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EFFECTS OF DIETARY FIBER INTAKE ON RISK FACTORS FOR CARDIOVASCULAR DISEASE IN SUBJECTS AT HIGH RISK

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1 **ABSTRACT**

2 **BACKGROUND:**

3 Epidemiological studies and feeding trials with **supplements suggest** that fibre intake is
4 associated with a reduction in cardiovascular risk. However, **the effects of changes in dietary**
5 **fibre on risk factor levels have not been evaluated in free-living individuals. Thus, we**
6 **assessed** the 3-month effects of changes in dietary fibre intake on cardiovascular risk factors
7 in free-living high-risk subjects.

8 **METHODS:**

9 772 high-risk subjects (age **69±5** years) were assigned to a low-fat diet or 2 Mediterranean-
10 style diets. All **participants** received behavioural and nutritional education, **including**
11 recommendations for increasing the consumption of vegetables, fruits, and legumes. **Changes**
12 **in food and nutrient intake, body weight, blood pressure, lipid profiles, glucose control, and**
13 **inflammatory markers were evaluated.**

14 **RESULTS:**

15 Most participants increased consumption of vegetable **products, but** the increase in dietary
16 fibre exhibited wide between-subject variability (6-65 g/day). **Body weight, waist**
17 **circumference, and mean systolic and diastolic blood pressure decreased across quintiles of**
18 **fibre intake** ($P < 0.005$; all). Reductions in fasting glucose and total cholesterol levels, and
19 increments in HDL cholesterol were **highest** among participants in the upper 20% of fibre
20 intake ($P = 0.04$ and 0.02 , respectively). Plasma concentrations of C-reactive protein, but not
21 those of inflammatory cytokines, **decreased** in parallel **with increasing** dietary fibre ($P = 0.04$).
22 Significant reductions in LDL cholesterol were observed only among participants with the
23 greatest increases in soluble fibre intake ($P = 0.04$).

24 **CONCLUSIONS:**

25 **Increasing** dietary fibre intake with natural foods **is** associated with reductions in classical and
26 novel cardiovascular risk factors **in a high risk cohort.**

27

28 *Number of words: 243*

29

30 **KEYWORDS:** Dietary fibre; Atherosclerosis; Risk factors; Cardiovascular disease; Nutrition

31

1 INTRODUCTION

2 The Mediterranean diet (Med-diet) has been widely considered as a model of healthy
3 eating. This dietary pattern is characterized by a high consumption of non-refined grains,
4 legumes, nuts, fruits and vegetables; relatively high intake of total fat, mainly derived from
5 olive oil; moderate to high intake of fish and poultry; dairy products (usually as yogurt or
6 cheese) in small amounts; low consumption of red meat and meat products; and moderate
7 alcohol intake, usually in the form of red wine with meals.[1] Thus, high consumption of
8 fibre-rich foods is one of the characteristic features of the Med-diet.

9 Dietary fibre (DF), a mixture of chemicals in indigestible vegetable residues,[2] has
10 received much attention in nutritional epidemiology. Observational studies have consistently
11 shown that DF intake is associated with reduced cardiovascular risk, including ischemic heart
12 disease [3-6] and stroke [5-8], and lower risk of diabetes [9-11]. Clinical trials have also
13 suggested that DF supplementation has beneficial effects on risk factors, such as blood
14 pressure, serum lipids, insulin sensitivity and diabetic metabolic control.[12-16] However, no
15 intervention study has evaluated the effects of DF on classical and novel risk factors in free-
16 living persons at high cardiovascular risk.

17 To address this issue, we evaluated the effects of 3-month changes in DF intake on
18 cardiovascular risk factors in a large sample of subjects at high risk for cardiovascular disease.

19 MATERIAL AND METHODS

20 STUDY DESIGN

21 The PREDIMED study (*PREvención con Dieta MEDiterránea*) is a large multi-centre,
22 randomized 5-year clinical trial aimed at assessing the effects of the Med-diet on the primary
23 prevention of cardiovascular disease (CVD) in Spain (<http://www.predimed.org>). Up to
24 September 2008, this trial includes 6,988 high-risk participants allocated to 3 interventions:
25 Med-diet plus virgin oil, Med-diet plus nuts, and control diet (low-fat diet). The main
26

1 outcome for the whole trial is an aggregate of cardiovascular events (cardiovascular death,
2 non-fatal myocardial infarction, or non-fatal stroke). The Institutional Review Boards of the
3 participating centres approved the study protocol. This trial has been registered with the
4 International Standard Randomised Controlled Trial Number (ISRCTN) 35739639. The trial
5 design has been described in detail elsewhere.[17]

6 The present study was designed as a short-term trial in a subset of participants, namely
7 those entering the PREDIMED trial during the first 6 months of recruitment, to assess the
8 effects of changes in dietary fibre intake on surrogate markers of atherosclerosis.

