Dietary energy density and body weight changes after three years in the PREDIMED study.

Cristina Razquin, Ana Sanchez-Tainta, Jordi Salas-Salvadó, Pilar Buil-Cosiales, Dolores Corella, Montserrat Fito, Emilio Ros, Ramón Estruch, Fernando Arós, Enrique Gómez-Gracia, Miquel Fiol, José Lapetra, Luis Serra-Majem, Xavier Pinto, Helmut Schroeder, Josep A. Tur, José. Vicente Sorlí, Rosa M. Lamuela-Raventós, Mónica Bulló, Maira Bes-Rastrollo, Miguel A. Martinez-Gonzalez. FOR THE PREDIMED GROUP.

Cristina Razquin. Department of Preventive Medicine and Public Health, University of Navarra. Irunlarrea 1, 31080 Pamplona, Navarra, Spain. Tel 0034 948 425 600, ext 806605. Fax: + 34 948 42 56 49. E-mail: crazquin@unav.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn) and PREDIMED Network (RD 06/0045), Instituto de Salud Carlos III (ISCIII), Madrid, Spain. Instituto de Investigación Sanitaria de Navarra (IdiSNA).

Ana Sanchez-Tainta Department of Preventive Medicine and Public Health, University of Navarra. Irunlarrea 1, 31080 Pamplona, Navarra, Spain. Tel 0034 948 425 600, ext 806596. Fax: + 34 948 42 56 49. E-mail: asanchez4@unav.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn) and PREDIMED Network (RD 06/0045), Instituto de Salud Carlos III (ISCIII), Madrid, Spain. Instituto de Investigación Sanitaria de Navarra (IdiSNA).

Jordi Salas-Salvadó. Human Nutrition Department, IISPV, Universitat Rovira i Virgili, Carrer de Sant Llorenç, 21, 43201 Reus, Tarragona, Spain. Phone: 0034 977759313; FAX: +34 977759322. E-mail: jordi.salas@urv.cat. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain

Pilar Buil-Cosiales. Servicio Navarro de Salud-Osasunbidea, Primary Health Care, Pamplona, Spain. E-mail: pilar.buil.cosiales@cfnavarra.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Dolores Corella. Department of Preventive Medicine and Public Health, Nutrition and Food Sciences, School of Medicine, University of Valencia, Av. de Blasco Ibáñez, 13, 46010 Valencia Spain. Phone: 34 963864417; FAX: 34 963864166. E-mail: dolores.corella@uv.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Montserrat Fito. Cardiovascular Risk and Nutrition Research Group, IMIM-Institut de Recerca del Hospital del Mar, Parc de Salut Mar Edifici PRBB, carrer Doctor Aiguader, 88 08003, Barcelona, Spain. Tel. 933 16 07 20; Fax +34 933 16 07 96. E-mail: mfito@imim.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Emilio Ros. Lipid Clinic, Endocrinology and Nutrition Service, IDIBAPS, Hospital Clinic, Carrer del Rosselló, 149, 08036 Barcelona, Spain. E-mail: eros@clinic.cat. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Ramón Estruch. Department of Internal Medicine, IDIBAPS, Hospital Clinic, Hospital Clinic, Carrer del Rosselló, 149, 08036, Barcelona, Spain. Tel +34932275539; Fax +34932279236.

E-mail: restruch@clinic.ub.es. University of Barcelona. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Fernando Arós. Department of Cardiology, Hospital Araba (Txagorritxu), c/ Jose Atxotegi, s/n 01009 Vitoria, Álava, Spain. Tel: 945 00 70 00. E-mail: aborau@secardiologia.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Enrique Gómez-Gracia. Department of Epidemiology, School of Medicine, University of Malaga, Avda. de Cervantes, 2, 29016 Málaga, Spain. Tel: 952131609. E-mail: egomezgracia@uma.es.

Miquel Fiol. Instituto de Investigación Sanitaria de Palma (IdISPa). Hospital Son Espases, Ctra de Valldemossa, 79, 07010 Palma de Mallorca, Spain. Tel: 871205987/871205050, ext 75987. E.mail: miguel.fiol@ssib.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

José Lapetra. Department of Family Medicine, Primary Care Division of Sevilla, San Pablo Health Center, Calle Jerusalén, s/n, 41007, Sevilla Spain. E.mail: jlapetra@ono.com. Tel: 954 99 41 40. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Luis Serra-Majem. Department of Clinical Sciences, University of Las Palmas de Gran Canaria, Pso. Blas Cabrera Felipe "Físico" s/n, 35016, Las Palmas de Gran Canaria Las

Palmas, Spain. E-mail: lluis.serra@ulpgc.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Xavier Pinto. Lipids and Vascular Risk Unit, Internal Medicine, Hospital Universitario de Bellvitge, Carrer de la Feixa Llarga, s/n, 08907 L'Hospitalet de Llobregat, Barcelona, Spain. E-mail: xpinto@bellvitgehospital.cat. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Helmut Schroeder. Cardiovascular and Nutrition Research Group, Institut de Recerca Hospital del Mar-IMIM, Parc de Salut Mar Edifici PRBB, carrer Doctor Aiguader, 88 08003, Barcelona, Spain; Tel. 933 16 07 20; Fax +34 933 16 07 96. E-mail: hschoeder@imim.es. CIBER Epidemiologia y Salud Pública (CIBERESP), Spain.

