6.0	<0.001
Energy expenditure[f] **(MET-h/d)**	4.0 ± 4.2	3.9 ± 4.0	3.7 ± 3.7	0.04

Dietary pattern (g/day)	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	***P value*[e]**
Mediterranean diet adherence score	8.5 ± 1.9	8.7 ± 1.9	8.7 ± 1.9	0.61
Total dairy	279.0 ± 207.1	378.9 ± 204.1	494.9 ± 228.2	<0.001
Yogurt, total	0.0 ± 0.0	65.3 ± 38.6	196.6 ± 94.6	<0.001
Low-fat yogurt	0.0 ± 0.0	44.5 ± 44.2	142.3 ± 116.1	<0.001
Milk, total	235.5 ± 194.1	266.7 ± 185.8	271.6 ± 184.0	0.37
Low-fat milk	174.8 ± 194.9	221.1 ± 198.5	234.9 ± 196.1	0.02
Cream and whipped cream	0.39 ± 3.39	0.65 ± 5.79	0.30 ± 2.0	0.01
Cheese	15.1 ± 17.1	14.6 ± 15.6	12.6 ± 15.7	<0.001
Low-fat cheese	11.2 ± 21.5	13.7 ± 18.9	17.2 ± 23.0	<0.001
Dairy desserts	13.7 ± 43.3	10.5 ± 26.1	9.1 ± 28.5	0.07
Other dairy[g]	1.75 ± 6.7	1.76 ± 5.3	1.97 ± 6.7	0.23
Soft drinks	21.7 ± 72.6	18.7 ± 63.8	14.1 ± 47.5	0.008
Nutrient intake [h]				
Total energy (Kcal/day)	2300 ± 600	2351.6 ± 581.6	2046.6 ± 483.5	<0.001
Carbohydrates (g/day)	234.7 ± 46.3	238.0 ± 42.9	242.6 ± 36.0	<0.001
Protein (g/day)	87.8 ± 14.4	92.3 ± 13.9	96.6 ± 13.4	<0.001
SFA[i] (g/day)	25.8 ± 6.4	25.3 ± 6.0	24.4 ± 5.1	<0.001
MUFA[j] (g/day)	50.1 ± 11.6	48.8 ± 11.3	47.2± 10.4	<0.001
PUFA[k] (g/day)	16.2 ± 5.5	15.8 ± 5.3	15.2 ± 4.7	<0.001
Fiber (g/day)	24.6 ± 7.6	25.5 ± 7.8	26.3 ± 7.0	<0.001

Total cholesterol (mg/day)	368.9 ± 111.1	368.9 ± 116.5	357.5 ± 91.9	<0.001
n-3 fatty acids (g/day)	2.2 ± 0.79	2.2 ± 0.80	2.2 ± 0.73	0.07
Lignan intake (mg/day)	0.59 ± 0.2	0.60 ± 0.2	0.61 ± 0.2	0.04
Cardiovascular risk parameters	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	***P value*[e]**
Body Mass Index (Kg/m^2)	29.6 ± 3.5	29.9 ± 3.7	30.0 ± 3.7	0.50
Systolic blood presure (mmHg)	149.7 ± 19.1	148.6 ± 19.0	148.2 ± 19.1	0.40
Diastolic blood pressure (mmHg)	83.2 ± 10.2	82.9 ± 10.0	82.2 ± 10.5	0.01
Glucose (mg/dL)	123.5 ± 39.8	121.1 ± 42.0	122.1 ± 41.3	0.44
Lipid profile (mg/dL)	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	***P value*[e]**
Total cholesterol	210.7 ± 38.3	210.7 ± 38.1	212.2 ± 38.2	0.22
HDL-cholesterol	52.8 ± 13.0	53.8 ± 14.3	55.6 ± 13.9	<0.001
LDL-cholesterol	130.3 ± 33.5	130.2 ± 33.4	130.2 ± 34.4	0.99
Triglycerides	142.1 ± 79.1	136.8 ± 83.7	132.5 ± 67.3	0.08

[a] χ^2 tests

[b] Arterial hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg, or taking antihypertensive medication)

[c] Diabetes was diagnosed when fasting plasma glucose concentrations of ≥7.0 mmol/L (≥126.1 mg/dL), 2-h plasma glucose concentrations of ≥11.1 mmol/L (≥200.0 mg/dL) after an oral dose of 75 g glucose, or insulin treatment.