9 PARTICIPANTS AND RECRUITMENT

10 Nine hundred thirty possible participants were evaluated. Eligible subjects were community-
11 dwelling persons, aged 55-80 years for men and 60-80 years for women, who had either type
12 2 diabetes or 3 or more of the following CHD risk factors: current smoking, hypertension
13 (blood pressure >140/90 mmHg), LDL cholesterol \geq 160 mg/dL, low HDL cholesterol (\leq 40
14 mg/dL), body mass index ($\text{BMI} \geq 25 \text{ kg/m}^2$), or family history of premature CHD. Exclusion
15 criteria were: previous history of cardiovascular disease, any severe chronic illness, illegal
16 drug use or alcoholism, and low predicted likelihood of changing dietary habits.[18]

17 The primary care physicians based participants' eligibility on review of clinical records
18 and a screening visit. Suitable candidates were invited to attend a screening visit. This
19 included a face-to-face interview to inquire about medical conditions and risk factors related
20 to eligibility. More than 95 % of eligible candidates who met entry requirements signed an
21 informed consent and agreed to return for the baseline visit.

22 BASELINE ASSESSMENT AND INTERVENTION

23 We administered a validated 137-item food frequency questionnaire (FFQ),[19] and the
24 validated Spanish version[20] of the Minnesota Leisure Time Physical Activity questionnaire
25 in the baseline assessment. For each food included in the FFQ, a standard portion size

1 (representing the serving size of that item most frequently consumed currently in Spain) was
2 specified. DF intake was calculated by multiplying the frequency of consumption of each item
3 by the fibre content of the specified serving, according to Spanish food composition
4 tables.[21] The intra-class correlation coefficient comparing DF intake by FFQ with the
5 average of four 3-day dietary records was 0.75. Anthropometric measurements, blood
6 pressure, spot urine and fasting blood samples were obtained. All examinations were repeated
7 at 3 months.

8 Trained dieticians were responsible for all aspects of the interventions and assisted
9 participants in completing the FFQ.[22] Participants assigned to the control group received
10 personal advice together with a leaflet with written recommendations to follow a low-fat
11 diet.[23] Participants in the 2 Med-Diet intervention groups were given personalized advice
12 for dietary changes directed to achieve a diet closest to the traditional Med-diet.[22]
13 Depending on group assignment, participants were given free virgin olive oil or free sachets
14 of walnuts, hazelnuts, and almonds. In the 3 groups, the general guidelines included positive
15 recommendations for increase consumption of vegetables, fruits, legumes, fish and seafood,
16 and white meats instead of red meats. Negative recommendations included limiting and/or
17 eliminating presumed detrimental foods (red and processed meats, fat-rich dairy products,
18 commercial pastries, snacks, and sugar-sweetened beverages). Thus, all intervention diets
19 coincided in the recommendation to increase fibre-rich foods, a reason why the 3 intervention
20 groups are grouped as a single one for the comparisons of fibre intake and change in risk
21 factor levels.

22 A one-hour group session with up to 20 participants, with separate sessions for each
23 intervention group, was scheduled after inclusion. Group sessions consisted of informative
24 talks and provision of written material with descriptions of main foods, seasonal shopping
25 lists, meal plans, and cooking recipes.[22]

1 MEASUREMENTS

2 Weight and height were measured with calibrated scales and a wall-mounted stadiometer,
3 respectively. Waist circumference was measured midway between the lowest rib and the iliac
4 crest using an anthropometric tape. Trained personnel measured blood pressure in triplicate
5 with a validated semi-automatic oscillometer (Omron HEM-705CP, The Netherlands).