Josep A. Tur. Department of Fundamental Biology & Health Sciences, University of Balearic Islands, Guillem Colom Bldg, Campus, 07122 Palma de Mallorca, Spain. Tel: +34 971 73146 Fax: +34 971 173184. E-mail: pep.tur@uib.es. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

José V. Sorlí. Department of Preventive Medicine and Public Health, Nutrition and Food Sciences, School of Medicine, University of Valencia, Av. de Blasco Ibáñez, 13, 46010 Valencia Spain. Phone: 34 963864417; FAX: 34 963864166. E-mail: Jose.Sorli@uv.es CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Rosa M. Lamuela-Raventós. Department of Nutrition and Food Science, School of Pharmacy, XaRTA, INSA, University of Barcelona, Department of Nutrition and Food Science School of Pharmacy, University of Barcelona, Av Joan XXIII s/n, 08028-Barcelona, Spain. Tel:+34934034843, Fax:+34934035931. E-mail: lamuela@ub.edu. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Maira Bes-Rastrollo. Department of Preventive Medicine and Public Health, Facultad de Medicina, Universidad de Navarra, Irunlarrea 1, 31080 Pamplona, Navarra, Spain. E-mail: mbes@unav.es. Tel: +34 948 42 56 00 Ext: 806602. Fax: + 34 948 42 56 49. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Miguel A. Martinez-Gonzalez. Department of Preventive Medicine and Public Health, Facultad de Medicina, Universidad de Navarra, Irunlarrea 1, 31080 Pamplona, Navarra, Spain. E-mail: mamartinez@unav.es. Tel: +34 948 42 56 00 Ext: 806463. Fax: + 34 948 42 56 49. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

Author to whom correspondence should be addressed:

Miguel A. Martinez-Gonzalez. Department of Preventive Medicine and Public Health, Facultad de Medicina, Universidad de Navarra, Irunlarrea 1, 31080 Pamplona, Navarra, Spain. E-mail: mamartinez@unav.es. Tel: +34 948 42 56 00 Ext: 806463. Fax: + 34 948 42 56 49. CIBER Fisiopatología de la Obesidad y Nutrición (CIBERobn), Instituto de Salud Carlos III (ISCIII), Madrid, Spain.

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KEYWORDS

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ABSTRACT

The association of dietary energy density (ED) and overweight is not clear in the literature. Our aim was to study in 4259 of the PREDIMED trial whether an increase in dietary ED based on a higher adherence to a Mediterranean dietary pattern was associated with 3-y weight gain.

A validated 137-item food-frequency questionnaire was administered. Multivariable-adjusted models were used to analyze the association between 3-y ED change and the subsequent 3-y body weight change.

The most important weight reduction after 3-y follow-up was observed in the two lowest quintiles and the highest quintile of ED change. The highest ED increase was characterized by an increased intake of extra virgin olive oil (EVOO) and nuts and a decreased intake of other oils, vegetable and fruit consumption ($p<0.001$).

In conclusion, increased 3-y ED in the PREDIMED study, associated with a higher EVOO and nuts consumption, was not associated with weight gain.

1. Introduction

The prevalence of obesity, a major risk for cardiovascular disease and other chronic diseases, is rapidly increasing and becoming an important public health problem with more than 1.4 billion overweight adults worldwide in 2008 (WHO 2008) . The magnitude of the problem has led to search different approaches to prevent and reduce weight gain. In this context, it has been proposed that dietary energy density (ED) may determine the overconsumption associated to overweight more than the amount of food (Bes-Rastrollo et al. 2008). Previous interventional studies analyzing dietary ED suggest that an increase in low ED foods and a decrease of high ED food consumption may lead to body weight loss (Rolls et al. 2005; Ledikwe et al. 2007) . However, there also interventional studies that did not observe this association (Saquib et al. 2008) . We hypothesized that it may be that not only the dietary ED but the sources of the high density elements may be influencing weight gain.

The PREDIMED study showed that a Mediterranean dietary pattern rich in fat (mono and polyunsaturated fat) lead to a reduction in the risk of cardiovascular clinical events (Estruch et al. 2013). Thus, our aim was to assess in this trial whether an increase in dietary ED based on a higher adherence to a Mediterranean dietary pattern, increasing both low ED foods such as vegetables and fruit but also increasing the consumption of energy-dense foods such as extra-virgin olive oil (EVOO) or nuts, was associated to body weight changes.