[d] Hypercholesterolemia was defined as LDL-cholesterol ≥ 160 mg/dL, HDL-cholesterol≤ 40 mg/dL, or antihyperlipidemic medication.

[e] One-way ANOVA tests

[f] In physical activity at leisure time.

[g] Cream cheese and condensed milk.

[h] FFQ was used to estimate the dietary pattern by multiplying the frequency of consumption of all food items by the average portion size using Spanish food composition tables and was carried out by trained dietitians.

[i] SFA: Saturated Fatty Acids

[j] MUFA: Monounsaturated Fatty Acids

[k] PUFA: Polyunsaturated Fatty Acids

Table 2. Association between yogurt, dairy or lignans consumption and CVR-P of 7169 elderly Spanish participants at high cardiovascular risk from the PREDIMED cohort.

General Linear Models		**Model^a**	**Group 1 vs Group 0^b**		**Group 2 vs Group 0^b**		**P-trend**
			β (95%CI)	**P-value**	**β (95%CI)**	**P-value**	
Lignans intake	Total cholesterol (mg/dL)	**1**	1.08 (-1.26, 3.42)	0.37	1.50 (-0.83, 3.84)	0.21	
		2	1.19 (-1.20, -3.60)	0.73	2.42 (-0.20, 5.05)	0.07	0.60
	HDL-cholesterol (mg/dL)	**1**	0.34 (-0.49, 1.19)	0.42	1.04 (0.20, 1.88)	0.01	
		2	-0.15 (-1.01, 0.71)	0.20	0.05 (-0.89, 0.99)	0.92	0.81
	LDL-cholesterol (mg/dL)	**1**	-2.46 (-7.42, 2.49)	0.33	-5.51 (-10.45, -0.57)	0.03	
		2	0.96 (-1.25, 3.18)	0.20	2.38 (-0.03, 4.80)	0.05	0.29
	Triglycerides (mg/dL)	**1**	-2.46 (-7.42, 2.49)	0.33	-5.51 (-10.45, -0.57)	0.03	
		2	-1.68 (-6.77, 3.40)	0.51	-2.57 (-8.14, 2.98)	0.36	0.03
	Glucose (mg/dL)	**1**	-2.93 (-5.51, -0.34)	0.03	-2.46 (-5.04, 0.12)	0.62	
		2	-4.16 (-6.78, 1.54)	0.002	-6.08 (-8.95, -3.21)	<.001	0.02
	BMI^c (kg/m^2)	**1**	-0.10 (-0.31, 0.10)	0.32	-0.17 (-0.37, 0.037)	0.11	
		2	0.01 (-0.20, 0.22)	0.92	0.11 (-0.12, 0.34)	0.36	0.29
	Weight (kg)	**1**	-0.12 (0.72, 0.47)	0.68	-0.086 (-0.68, 0.51)	0.78	
		2	0.45 (-0.17, 1.08)	0.53	0.65 (-0.03, 1.32)	0.06	0.57
	Waist circumference (cm)	**1**	-0.49 (-1.06, 0.09)	0.10	-0.99 (-1.57, -0.41)	0.001	
		2	-0.22 (-0.82, 0.37)	0.46	-0.26 (-0.92, 0.40)	0.44	0.005
	SBP^d (mmHg)	**1**	0.94 (-0.25, 2.14)	0.12	0.67 (-0.53, 1.88)	0.27	
		2	0.97 (-0.26, 2.19)	0.12	1.31 (-2.06, 2.67)	0.06	0.90