6 Blood and urine samples were obtained after an overnight fast. Serum, EDTA- plasma, and
7 urine samples were coded, shipped to central laboratories, and stored at -80°C until assay. The
8 clinical investigators and laboratory technicians were blinded to intervention. **Analyses**
9 determined by subject in frozen samples of whole serum or plasma as appropriate were: blood
10 glucose by the glucose-oxidase method; serum insulin by radioimmunoassay; cholesterol and
11 triglycerides by enzymatic procedures; HDL cholesterol after precipitation with
12 phosphotungstic acid and magnesium chloride; soluble intercellular adhesion molecule-1
13 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and interleukin-6 (IL-6) by
14 standard ELISA assays; and high sensitivity C-reactive protein (CRP) by particle-enhanced
15 immunonephelometry.

16 STATISTICAL ANALYSES

17 For the comparison of changes in risk factors, the average of **two** baseline measurements was
18 used as the baseline value and the average of the **two 3-month measurements** was used as the
19 final variable. Values with a skewed distribution (CRP, VCAM-1, ICAM-1 and IL-6) were
20 transformed to their natural logarithm for analyses. Those subjects whose energy intake, as
21 derived from food frequency questionnaires, was outside pre-specified ranges (2510 to 14 644
22 kJ for women and 3347 to 17 573 kJ for men) were excluded from the calculations of energy
23 and nutrient intake, as recommended in nutritional epidemiology.[24] Multiple linear
24 regression models were used to study the relationship between **DF** and changes in risk factors.
25 Mean differences in the changes **of** these variables (post-trial minus pre-trial values) were

1 compared by quintiles of change in DF intake. We adjusted for intervention group, age,
2 gender, body weight, smoking, alcohol intake and physical activity. The treatment effects are
3 expressed as average changes and 95% confidence intervals (CI).

4

5 RESULTS

6 Of the 930 eligible subjects, 158 were excluded for the following reasons: not meeting
7 inclusion criteria (n=86), not accepting to change their dietary habits (n=18), excessive
8 alcohol intake (n=14), gastrointestinal disease (n=4), food allergies (n=3) or refusing to
9 participate (n=33). Table 1 shows the baseline characteristics of the 772 participants (348
10 men and 424 women) who entered the study. Most of them were overweight or obese (90%),
11 more than three quarters had hypertension, one fourth had family history of cardiovascular
12 disease and one fifth were smokers. There were only 3 withdrawals before study completion.
13 The baseline data of these subjects were similar to the mean values for the overall group.
14 Subsequent data refer only to the 769 participants who completed the study.

15 FOOD, ENERGY, AND NUTRIENT INTAKE

16 We excluded 48 participants from food, energy and nutrient calculations because they
17 reported unrealistic energy intakes.[21] Following the advice of the dieticians, most of the
18 participants increased consumption of vegetables, legumes, fruits, and fish and decreased
19 intake of meat and dairy products (Table 2). Cereal intake also decreased due to reduced
20 consumption of white bread, which is the main cereal food in the Spanish diet. A large
21 increase in the consumption of nuts, one of the supplemental foods given, was observed,
22 whereas the total amount of olive oil did not change because participants replaced customarily
23 used refined olive oil by the virgin variety supplied. Alcohol intake increased slightly at the
24 expense of wine, one of the components of the Med-diet recommended in moderation to
25 participants who were not abstainers at baseline. The results did not materially change when
26 we included in the calculations the participants whose energy consumption was out of range.

1 **Table 2** also shows 3-month changes in energy and nutrient intake. The reduction from
2 baseline in reported energy intake was due to decreases in intake of carbohydrate and total fat,
3 while protein intake increased. Increases in intake of monounsaturated fatty acids (MUFA)
4 and polyunsaturated fatty acids (PUFA), including both vegetable and marine n-3 fatty acids,
5 and a decrease in saturated fatty acid (SFA) intake occurred. Estimated energy expenditure
6 from physical activity was similar at baseline and after 3 months.

7 FIBRE AND VASCULAR RISK FACTORS

8 A significant increase in total and soluble DF intake was observed at the 3-month assessment
9 (**Table 2**). However, the consumption of DF exhibited wide between-subject variability. In
10 fact, daily DF intake ranged from 6 to 65 g at the 3-month assessment. Because energy and
11 DF intake increased in parallel, changes in DF intake categorized in quintiles were energy-
12 adjusted to assess associations with other variables (**Table 3**). Demographic characteristics,
13 adiposity and cardiovascular risk factors were similar across the range of DF intake.
14 Predictably, increasing DF intake was associated directly with carbohydrate intake and
15 inversely with intake of total fat, MUFA and SFA. There were no differences in alcohol
16 intake or sedentariness by categories of DF intake.