2. Methods

The design and methods of the PREDIMED trial have been reported in a specific publication (Martinez-Gonzalez et al. 2012). PREDIMED is a randomized, cardiovascular primary prevention trial conducted in 11 Spanish recruiting centers (www.predimed.es). The protocol was approved by the Institutional Review Boards at all study locations. The trial is registered at http://www.controlled-trials.com/ISRCTN 35739639. The PREDIMED trial included 7,447 participants who were randomly allocated to one of three arms: 1) a traditional Mediterranean diet (MedDiet) supplemented with EVOO; 2) a traditional MedDiet supplemented with tree nuts; or 3) a control (low-fat) diet. Participants in the two MedDiet groups received either EVOO (to consume 50 g/d) or mixed nuts per day (15 g/d walnuts, 7.5 g/d hazelnuts, and 7.5 g/d almonds) at no cost. They received instructions directed to upscale the traditional MedDiet 14-item score (Schroder et al. 2011), including 1) the use of olive oil for cooking and dressing; 2) increased consumption of vegetables, nuts, and fish products; 3) consumption of white meat instead of red or processed meat; 4) preparation of home-made sauce by simmering tomato, garlic, onion and aromatic herbs with olive oil to dress vegetables, pasta, rice and other dishes; and 5) for alcohol drinkers, to follow a moderate pattern of red wine consumption. Participants allocated to the control group received small nonfood gifts and were advised to reduce all types of fat and were given written recommendations according to American Heart Association guidelines.

For the present study, body weight changes between 3-y and baseline were analyzed due to the fact that all the recruitment centers achieve the 3-y follow-up. After that, the total sample size will be significantly reduced.

2.1 Subjects

Eligible participants were men aged 55-80 years and women aged 60-80 years without previous cardiovascular disease who fulfilled at least one of the following criteria: type-2 diabetes or 3 or more cardiovascular risk factors, namely smoking, hypertension, dyslipidemia, overweight (BMI $\geq$ 25 kg/m2) or a family history of premature cardiovascular disease. For the present study we excluded 232 participants, 79 of them because their baseline food-frequency questionnaires (FFQ) were missing and 152 had total energy intake out-of predefined limits (<500 or >3500 kcal/d in women or <800 or >4000 kcal/d in men) (Willet & Stampfer 1998) and one had 9 or more missing data in the FFQ .

Moreover, 2888 participants had their 3-y FFQ missing and 17 subjects had 3-y total energy intake out-of predefined limits and were excluded. Regarding body weight, 51 subjects were excluded because of missing body weight data (baseline or third year follow-up) or implausible body weight recorded. Consequently, the final sample size included 4259 subjects.

2.2 Dietary assessment

Data on dietary intake were collected at baseline with a semi-quantitative 137-item validated FFQ (Fernandez-Ballart et al. 2010) and the PREDIMED 14-item questionnaire assessing the degree of adherence to the Mediterranean diet (values of 0 to 1 were assigned to each item, so that a score of 14 points meant the maximum adherence) (Schroder et al. 2011); this was an extension of a previously validated questionnaire (Martinez-Gonzalez et al. 2002) .

Dietary ED was calculated by dividing each subject's daily intake (kcal) by the reported weight (g) of all foods consumed based on the serving size and daily frequency of consumption. Caloric and noncaloric beverages were excluded from the calculation (Ledikwe et al. 2005) because energy intake from beverages is regulated differently from energy intake from foods (Mattes 1996). In addition, this method of calculating dietary ED has been demonstrated to provide the best correlations to measures of obesity in previous cross-sectional studies (Ledikwe et al. 2005; Mendoza et al. 2007).

2.3 Assessment of non-dietary variables

At baseline examination and yearly in follow-up visits, trained personnel performed anthropometric and blood pressure measurements and obtained samples of fasting blood. Weight and height were measured with light clothing and no shoes with calibrated scales and a wall-mounted stadiometer.

Several questionnaires were used at baseline examination to collect sociodemographic data, lifestyle variables, history of illnesses, and medication use. A validated questionnaire (Elosua et al. 1994) was used to collect information on physical activity.

2.4 Statistical analysis

Baseline characteristics and nutritional habits of participants according to their quintiles of 3-y ED change were analyzed (table 1) and p values for linear trend tests were calculated for each variable.

Changes between baseline and 3-y follow-up Mediterranean dietary pattern main characteristics are shown in table 2.

ANCOVA analysis was used to obtain 3-y body weight changes adjusted means for age and sex or age, sex, baseline BMI, baseline ED, center, intervention group, baseline physical activity, and the 14-item Mediterranean diet score of PREDIMED.