	DBP^{e} (mmHg)	**1**	0.06 (-0.58, 0.71)	0.35	-0.26 (-0.91, 0.38)	0.42	
		2	0.18 (-0.48, 0.84)	0.59	0.27 (-0.46, 1.01)	0.46	0.09
General Linear Models		**Model^{a*}**	**<1 yogurt/day vs non consumers**		**≥1 yogurt/day vs non consumers**		**P-trend**
			β (95%CI)	**P-value**	**β (95%CI)**	**P-value**	
Total Yogurt	Total cholesterol (mg/dL)	**1**	-3.00 (-5.40, 0.62)	0.01	-3.34 (-6.17, -0.51)	0.02	
		2	-2.92 (-5.30, -0.53)	0.02	-3.33 (-6.20, -0.48)	0.02	0.03
	HDL-cholesterol (mg/dL)	**1**	-0.31 (-1.17, 0.54)	0.48	0.08 (-0.93, 1.10)	0.87	
		2	-0.41 (-1.27, 0.44)	0.34	-0.14 (-1.16, 0.88)	0.78	0.81
	LDL-cholesterol (mg/dL)	**1**	-1.74 (-3.94, 0.46)	0.12	-2.45 (-5.05, 0.15)	0.06	
		2	-1.65 (-3.87, 0.55)	0.14	-2.39 (-5.04, 0.23)	0.07	0.06
	Triglycerides (mg/dL)	**1**	-5.10 (-10.16, -0.06)	0.05	-8.47 (-14.46, -2.48)	0.005	
		2	-4.14 (-9.19, 0.91)	0.11	-6.94 (-12.97, -0.91)	0.02	0.07
	Glucose (mg/dL)	**1**	-0.93 (-3.56, 1.71)	0.49	1.33 (-1.79, 4.45)	0.40	
		2	-0.87 (-3.51, 1.72)	0.50	1.82 (-1.30, 4.94)	0.25	0.50
	BMI^{c} (kg/m^{2})	**1**	0.14 (-0.06, 0.35)	0.18	0.11 (-0.14, 0.36)	0.39	
		2	0.14 (-0.06, 0.35)	0.18	0.13 (-0.12, 0.38)	0.32	0.11
	Weight (kg)	**1**	0.88 (0.26, 1.49)	0.005	0.75 (0.02, 1.48)	0.04	
		2	0.90 (0.29, 1.52)	0.004	0.88 (0.15, 1.69)	0.02	0.007
	Waist circumference (cm)	**1**	0.51 (-0.088, 1.11)	0.09	-0.17 (-0.88, 0.54)	0.63	
		2	0.59 (-0.01, 1.19)	0.055	0.04 (-0.67, 0.76)	0.90	0.42
	SBP^{d} (mmHg)	**1**	-0.33 (1.57, 0.91)	0.60	-0.42 (-1.89, 1.06)	0.58	
		2	-0.37 (-1.61, 0.87)	0.55	-0.48 (-1.96, 0.99)	0.52	0.62
	DBP^{e} (mmHg)	**1**	-0.04 (-0.71, 0.62)	0.89	-0.25 (-1.04, 0.54)	0.53	