17 **Table 4** shows adjusted changes in risk factors according to quintiles of change in DF. The
18 higher the increment in DF intake, the greater was the weight loss and the reduction in waist
19 circumference and systolic and diastolic blood pressure. In addition, fasting glucose and total
20 cholesterol levels decreased, and HDL cholesterol increased with increasing DF intake.
21 Reductions in serum LDL cholesterol concentrations, but not in triglycerides, were
22 nonsignificantly higher for participants with greater increases in DF. The plasma levels of
23 CRP, a systemic biomarker of inflammation, but not those of other inflammatory biomarkers,
24 also decreased in parallel with increases in DF.

1 **Table 5** shows changes in cardiovascular risk factors between extreme quintiles of DF
2 intake. The differences were statistically significant for body weight, waist circumference,
3 systolic and diastolic blood pressure, fasting glucose and total cholesterol. When the same
4 analysis was performed for changes in soluble DF intake, the results were similar, except for
5 changes in LDL cholesterol, which were -8.06 mg/dL (95% CI -15.83 to -2.87) significantly
6 (P=0.042) different between extreme quintiles. Changes of cardiovascular risk factors in
7 quintile 5 versus quintile 1 of DF intake ranged from nearly 1 kg reduction in body weight to
8 close to a 9 mm decrease in systolic blood pressure.

9

10 **DISCUSSION**

11 We tested the hypothesis that the provision of increasing amounts of DF from natural foods
12 might be instrumental in the effect of a Mediterranean-style diet to reduce the levels of
13 cardiovascular risk factors. The rationale underlying this substudy of the PREDIMED feeding
14 trial was the available epidemiological and clinical trial evidence supporting the association of
15 DF intake with beneficial effects on surrogate markers of cardiometabolic risk, including
16 systemic inflammation.[12,14,25-27] In fact, DF intake after a 3-month behavioural
17 intervention to enhance the Med-diet was associated with significant reductions in body
18 weight, waist circumference, systolic and diastolic blood pressure and fasting glucose, as well
19 as a greater increase in HDL cholesterol. In addition, when we specifically assessed changes
20 in the consumption of soluble DF, participants in the highest quintile also showed a
21 significantly greater reduction in serum LDL cholesterol concentration than those in the
22 lowest quintile.

23 Many epidemiological studies have evaluated the effects of DF on the risk of coronary
24 heart disease.[3-6] In a pooled analysis of 10 prospective cohorts,[28] each 10-g/day
25 increment of energy-adjusted total DF was associated with a 14% decrease in risk of coronary

1 events and a 27% decrease in risk of coronary death. However, in the only randomised
2 clinical trial designed to examine whether increased intake of DF reduces the risk of
3 myocardial infarction, the DART study,[29] patients with existing coronary heart disease
4 advised to increase DF did not have lower reinfarction rates over a 2-year period.
5 Furthermore, DF advice had no clear effect on coronary or all-cause mortality after longer
6 follow-up.[30] Most likely, as assessed in prospective studies,[28] DF intake with the usual
7 diet is a marker of healthy food choices with an overall cardiovascular benefit, while changing
8 the diet to increase DF at late stages, when clinical consequences of atherosclerosis have
9 developed, may not be protective, as has been shown in a similar situation for antioxidant
10 supplements as opposed to the antioxidant content of the habitual diet.[32] Indeed, a plant-
11 based diet is rich in both fibre and antioxidants. At any rate, increasing DF during 3 months
12 by older individuals at high cardiovascular risk has measurable beneficial effects on several
13 risk factors.

14 Reduced adiposity, particularly in the highest category of DF intake (Tables 4 and 5), was
15 observed in our study. Large prospective studies have reported that consumption of DF is
16 inversely associated with weight and weight gain, [32-34]. A high intake of DF may assist
17 weight loss because of the incomplete digestion and absorption of energy from this type of
18 carbohydrate and the bulky nature of high-fibre foods, with increased demands on chewing
19 and subsequent distension and delayed emptying of the stomach, promoting satiety and thus
20 curtailing energy intake.[25,26,35] Our results further support a beneficial role of fibre-rich
21 diets on weight control.