Linear multiple regression models were used to analyze the association between dietary ED changes and body weight changes after three years of intervention adjusting for the same potential confounders. Those participants in the third quintile of change (roughly no change in dietary ED) were considered as the reference category.

To achieve a statistical power of 80%, assuming a minimum difference of 0.8kg between groups of comparison and a standard deviation of 5, a sample size of 614 is needed in each group (quintile).

3. Results

Baseline characteristics of participants according to quintiles of ED changes are presented in table 1. We observed that an increase in dietary ED after three years in the PREDIMED study was significantly associated with lower baseline ED, total energy intake from solid foods and higher total amount of ingested food. Moreover, this increase was observed more frequently in females, older subjects and especially those allocated to the active arms of the intervention with MedDiet+EVOO and MedDiet+nuts.

In table 2, changes in dietary habits related to the Mediterranean dietary score according to quintiles of 3-y changes in ED are shown. The most important changes in the upper quintiles of energy density change were related to an increased consumption of EVOO and nuts, a decreased intake of other oils and a reduction in vegetable and fruit consumption ($p<0.001$). In parallel, a higher intake of monounsaturated and polyunsaturated fat was observed in the upper quintiles of ED change ($p<0.001$), with a parallel lower intake of carbohydrate and protein ($p<0.001$).

Our main aim was to observe if changes in ED were associated with body weight changes after 3-year follow-up. Thus, in table 3 mean body weight changes adjusted for age and sex or additionally adjusted for baseline BMI, baseline ED, center, intervention group, baseline physical activity and the 14-item Mediterranean diet score of PREDIMED are presented. We observed the most important weight reduction after 3-y follow-up in the two lowest quintiles and also in the fifth quintile of ED change (Figure 1).

This finding was corroborated with the linear regression models fitted to observe 3-y body weight changes (table 4). In fact, the fifth quintile (those who increased the most their dietary ED) showed similar coefficient and 95% CI than the first quintile (those who decreased the most their dietary ED) when compared to quintile 3 (reference; roughly no change).

The analysis of food ED and its association with weight changes showed that increased consumption of those foods with the highest ED (oils) was associated with the highest body weight change, not only as expected with weight gain, but also with weight loss (Figure 2). Thus, in this study, it seems that changes in the consumption of oils are highly determining body weight changes.

4. Discussion

In this study, we present the association between ED changes and 3-y body weight changes in the frame of a controlled and randomized nutritional intervention trial (PREDIMED). Interestingly, we did not observe a linear relationship between increasing ED changes and increasing body weight gain. The results showed an inverse “V-shaped” pattern for the dose-response trend, this means that, increasing ED was initially associated with higher body weight loss that decreased until approximately the third quintile of ED changes (minimum weight loss), and after that, weight loss was, again, progressively increasing.

When analyzing Mediterranean score relevant foods, the highest quintile of ED change was characterized by a higher increase specially, in EVOO and nuts consumption, but also in legumes and commercial bakery compared to lower quintiles. On average, some subjects with the highest ED increase seemed to change their dietary habits in order to achieve higher intake of EVOO, nuts, legumes, poultry, and lower red meats according to a Mediterranean dietary pattern, but, other subjects in the same quintile reduced vegetables and fruit consumption and increased bakery consumption, what negatively accounted to the Mediterranean dietary score. Despite this undesirable changes, it seemed that the high intake of nuts, and specially, EVOO were able to lead to body weight loss, though in a lesser amount. Indeed, we observed that either when ED intake was reduced by means of a drastic reduction of fat (mono and polyunsaturated fat) or either when the ED intake was increased by means of a strong increase of these fat types, the effect appeared to be a similar weight loss.

There are a few prospective studies that have analyzed the association between dietary ED and weight change. In the Nurses' cohort, they found that an increase in ED was associated with body weight gain after 4-y and 8-y follow up (Bes-Rastrollo et al. 2008). However, an increase in olive oil salad dressing was associated with a statistically significant 8-y weight loss. In the MONICA study no association was found between baseline ED and weight gain, but they found partial associations in women or obese subjects (Iqbal et al. 2006) . In a large European cohort, the EPIC study, no association was found between ED and weight changes but a positive association with waist circumference change was reported (Du et al. 2009).

Previous intervention studies analyzing ED change and weight change suggested a potential beneficial effect of reducing ED of meals (Rolls et al. 2005; Ledikwe et al. 2007). However, in the study published by Rolls *et al*, the high dense food tested were snacks (Rolls et al. 2005) and in the PREMIER trial all the interventions led to a reduced consumption of fats and oils (Ledikwe et al. 2007). On the other hand, in the frame of the WHEL study, it was found that an intervention with a significant decrease in dietary energy density did not lead to body weight loss after 4 years of follow-up (Saquib et al. 2008).