		2	-0.04 (-0.71, 0.62)	0.90	-0.22 (-1.01, 0.58)	0.59	0.65
Full-fat Yogurt	Total cholesterol (mg/dL)	**1**	1.70 (-0.63, 4.04)	0.15	-1.72 (-5.65, 2.22)	0.39	
		2	1.19 (-1.28, 3.66)	0.34	-2.43 (-6.47, 1.61)	0.24	0.047
	HDL-cholesterol (mg/dL)	**1**	0.36 (-0.47, 1.20)	0.39	0.95 (-0.46, 2.36)	0.19	
		2	0.56 (-0.32, 1.44)	0.21	0.99 (-0.45, 2.44)	0.18	0.12
	LDL-cholesterol (mg/dL)	**1**	2.11 (-0.03, 4.25)	0.05	-1.95 (-5.58, 1.67)	0.29	
		2	1.81 (-0.45, 4.08)	0.12	-2.38 (-6.10, 1.34)	0.21	0.047
	Triglycerides (mg/dL)	**1**	0.03 (-4.91, 4.97)	0.99	-7.60 (-15.94, 0.73)	0.07	
		2	-1.90 (-7.12, 3.31)	0.47	-9.33 (-17.87, -0.79)	0.03	0.02
	Glucose (mg/dL)	**1**	-2.27 (-4.84, 0.30)	0.08	-0.81 (-5.14, 3.51)	0.71	
		2	-1.85 (-4.55, 0.84)	0.18	0.63 (-3.77, 5.03)	0.78	0.98
	BMI^c (kg/m^2)	**1**	0.23 (0.03, 0.44)	0.03	0.24 (-0.11, 0.58)	0.18	
		2	0.19 (-0.03, 0.40)	0.08	0.22 (-0.13, 0.58)	0.22	0.06
	Weight (kg)	**1**	0.72 (0.13, 1.32)	0.02	0.51 (-0.50, 1.52)	0.32	
		2	0.78 (0.15, 1.41)	0.01	0.70 (-0.33,1.74)	0.18	0.037
	Waist circumference (cm)	**1**	0.70 (0.12, 1.28)	0.02	0.25 (-0.74, 1.24)	0.61	
		2	0.48 (-0.14, 1.09)	0.13	0.16 (-0.85, 1.17)	0.75	0.30
	SBP^d (mmHg)	**1**	0.82 (-0.38, 2.02)	0.18	1.84 (-0.22, 3.91)	0.08	
		2	0.43 (-0.83, 1.70)	0.50	1.33 (-0.77, 3.44)	0.21	0.42
	DBP^e (mmHg)	**1**	1.06 (0.41, 1.70)	0.001	0.63 (-0.48, 1.76)	0.27	
		2	0.81 (0.13, 1.49)	0.02	0.36 (-0.76, 1.50)	0.52	0.31
Low-fat Yogurt	Total cholesterol (mg/dL)	**1**	-3.51 (-5.62, -1.40)	0.001	-1.79 (-4.51, 0.93)	0.20	
		2	-4.40 (-6.65, -2.15)	<.001	-2.87 (-5.75, 0.01)	0.05	0.08
	HDL-cholesterol	**1**	-0.89 (-1.64, -0.13)	0.02	-0.38 (-1.35, 0.59)	0.44	

	(mg/dL)	**2**	-1.05 (-1.85, -0.24)	0.01	-0.63 (-1.65, 0.40)	0.23	0.57
	LDL-cholesterol (mg/dL)	**1**	-3.00 (-4.93, -1.06)	0.002	-1.17 (-3.65, 1.31)	0.36	
		2	-3.80 (-5.87, -1.72)	<.001	-2.11 (-4.75, 0.52)	0.11	0.20
	Triglycerides (mg/dL)	**1**	-0.43 (-4.89, 4.03)	0.85	-4.36 (-10.13, 1.40)	0.14	
		2	-0.82 (-5.59, 3.95)	0.73	-4.53 (-10.60,1.56)	0.14	0.34
	Glucose (mg/dL)	**1**	1.56 (-0.76, 3.88)	0.19	2.69 (-0.33, 5.70)	0.08	
		2	1.29 (-1.18, 3.76)	0.31	2.80 (-0.36, 5.97)	0.08	0.39
	BMI[c] (kg/m^2)	**1**	0.0007 (-0.18, 0.18)	0.99	-0.104 (-0.35, 0.14)	0.40	
		2	0.12 (-0.08, 0.32)	0.23	0.04 (-0.21, 0.30)	0.72	0.35
	Weight (kg)	**1**	0.24 (-0.29, 0.78)	0.38	0.058 (-0.64, 0.76)	0.87	
		2	0.64 (0.06, 1.21)	0.03	0.55 (-0.18, 1.30)	0.14	0.025
	Waist circumference (cm)	**1**	0.18 (-0.35, 0.71)	0.51	-0.80 (-1.49, -0.11)	0.02	
		2	0.55 (-0.02, 1.12)	0.06	-0.30 (-1.02, 0.42)	0.42	0.67
	SBP[d] (mmHg)	**1**	-0.87 (-1.96, 0.22)	0.12	-1.37 (-2.79, 0.04)	0.06	
		2	-0.62 (-1.79, 0.55)	0.30	-1.12 (-2.62, 0.37)	0.14	0.28
	DBP[e] (mmHg)	**1**	-0.94 (-1.52, -0.35)	0.001	-0.96 (-1.72, -0.20)	0.01	
		2	-0.076 (-1.38, -0.13)	0.02	-0.76 (-1.56, 0.04)	0.06	0.25
General Linear Models		**Model[a*]**	**Group 1 vs Group 0[f]**		**Group 2 vs Group 0[f]**		**P-trend**
			β (95%CI)	**P value**	**β (95%CI)**	**P value**	
Total dairy[g]	Total cholesterol (mg/dL)	**1**	-4.34 (-6.70, -2.17)	<.001	-4.52 (-7.18, -1.86)	<.001	
		2	-4.30 (-6.60, -2.01)	<.001	-4.36 (-7.09, -1.62)	0.002	<.001
	HDL-cholesterol (mg/dL)	**1**	-1.06 (-1.87, -0.25)	0.01	-1.07 (-2.02, -0.11)	0.03	
		2	-0.87 (-1.69, -	0.04	-0.65 (-1.63, 0.33)	0.19	0.005