22 Increasing DF intake was associated with significant blood pressure lowering in our
23 mostly hypertensive participants. Consistently, large prospective studies have reported that
24 increased DF was associated with lower risk of hypertension [36] or lower self-reported blood
25 pressure.[37] A meta-analysis of clinical studies of fibre supplementation[12] also supports an

1 inverse association between fibre and blood pressure. Accordingly, an increase in DF has
2 been recommended by the World Health Organization as a safe and practical approach to
3 cardiovascular risk reduction in hypertensive populations.[38]

4 Our participants who increased DF intake also showed a reduction in fasting glucose
5 levels, extending previous observations of the favourable effects of a diet with abundant fibre-
6 rich foods, particularly whole grain, bran and germ intake, on the risk of type 2 diabetes.[9-
7 11,39,40] DF reduces the glycemic index of foods, thereby attenuating insulin responses and
8 enhancing insulin sensitivity,[41,42] to which associated weight loss is likely to contribute.

9 Structural fibre is insoluble, whereas natural gel-forming fibres are soluble,[2] and
10 increasing consumption of this particular variety of DF has a modest cholesterol lowering
11 effect that is attributable to interference with intestinal bile acid absorption and enhancement
12 of faecal cholesterol excretion, although other mechanisms can be operative.[42] Thus,
13 increasing soluble fibre intake by 1 g/day is associated with a mean reduction in serum LDL
14 cholesterol level of about 2 mg/dL (0.052 mmol/L), according to a meta-analysis of
15 randomized trials of soluble fibre supplementation.[13] In support of these evidences, our
16 study shows a significant -8.06 mg/dL LDL cholesterol decrease between extreme quintiles of
17 soluble fibre intake.

18 Since atherosclerosis is considered a low-grade inflammatory disease,[43] the relationship
19 between DF intake and serum inflammatory markers has also been evaluated in epidemiologic
20 and clinical studies, as reviewed.[25-27] Results from recent epidemiologic studies have
21 consistently shown an inverse association between DF intake and plasma CRP levels.[44-47]
22 In a recent study, both increasing fibre intake by about 30 g/day from a diet naturally rich in
23 fibre or from a supplement reduced levels of CRP.[48] Thus, it was not surprising that we
24 observed in the upper quintile of energy-adjusted DF intake (≤ 26 g/day) a nearly 1 mg/L
25 reduction in CRP levels after adjustment for sex, age, BMI and relevant lifestyle

1 characteristics. However, no changes were observed in other inflammatory biomarkers. The
2 mechanisms of change in CRP levels as a result of DF intake are still largely unknown.
3 Possibilities include DF slowing absorption of glucose, fibre-rich meal modulation of
4 cytokine responses blunting oxidative stress and inflammation, and production of anti-
5 inflammatory cytokines by gut flora exposed to fibre.[26,27]

6 Our study has limitations. Since no biomarker of DF intake is available, FFQ data was the
7 only source of information on food consumption, including DF. FFQs are known to contain
8 measurement errors, a reason why energy intake was included as a covariate in the models to
9 achieve the equivalent of an isoenergetic diet and thus overcome this problem. At any rate,
10 measurement error most likely would have introduced non-differential misclassification, and
11 the implications for the results of this error would have been to bias the estimates towards the
12 null. The duration of follow-up lasting only 3 months cannot be considered a major limitation,
13 because the effects of dietary interventions on risk factors do not need a long induction
14 period.[49] The study also has strengths, such as reproducing real-life conditions with home-
15 prepared foods in free-living individuals, as in usual clinical practice. Other strengths are the
16 high response and low drop-out rates, which can be partly explained because participants
17 belonging to a Mediterranean culture, where people are accustomed to using olive oil and
18 nuts, the supplemental foods provided at no cost, and enjoy eating fibre-rich vegetables, fruits
19 and legumes.

20 In summary, the results of this study show that an increase in DF intake achieved with
21 natural foods in the setting of a Mediterranean-style diet can reduce cardiovascular risk
22 factors. Except for subjects in the highest 20% of DF intake, the effects on each individual
23 risk factor were modest but, taken together, they suggest that increasing DF consumption may
24 be instrumental in modifying the population cardiovascular risk profile, therefore preventing
25 or delaying future cardiovascular events.

26

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7 analyses. CIBEROBN is an initiative of Instituto de Salud Carlos III, Spain.