Thus, it seems that neither observational nor interventional studies have found a clear association between ED and weight changes.

The PREDIMED trial was not designed as weight loss program (Martinez-Gonzalez et al. 2012), however, following a Mediterranean-style dietary pattern without energy restriction led to body weight control and even to weight loss (Babio et al. 2014; Estruch et al. 2016; Álvarez-Pérez et al. 2016). Both MedDiets tested in the PREDIMED trial were aimed to strongly increase EVOO and nuts (high ED foods) consumption as the principal fat sources, what at least contrasted with the most usual traditional (low fat) approach for weight loss diets. The idea that following a MedDiet does not lead to weight gain despite the high content of high ED components has been published also in other studies (Yang et al. 2014; Roswall et al. 2014).

Thus, this study suggests that the effects of dietary ED on weight change depend on the particular high dense foods consumed, in a context of a specific dietary pattern. In fact, if these energy-dense foods of the diet are mainly sources of mono and polyunsaturated fat, this diet may lead to body weight loss.

In conclusion, increased dietary ED after three years in the PREDIMED study was not associated with body weight gain. Indeed, the highest ED increase based on higher EVOO and nuts consumption was linked to a mean body weight loss similar to that associated with the highest ED decrease.

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Declarations

Ethics approval and consent to participate. The PREDIMED trial was conducted according to the guidelines laid down in the Declaration of Helsinki and the Institutional Review Board of each recruitment center approved the study protocol.

Consent for publication. Not applicable.

Availability of data and material. Please contact author for data requests.

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Table legends

Table 1. Baseline characteristics of the participants across quintiles of 3-y ED change (n=4242)

Table 2. 3y-changes in dietary habits related to the Mediterranean diet across quintiles of change in ED

Table 3. 3-y mean weight changes according to quintiles of change in dietary ED

Table 4. Association between ED changes and body weight changes after three years in the PREDIMED study

Figure legend

Figure 1. Weight change (3-y) according to quintiles of dietary ED changes in the PREDIMED study.

Legend: Mean body weight change according to quintiles of changes in dietary ED after three years in the PREDIMED study, adjusted for age, sex, baseline BMI, baseline energy density, center, intervention group, baseline physical activity, 14-item Mediterranean diet score.

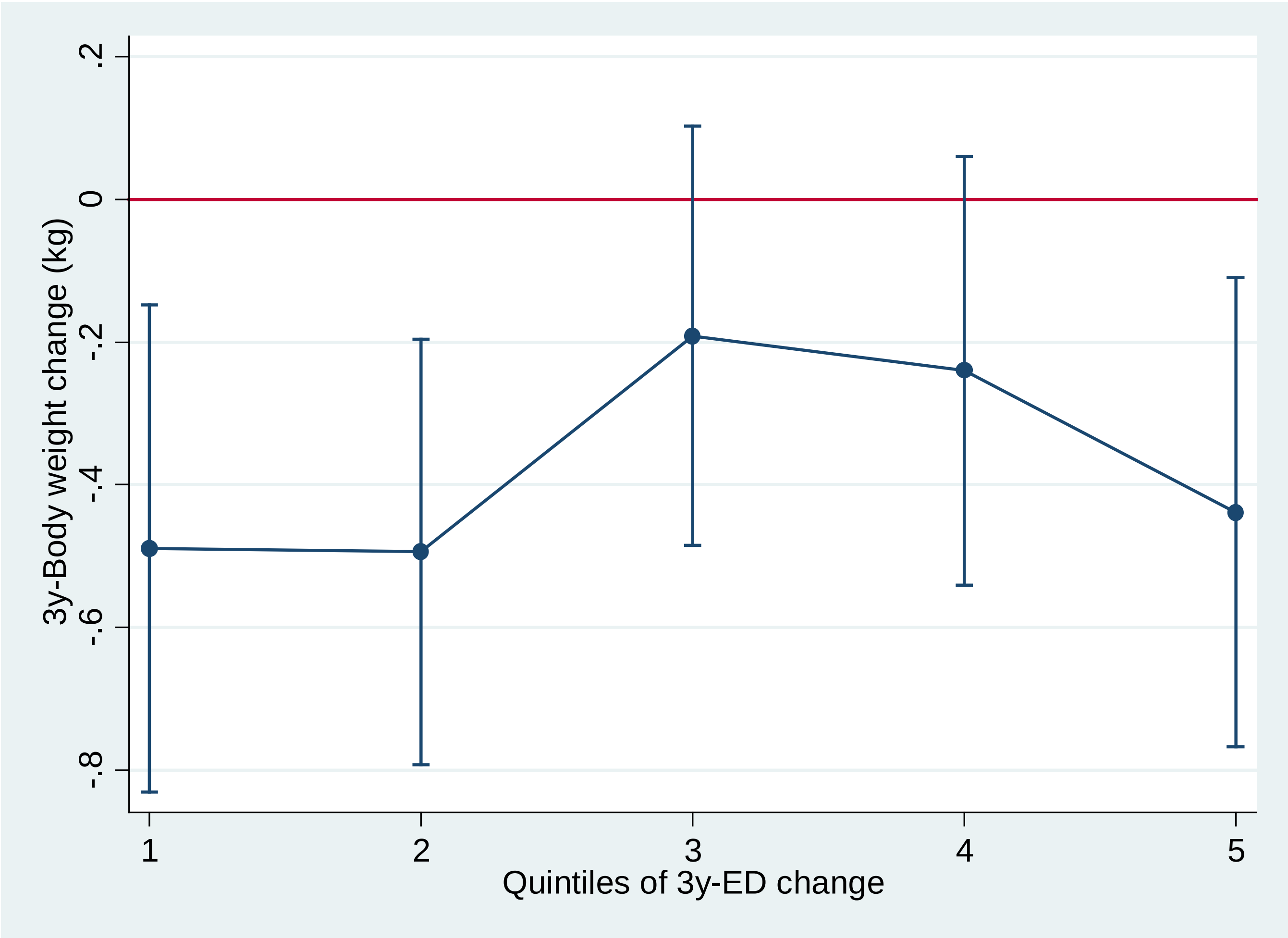
ED: Energy density; BMI: Body mass index