			0.005)				
	LDL-cholesterol (mg/dL)	**1**	-2.41 (-4.50, -0.32)	0.02	-2.23 (-4.68, 0.22)	0.07	
		2	-2.34 (-4.45, -0.22)	0.03	-2.18 (-4.70, 0.33)	0.09	0.048
	Triglycerides (mg/dL)	**1**	-4.35 (-9.15, 0.45)	0.07	-2.93 (-8.58, 2.71)	0.31	
		2	-4.74 (-9.58, 0.11)	0.06	-4.13 (-9.93, 1.65)	0.16	0.37
	Glucose (mg/dL)	**1**	3.35 (0.85, 5.85)	0.008	8.93 (5.99, 11.87)	<.001	
		2	2.64 (0.14, 5.14)	0.04	7.89 (4.89, 10.88)	<.001	<.001
	BMI[c] (kg/m^2)	**1**	0.15 (-0.05, 0.35)	0.15	0.11 (-0.12, 0.35)	0.34	
		2	0.075 (-0.13, 0.28)	0.46	-0.011 (-0.25, 0.23)	0.93	0.68
	Weight (kg)	**1**	0.12 (-0.46, 0.71)	0.67	-0.14 (-0.83, 0.56)	0.70	
		2	-0.08 (-0.67, 0.50)	0.78	-0.53 (-1.24, 0.18)	0.15	0.82
	Waist circumference (cm)	**1**	0.18 (-0.38, 0.75)	0.52	-0.22 (-0.90, 0.46)	0.52	
		2	-0.05 (-0.62, 0.52)	0.86	0.70 (-1.39, -0.003)	0.05	0.16
	SBP[d] (mmHg)	**1**	-0.25 (-1.43, 0.92)	0.67	-0.82 (-2.22, 0.59)	0.25	
		2	-0.28 (-1.46, 0.90)	0.64	-0.77 (-2.21, 0.67)	0.29	0.025
	DBP[e] (mmHg)	**1**	-0.14 (-0.77, 0.48)	0.65	-0.57 (-1.32, 0.19)	0.14	
		2	-0.22 (-0.85, 0.41)	0.50	-0.78 (-1.53, -0.019)	0.04	0.02

[a] Model 1: adjusted for recruitment center, sex and age; Model 2: adjusted for recruitment center, sex, age, smoking, soft drinks, carbohydrates, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, n-3 fatty acids, dairies. [*]Model 2 replacing dairies by fiber.

[b] Lignans groups were formed according to tertiles, group 0: <0.46 mg/day, group 1: 0.46-0.67 mg/day, and group 2: >0.67 mg/day

[c] BMI: Body Mass Index.