8

9 WHAT IS ALREADY KNOWN ON THIS SUBJECT?

- 10 • Epidemiological studies have suggested that dietary fibre intake is associated with
11 reduced incidence of ischemic heart disease, stroke **and diabetes**.
- 12 • Clinical trials have also pointed out that diets with fibre supplementation may reduce
13 blood pressure, improve lipid profile and increase insulin sensitivity.
- 14 • No intervention studies have evaluated the effects of dietary fibre on classical and
15 novel risk factors in free-living subjects at high cardiovascular risk.

16

17 WHAT DOES THIS PAPER ADD?

- 18 • The increase of dietary fibre in an intervention aimed to upgrade consumption of
19 fruits, vegetables and legumes in the setting of a Mediterranean-style diet was
20 associated with reductions in cardiovascular risk factors, such as body weight, waist
21 circumference, systolic and diastolic blood pressures, serum glucose, and C-reactive
22 protein.
- 23 • Reductions in total cholesterol and LDL cholesterol were observed only among
24 participants with greater increases in soluble fibre intake.
- 25 • These beneficial effects on surrogate markers of cardiovascular risk add biological
26 plausibility to the epidemiological evidence supporting a protective effect of dietary
27 fibre intake on the risk for cardiovascular diseases.

28

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Table 1. Baseline characteristics of the 772 subjects included in the study.

Characteristics	Participants
Age, mean (SD), years	68.8 (6.4)
Gender, men (%)	339 (44)
Family history of CHD, No. (%)	178 (23)
Current smokers, No. (%)	127 (16)
Type 2 diabetes mellitus, No. (%)	421 (54)
Hypertension, No (%)	605 (78)
Dyslipidemia, No. (%)	515 (67)
Body mass index, mean (SD), kg/m ²	29.9 (4.2)
Overweight or obesity (Body mass index > 25 kg/m ²), No. (%)	696 (90)
Medications, No. (%)	
ACE inhibitors	340 (44)
Diuretics	271 (35)
Other antihypertensive agents	160 (21)
Statins	326 (42)
Other lipid-lowering agents	51 (6)
Insulin	61 (8)
Oral hypoglycemic drugs	282 (37)
Aspirin or other antiplatelet drugs	138 (18)
Occupation, No. (%)	
Unskilled	179 (23)
Skilled manual	288 (37)
Skilled non-manual	172 (22)
Directive and professional	133 (17)
Education level, No. (%)	
Primary school	554 (72)
First degree high school	126 (16)
High school or university	91 (12)

Abbreviations: CHD, coronary heart disease; ACE, angiotensin-converting enzyme.

[†]Calculated as weight in kilograms divided by the square of height in meters.

Table 2. Baseline levels and 3-month changes in the consumption of key food items, energy and nutrients.

Variables	Baseline	3 months	Change, mean (95 % CI)	P
<i>Foods, daily consumption in grams</i>				
Fruits	262 ± 218	280 ± 153	18.1 (0.4 to 35.7)	0.044
Vegetables	357 ± 168	362 ± 164	5.1 (-8.0 to 18.2)	0.443
Legumes	14.3 ± 9.3	19.5 ± 21.5	5.2 (3.6 to 6.9)	< 0.001
Fish, seafood	111 ± 63	114 ± 87	2.6 (-3.6 to 8.8)	0.414
Meat, meat products	157 ± 75	136 ± 58	-20.6 (-26.6 to -15.2)	< 0.001
Cereals	263 ± 124	238 ± 115	-24.8 (-34.4 to -15.2)	< 0.001
Dairy products	403 ± 228	387 ± 226	-16.1 (-32.1 to -0.2)	0.047
Refined-mixed olive oil	20.5 ± 20.7	13.6 ± 19.5	-6.9 (-8.6 to -5.1)	< 0.001
Virgin olive oil	19.9 ± 23.9	27.6 ± 23.8	7.7 (5.9 to 9.4)	< 0.001
Total nuts	11.0 ± 16	22.1 ± 23.5	11.1 (9.1 to 13.1)	< 0.001
Alcohol	10.5 ± 17.3	12.3 ± 18.4	1.9 (0.6 to 3.1)	0.003
<i>Energy and Nutrients</i>				
Energy, kj/d	2538 ± 738	2393 ± 638	-145 (-200 to -88)	< 0.001
Protein, % En	17.1 ± 3.3	18.8 ± 6.0	1.7 (1.2 to 2.3)	< 0.001
Carbohydrate, % En	41.9 ± 7.7	41.0 ± 7.7	-0.9 (-1.5 to -0.3)	< 0.001
Total fibre, g/d	21.1 ± 7.6	22.2 ± 7.9	1.1 (0.4 to 1.7)	0.001
Soluble fibre, g/d	5.5 ± 2.1	5.9 ± 2.0	0.4 (0.2 to 0.6)	< 0.001
Total fat, % En	38.2 ± 7.3	37.2 ± 9.1	-0.8 (-1.5 to -0.1)	0.020
MUFA	18.8 ± 4.6	19.3 ± 4.6	0.5 (0.1 to 0.8)	0.009
PUFA	6.8 ± 2.2	7.2 ± 3.2	1.0 (0.8 to 1.3)	< 0.001
SFA	10.1 ± 2.4	9.2 ± 2.2	-0.8 (-1.0 to -0.7)	< 0.001
Alpha-linolenic acid, g/d	1.5 ± 0.9	1.9 ± 1.4	0.4 (0.3 to 0.5)	< 0.001
Marine n-3 fatty acids, g/d	0.8 ± 0.6	0.9 ± 0.9	0.1 (0.0 to 0.2)	0.009