Figure 2. Food consumption changes and 3-y body weight changes.

Legend: Estimates (B coefficient and 95% CIs) of 3-y body weight changes (kg) for the highest tertile of change of each food item compared to the lowest tertile. Adjusted for age, sex, baseline BMI, baseline energy density, center, baseline physical activity, 14-item Mediterranean diet score.

ED: Energy density; BMI: Body mass index

Figure 1



3y-Body weight change (kg)
.2
0
-.2
-.4
-.6
-.8
1
2
3
4
5
Quintiles of 3y-ED change

Figure 2.

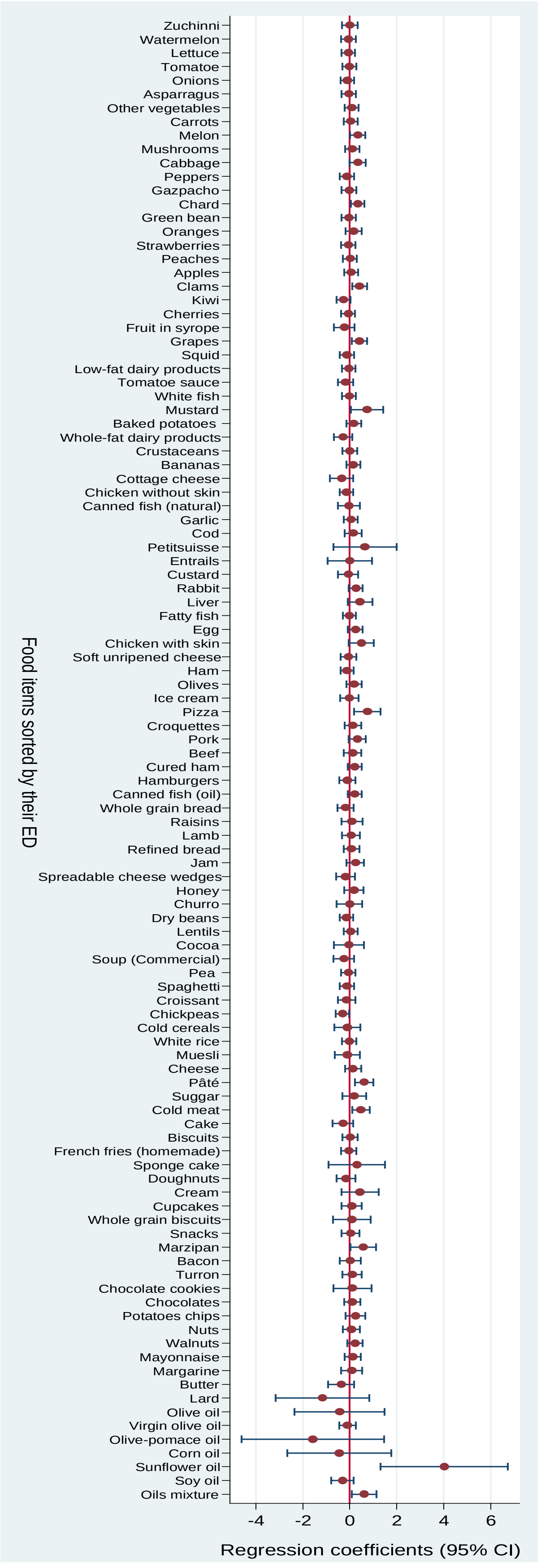

Zuchinni
Watermelon
Lettuce
Tomatoe
Onions
Asparragus
Other vegetables
Carrots
Melon
Mushrooms
Cabbage
Peppers
Gazpacho
Chard
Green bean
Oranges
Strawberries
Peaches
Apples
Clams
Kiwi
Cherries
Fruit in syrope
Grapes
Squid
Low-fat dairy products
Tomatoe sauce
White fish
Mustard
Baked potatoes
Whole-fat dairy products
Crustaceans
Bananas
Cottage cheese
Chicken without skin
Canned fish (natural)
Garlic
Cod
Petitsuisse
Entrails
Custard
Rabbit
Liver
Fatty fish
Egg
Chicken with skin
Soft unripened cheese
Ham
Olives
Ice cream
Pizza
Croquettes
Pork
Beef
Cured ham
Hamburgers
Canned fish (oil)
Whole grain bread
Raisins
Lamb
Refined bread
Jam
Spreadable cheese wedges
Honey
Churro
Dry beans
Lentils
Cocoa
Soup (Commercial)
Pea
Spaghetti
Croissant
Chickpeas
Cold cereals
White rice
Muesli
Cheese
Pâté
Suggar
Cold meat
Cake
Biscuits
French fries (homemade)
Sponge cake
Doughnuts
Cream
Cupcakes
Whole grain biscuits
Snacks
Marzipan
Bacon
Turron
Chocolate cookies
Chocolates
Potatoes chips
Nuts