[d] SBP: Systolic Blood Pressure.

[e] DBP: Diastolic Blood Pressure.

[f] Total dairy groups were formed according to tertiles, group 0: < 200g/day, group 1: 200-500 g/day, and group 2: >500g/day.

[g] Total dairy comprises whole/low-fat/skim milk, condensed milk, ice-cream, custard and all types of cheeses (ricotta, cured cheeses…).

Table 3. General linear models for the association between cardiovascular risk parameters and the joint intake of yogurt and lignans of 7169 elderly Spanish participants at high cardiovascular risk from the PREDIMED cohort.

GLM		**Low lignan intake (<0.6mg/day)** **(n = 3525)**		**High lignan intake (>0.6mg/day)** **(n = 3644)**		**P-interaction**
	Model^a	**β (95%CI)**	**P**	**β (95%CI)**	**P**	
Total cholesterol (mg/dl)	**Model 1**					0.05
	<1 yogurt/day vs non consumers	-2.22 (-5.74, 1.29)	0.21	-3.71 (-6.96, -0.46)	0.02	
	≥1 yogurt/day vs non consumers	0.63 (-3.61, 4.88)	0.77	-6.48 (-10.28, -2.67)	<0.001	
	Model 2					0.01
	<1 yogurt/day vs non consumers	-2.57 (-6.03, 0.89)	0.14	-3.83 (-7.05, -0.62)	0.02	
	≥1 yogurt/day vs non consumers	-0.59 (-3.63, 4.81)	0.78	-6.18 (-9.97, -2.40)	0.001	
HDL-cholesterol (mg/dl)	**Model 1**					0.27
	<1 yogurt/day vs non consumers	0.59 (-0.65, 1.83)	0.35	-1.17 (-2.36, 0.01)	0.05	
	≥1 yogurt/day vs non consumers	0.62 (-0.87, 2.12)	0.41	-0.49 (-1.87, 0.89)	0.49	
	Model 2					0.79
	<1 yogurt/day vs non consumers	0.07 (-1.18, 1.32)	0.91	-1.14 (-2.32, 0.04)	0.06	

	≥1 yogurt/day vs non consumers	-0.21 (-1.74, 1.32)	0.79	-0.48 (-1.87, 0.91)	0.50	
LDL-cholesterol (mg/dl)	**Model 1**					0.16
	<1 yogurt/day vs non consumers	-0.96 (-4.18, 2.25)	0.55	-2.45 (-5.48, 0.57)	0.11	
	≥1 yogurt/day vs non consumers	1.39 (-2.49, 5.28)	0.48	-5.54 (-9.06, -2.03)	0.002	
	Model 2					0.05
	<1 yogurt/day vs non consumers	-1.09 (-4.25, 2.08)	0.50	-2.74 (-5.72, 0.24)	0.07	
	≥1 yogurt/day vs non consumers	1.91 (-1.95, 5.76)	0.33	-4.92 (-8.41, -1.43)	0.005	
Triglycerides (mg/dl)	**Model 1**					0.05
	<1 yogurt/day vs non consumers	-9.41(-16.97, -1.86)	0.01	-1.07 (-7.86, 5.72	0.76	
	≥1 yogurt/day vs non consumers	-8.76 (-1.79, 0.38)	0.06	-7.36 (-15.30, 0.58)	0.07	
	Model 2					0.21
	<1 yogurt/day vs non consumers	-7.53 (-15.18, 0.11)	0.05	-1.31 (-8.15, 5.53)	0.71	
	≥1 yogurt/day vs non consumers	-5.93 (-15.19, 3.33)	0.21	-7.98 (-15.94, -0.015)	0.049	
Glucose (mg/dl)	**Model 1**					0.08
	<1 yogurt/day vs non consumers	-0.55 (-4.40, 3.30)	0.78	-1.19 (-4.80, 2.43)	0.52	