CI, Confidence Interval, MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids.

Table 3. Subjects characteristics and energy and nutrient intake according to quintiles of energy-adjusted dietary fibre intake at 3 months.

Variables	Quintiles of energy-adjusted total fibre intake at baseline					P*
	Q1	Q2	Q3	Q4	Q5	
N	144	146	143	143	145	
Dietary fibre intake, g/d (median)	≤ 16 (14)	16.1-19.9 (18)	20.0-21.9 (21)	22.0-25.9 (23)	≥ 26.0 (29)	
Age, years	68.7 ± 5.6	69.3 ± 6.0	68.4 ± 6.5	68.9 ± 6.0	69.2 ± 7.6	0.667
Sex, men	60	77	62	64	64	0.609
Smokers, n (%)	27 (19)	26 (18)	24 (17)	17 (12)	28 (19)	0.733
Diabetes, n (%)	79 (55)	95 (65)	77 (54)	75 (52)	85 (59)	0.470
Hypertension, n (%)	125 (87)	130 (89)	111 (78)	108 (76)	112 (77)	0.294
Dyslipidemia, n (%)	105 (73)	100 (69)	88 (62)	107 (75)	94 (65)	0.126
Body mass index, kg/m ²	29.6 ± 4.0	30.0 ± 4.5	30.0 ± 4.5	29.7 ± 4.0	29.3 ± 3.9	0.608
Waist circumference, cm	101 ± 10	101 ± 12	100 ± 11	99 ± 13	98 ± 10	0.174
Energy, kcal/d	2059 ± 590	2324 ± 520	2538 ± 598	2824 ± 724	3065 ± 886	<0.001
Protein, % En	17.6 ± 3.8	17.2 ± 2.9	16.9 ± 3.4	16.6 ± 2.9	16.8 ± 2.8	0.043
Carbohydrate, % En	40.6 ± 8.5	40.3 ± 7.6	41.5 ± 6.9	43.7 ± 6.8	45.2 ± 6.8	<0.001
Fat, % En	38.3 ± 7.9	39.7 ± 7.3	38.9 ± 7.2	37.4 ± 6.1	35.8 ± 6.1	<0.001
MUFA	18.8 ± 5.0	19.8 ± 2.5	19.3 ± 4.6	18.3 ± 4.1	16.9 ± 3.8	<0.001
PUFA	5.8 ± 2.1	6.2 ± 1.8	6.2 ± 2.2	6.0 ± 1.8	6.3 ± 2.7	0.215
SFA	10.7 ± 2.7	10.4 ± 2.5	10.1 ± 2.2	9.8 ± 2.1	9.6 ± 2.4	<0.001
Virgin olive oil, g/d	13.8 ± 20.9	18.8 ± 22.8	19.5 ± 23.1	24.1 ± 25.4	20.0 ± 23.4	0.010
Alcohol, g/d	11.8 ± 22.7	9.9 ± 16.7	10.8 ± 16.8	9.1 ± 13.5	9.2 ± 11.7	0.754
Low physical activity, n (%)**	47 (34)	45 (32)	46 (33)	35 (25)	32 (23)	0.155

Abbreviations as in Table 2.

Values are means ± standard deviations unless otherwise stated

* P value for linear trend by ANOVA or chi-square test.