Walnuts
Mayonnaise
Margarine
Butter
Lard
Olive oil
Virgin olive oil
Olive-pomace oil
Corn oil
Sunflower oil
Soy oil
Oils mixture
Food items sorted by their ED
-4
-2
0
2
4
6
Regression coefficients (95% CI)

Table 1. Baseline characteristics of the participants across quintiles of 3-y ED change (n=4242)

	Q1 (n=851)	**Q2 (n=850)**	**Q3 (n=853)**	**Q4 (n=853)**	**Q5 (n=852)**
Change in energy density (kcal/g)	-0.45 (0.18)	-0.18 (0.05)	-0.03 (0.04)	0.10 (0.05)	0.37 (0.16)
Baseline energy density (kcal/g)	1.7 (0.3)	1.5 (0.2)	1.4 (0.2)	1.3 (0.2)	1.2 (0.2)**
Total energy intake from solid foods (kcal/d)	2185.92 (511.9)	2079.0 (467.7)	2023.4 (472.0)	1976.1 (461.9)	1891.4 (487.0)**
Amount of food (g/d)	1311.9 (323.2)	1416.5 (333.6)	1480.4 (349.6)	1523.8 (375.9)	1552.3 (414.5)**
Age (y)	66.8 (6.0)	67.0 (6.0)	67.1 (6.1)	67.0 (5.9)	67.5 (6.2)*
Sex (%female)	52	59	59	61	57*
Physical activity (METS-min/d)	228.5 (230.8)	249.6 (239.6)	259.6 (266.9)	239.3 (242.8)	234.6 (255.9)
Mediterranean dietary pattern (score)	8.6 (1.9)	8.8 (1.9)	8.9 (1.9)	8.9 (1.9)	8.7 (1.9)
Baseline weight (kg)	77.2 (12.0)	76.3 (11.5)	76.5 (11.6)	76.4 (11.8)	76.3 (11.7)
Baseline BMI (kg/m2)	30.0 (3.9)	29.7 (3.7)	29.9 (3.8)	30.0 (3.7)	29.9 (3.7)

Intervention groups (%)					
Control	34	29	21	21	21**
MeDiet+EVOO	39	41	45	43	45**
MeDiet+Nuts	27	30	33	35	34**
Smoking (%)					
Never	59	67	63	63	61*
Current	16	12	13	11	12*
Former	25	21	24	25	27

*p<0.05, **p<0.001

Table 2. 3y-changes in dietary habits related to the Mediterranean diet across quintiles of change in ED