	≥1 yogurt/day vs non consumers	1.91 (-2.73, 6.56)	0.42	0.98 (-3.25, 5.22)	0.65	
	Model 2					0.07
	<1 yogurt/day vs non consumers	-0.47 (-3.66, 2.71)	0.77	-0.89 (-4.76, 2.99)	0.65	
	≥1 yogurt/day vs non consumers	-2.20 (-5.15, 0.75)	0.14	-1.92 (-5.41, 1.57)	0.28	
BMI[b] (kg/m^2)	**Model 1**					0.11
	<1 yogurt/day vs non consumers	0.22 (-0.08, 0.52)	0.14	0.07 (-0.22, 0.37)	0.63	
	≥1 yogurt/day vs non consumers	0.25 (-0.11, 0.61)	0.18	-0.003 (-0.35, 0.34)	0.98	
	Model 2					0.44
	<1 yogurt/day vs non consumers	0.28 (-0.02, 0.58)	0.007	0.06 (-0.23, 0.36)	0.65	
	≥1 yogurt/day vs non consumers	0.51 (0.15, 0.88)	0.006	-0.04 (-0.39, 0.31)	0.81	
Weight (kg)	**Model 1**					0.94
	<1 yogurt/day vs non consumers	1.21 (0.33, 2.09)	0.006	0.56 (-0.30, 1.42)	0.20	
	≥1 yogurt/day vs non consumers	1.05 (-0.01, 2.10)	0.05	0.47 (-0.53, 1.48)	0.35	
	Model 2					0.42
	<1 yogurt/day vs non consumers	1.20 (0.32, 2.09)	0.008	0.57 (-0.29, 1.43)	0.20	

	≥1 yogurt/day vs non consumers	1.35 (0.27, 2.43)	0.01	0.39 (-0.62, 1.41)	0.45	
Waist circumference (cm)	**Model 1**					0.05
	<1 yogurt/day vs non consumers	0.70 (-0.14, 1.54)	0.10	0.36 (-0.49, 1.22)	0.40	
	≥1 yogurt/day vs non consumers	0.25 (-0.76, 1.26)	0.63	-0.42 (-1.42, 0.58)	0.41	
	Model 2					0.37
	<1 yogurt/day vs non consumers	0.70 (-0.15, 1.55)	0.11	0.35 (-0.51, 1.21)	0.42	
	≥1 yogurt/day vs non consumers	0.42 (-0.61, 1.46)	0.42	-0.54 (-1.55, 0.47)	0.29	
SBP[c] (mmHg)	**Model 1**					0.96
	<1 yogurt/day vs non consumers	0.26 (-1.50, 2.02)	0.77	-0.88 (-2.63, 0.87)	0.32	
	≥1 yogurt/day vs non consumers	-0.05 (-2.18, 2.08)	0.96	-0.72 (-2.77, 1.34)	0.49	
	Model 2					0.69
	<1 yogurt/day vs non consumers	-0.26 (-2.03, 1.50)	0.77	-1.14 (-2.86, 0.59)	0.20	
	≥1 yogurt/day vs non consumers	-0.23 (-2.38, 1.93)	0.84	-1.09 (-3.13, 0.95)	0.30	
DBP[d] (mmHg)	**Model 1**					0.08
	<1 yogurt/day vs non consumers	0.09 (-0.85, 1.04)	0.85	-0.15 (-1.09, 0.79)	0.76	

	≥1 yogurt/day vs non consumers	-0.02 (-1.16, 1.12)	0.97	-0.34 (-1.45, 0.76)	0.54	
	Model 2					0.08
	<1 yogurt/day vs non consumers	-0.08 (-1.03, 0.86)	0.86	-0.12 (-1.05, 0.82)	0.80	
	≥1 yogurt/day vs non consumers	0.16 (-0.99, 1.32)	0.78	-0.12 (-1.23, 0.99)	0.83	

[a] Model 1: adjusted for recruitment center, sex and age; Model 2: additionally adjusted for smoking, soft drinks, carbohydrates, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, family history of heart disease, diabetes and hypertension.

[b] BMI: Body Mass Index.

[c] SBP: Systolic Blood Pressure.

[d] DBP: Diastolic Blood Pressure.