**Lowest tertile.

Table 4. Three-month changes in risk factors by quintiles of change in dietary fibre intake.

Variable changes	Quintiles of change in dietary fibre intake					P*	P**
	Q1	Q2	Q3	Q4	Q5		
Fibre intake, range (g/d)	<-2.5	-2.5 to 0.2	0.2 to 1.8	1.8 to 5.3	>5.3		
Fibre intake, median (g/d)	-5.7	-1.3	0.3	2.6	8.3		
N	122	123	123	122	123		
Weight, kg	0.02	-0.19	-0.23	-0.38	-0.90	<0.001	0.001
Waist circumference, cm	0.74	-0.17	-0.83	-1.27	-1.90	<0.001	<0.001
Systolic BP, mm Hg	-0.19	-2.67	-2.95	-2.43	-9.08	<0.001	<0.001
Diastolic BP, mm Hg	-1.25	-1.33	-2.04	-2.01	-4.76	0.002	0.005
Fasting glucose, mg/dL	5.72	1.84	-3.56	-1.65	-7.67	0.05	0.04
Fasting insulin, pmol/L	-0.53	0.51	-0.68	-0.52	-0.77	0.81	0.76
Total cholesterol, mg/dL	0.94	-2.75	0.95	-5.52	-8.78	0.14	0.19
LDL cholesterol , mg/dL	-1.66	-2.15	-3.77	-5.09	-8.63	0.14	0.14
HDL cholesterol , mg/dL	1.29	0.81	1.46	1.51	2.32	0.07	0.02
Triglycerides, mg/dL	-5.09	-4.20	0.70	-2.23	-3.62	0.80	0.70
C-reactive protein, mg/L	-0.02	-0.03	-0.18	-0.21	-1.01	0.07	0.04
Interleukin-6 , pg/mL	-0.46	-1.18	0.21	-0.65	-0.69	0.90	0.88
ICAM-1, ng/mL	-14.6	-27.1	-39.6	-23.3	-22.6	0.81	0.82
VCAM-1, ng/mL	-21	-17	22	-117	-77	0.19	0.23

BP, blood pressure; ICAM, intercellular adhesion molecule; VCAM, vascular cell adhesion molecule.

* P value for linear trend adjusted for age, gender and energy intake.

** Additionally adjusted for intervention group and baseline body mass index, smoking, alcohol intake and physical activity.

Table 5. Mean changes (95% confidence intervals) and mean differences (95% confidence intervals) in changes in adiposity, blood pressure and other risk factors between the lowest (Q1) and the highest (Q5) quintile of changes in total dietary fibre intake.

Variable changes	Extremes of changes in dietary fibre intake			P**
	Q1	Q5	Change Q5 versus Q1*	
Weight, kg	0.02 (-0.36 to 0.32)	-0.90 (-1.40 to -0.42)	-0.92 (-1.52 to -0.33)	0.002
Waist circumference, cm	0.74 (-0.20 to 1.68)	-1.90 (-3.18 to -0.60)	-2.63 (-4.20 to -1.07)	0.001
Systolic blood pressure, mm Hg	-0.19 (-3.41 to 3.03)	-9.08(-12.21 to -5.95)	-8.89 (-13.37 to -4.41)	< 0.001
Diastolic blood pressure, mm Hg	-1.25 (-2.70 to 0.21)	-4.76 (-6.46 to -3.08)	-3.52 (-5.73 to -1.31)	0.002
Fasting glucose, mg/dL	5.72 (0.64 to 10.79)	-7.67 (-11.84 to -3.50)	-13.39 (-19.86 to -6.93)	< 0.001
Total cholesterol, mg/dL	0.94 (-5.24 to 7.12)	-8.78 (-14.30 to -3.27)	-9.73 (-17.96 to -1.49)	0.021
LDL cholesterol, mg/dL	-1.66 (-6.96 to 3.64)	-8.63 (-14.26 to -3.00)	-7.90 (-14.96 to 0.72)	0.075
HDL cholesterol, mg/dL	1.29 (0.08 to 2.52)	2.32 (1.08 to 3.57)	1.03 (-0.70 to 2.76)	0.242
C-reactive protein, mg/L	-0.02 (-0.51 to 0.48)	-1.01 (-1.53 to -0.49)	-1.08 (-1.80 to -0.48)	0.004

* Differences between baseline and 3-month follow-up evaluation.