	Q1 (n=851)	Q2 (n=850)	Q3 (n=853)	Q4 (n=853)	Q5 (n=852)
Change in energy density (kcal/g)	-0.45 (0.18)	-0.18 (0.05)	-0.03 (0.04)	0.11 (0.05)	0.37 (0.16)**
Extra-virgin olive oil (g/d)	9.9 (31.9)	13.7 (29.7)	19.0 (28.4)	17.5 (29.1)	21.3 (27.4)**
Nuts (g/d)	1.6 (21.6)	3.4 (19.2)	6.6 (20.3)	6.8 (18.6)	7.5 (24.0)**
Vegetables (g/d)	96.3 (149.7)	42.6 (131.7)	15.9 (143.9)	-38.2 (141.9)	-116.9 (172.3)**
Fruits (g/d)	200.7 (191.6)	87.0 (168.1)	24.5 (192.2)	-39.9 (201.3)	-152.8 (218.5)**
Legumes (g/d)	1.6 (20.9)	1.7 (12.4)	1.8 (14.2)	3.6 (14.6)	2.2 (14.6)
Red meats (g/d)	-17.4 (39.7)	-12.0 (36.5)	-13.1 (35.0)	-12.8 (38.9)	-10.0 (39.6)**
Poultry (g/d)	9.2 (35.5)	5.9 (35.4)	5.7 (35.8)	3.6 (35.1)	2.4 (36.0)**
Fish (g/d)	10.5 (53.8)	5.5 (46.6)	8.2 (49.9)	-2.3 (54.0)	-7.2 (62.2)**
Commercial bakery (g/d)	-20.7 (40.0)	-9.8 (32.5)	-5.2 (29.9)	0.6 (28.9)	5.2 (34.5)**
Other olive oils (g/d)	-14.0 (24.9)	-11.4 (24.0)	-10.9 (22.5)	-9.0 (23.9)	-4.5 (22.0)**
Vegetable oils (not olive)	-2.5 (9.6)	-2.3 (8.0)	-1.7 (7.2)	-1.7 (6.6)	-1.3 (6.9)**
Butter (g/d)	-0.1 (2.4)	-0.2 (2.4)	-0.1 (2.1)	-0.1 (2.1)	-0.1 (2.8)
Carbohydrate intake (% total energy)	0.7 (8.1)	-0.3 (7.4)	-1.2 (7.1)	-0.9 (7.5)	-2.4 (8.2)**

Protein intake (% total energy)	1.7 (2.9)	0.7 (2.6)	-0.0 (2.6)	-0.7 (2.8)	-1.8 (2.9)**
Fat intake (% total energy)	-2.3 (8.1)	-0.3 (7.4)	1.4 (7.0)	1.9 (7.3)	4.5 (7.8)**
Monounsaturated fatty acid intake (% total energy)	-0.8 (5.7)	0.5 (5.1)	1.6 (4.8)	1.9 (5.2)	3.6 (5.2)**
Polyunsaturated fatty acid intake (% total energy)	-0.3 (2.6)	-0.1 (2.5)	0.4 (2.4)	0.5 (2.2)	0.9 (2.7)**
Saturated fatty acid intake (% total energy)	-1.2 (2.5)	-0.7 (2.2)	-0.5 (2.2)	-0.5 (2.2)	-0.0 (2.4)**
Total energy intake from solid foods (kcal/d)	-309.2 (556.7)	-127.2 (521.4)	-19.3 (512.2)	28.8 (526.4)	154.5 (538.2)**

Table 3. 3-y mean weight changes according to quintiles of change in dietary ED

	Q1 (n=851)	**Q2 (n=850)**	**Q3 (n=853)**	**Q4 (n=853)**	**Q5 (n=852)**
Median change in energy density (kcal/g)	-0.40	-0.17	-0.03	0.10	0.33
Age and Sex-adjusted weight change (mean (95% CI))	-0.54 (-0.84 to -0.24)	-0.50 (-0.78 to -0.19)	-0.18 (-0.48 to 0.11)	-0.24 (-0.53 to 0.06)	-0.41 (-0.70 to -0.11)
Multivariate[1] adjusted weight change (mean (95% CI))	-0.49 (-0.83 to -0.15)	-0.49 (-0.79 to -0.20)	-0.19 (-0.48 to 0.10)	-0.24 (-0.54 to -0.06)	-0.44 (-0.77 to -0.11)

[1]age, sex, baseline BMI, baseline energy density, center, intervention group, baseline physical activity, 14-item Mediterranean diet score

Table 4. Association between ED changes and body weight changes after three years in the PREDIMED study

3-year weight change	Q1 (n=851)	Q2 (n=850)	Q3 (n=853)	Q4 (n=853)	Q5 (n=852)
Median change in energy density (kcal/g)	-0.40	-0.17	-0.03	0.10	0.33
Multivariable model[1]	-0.36 (-0.78 to 0.06)	-0.30 (-0.72 to 0.11)	0 (ref)	-0.06 (-0.47 to 0.36)	-0.23 (-0.65 to 0.19)
Multivariable model[2]	-0.30 (-0.75 to 0.16)	-0.30 (-0.72 to 0.12)	0 (ref)	-0.05 (-0.47 to 0.37)	-0.25 (-0.69 to 0.19)

[1]Multiple linear regression adjusted for age and sex. Reference category: third quintile

[2] Multiple linear regression adjusted for age, sex, baseline BMI, baseline energy density, center, intervention group, baseline physical activity, 14-item Mediterranean diet score. Reference category: third quintile