

Changes in bread consumption and 4-year changes in adiposity in Spanish subjects at high cardiovascular risk

I. Bautista-Castaño^{1,2†}, A. Sánchez-Villegas^{1,2†}, R. Estruch^{2,3,4}, M. A. Martínez-González^{2,5}, D. Corella^{4,6}, J. Salas-Salvadó^{2,4,7}, M. I. Covas^{4,8}, H. Schroder^{4,8}, J. Alvarez-Pérez^{1,2}, J. Quilez^{4,7}, R. M. Lamuela-Raventós^{2,4,9}, E. Ros^{4,10}, F. Arós^{2,11}, M. Fiol^{4,12}, J. Lapetra^{4,13}, M. A. Muñoz^{4,14}, E. Gómez-Gracia^{2,15}, J. Tur^{2,16}, X. Pinto^{2,17}, V. Ruiz-Gutierrez¹⁸, M. P. Portillo-Baquedano¹⁹ and L. Serra-Majem^{1,2*} on behalf of the PREDIMED Study Investigators

¹Department of Clinical Sciences, University of Las Palmas de Gran Canaria, PO Box 550, 35080 Las Palmas de Gran Canaria, Spain

²RETIC Alimentación saludable en la prevención primaria de enfermedades crónicas: la Red Predimed (RD06/0045), Spain

³Department of Internal Medicine, Hospital Clinic, Institut d'Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Barcelona, Spain

⁴Ciber Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III, Madrid, Spain

⁵Department of Preventive Medicine and Public Health, University of Navarra, Pamplona, Spain

⁶Department of Preventive Medicine and Public Health, University of Valencia, Valencia, Spain

⁷Human Nutrition Department, School of Medicine, University Rovira i Virgili, Reus, Spain

⁸Cardiovascular Risk and Nutrition Research Group, IMIM – Institut de Recerca del Hospital del Mar, Barcelona, Spain

⁹Department of Nutrition and Bromatology, University of Barcelona, Barcelona, Spain

¹⁰Lipid Clinic, Endocrinology and Nutrition Service, Institut d'Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Hospital Clinic, Barcelona, Spain

¹¹Department of Cardiology, Hospital Txagorritxu, Vitoria, Spain

¹²University Institute for Health Sciences Investigation, Palma de Mallorca, Spain

¹³Department of Family Medicine, Primary Care Division of Sevilla, San Pablo Health Center, Sevilla, Spain

¹⁴Primary Health Care Division and Research, IDIAP-Jordi Gol, Barcelona, Spain

¹⁵Department of Preventive Medicine, University of Málaga, Málaga, Spain

¹⁶Research Group on Community Nutrition and Oxidative Stress, University of Balearic Islands, Palma de Mallorca, Spain

¹⁷Internal Medicine Service, Hospital of Bellvitge, Hospitalet de Llobregat, Barcelona, Spain

¹⁸Instituto de la Grasa, CSIC, Sevilla, Spain

¹⁹Department of Pharmacy and Food Sciences, University of the Basque Country, Bilbao, Spain

(Submitted 3 February 2012 – Final revision received 20 September 2012 – Accepted 20 September 2012 – First published online 3 December 2012)

Abstract

The effects of bread consumption change over time on anthropometric measures have been scarcely studied. We analysed 2213 participants at high risk for CVD from the PREvención con Dieta MEDiterránea (PREDIMED) trial to assess the association between changes in the consumption of bread and weight and waist circumference gain over time. Dietary habits were assessed with validated FFQ at baseline and repeatedly every year during 4 years of follow-up. Using multivariate models to adjust for covariates, long-term weight and waist circumference changes according to quartiles of change in energy-adjusted white and whole-grain bread consumption were calculated. The present results showed that over 4 years, participants in the highest quartile of change in white bread intake gained 0.76 kg more than those in the lowest quartile (P for trend=0.003) and 1.28 cm more than those in the lowest quartile (P for trend <0.001). No significant dose–response relationships were observed for change in whole-bread consumption and anthropometric measures. Gaining weight (>2 kg) and gaining waist circumference (>2 cm) during follow-up was not associated with increase in bread consumption, but participants in the highest quartile of changes in white bread intake had a reduction of 33% in the odds of losing weight (>2 kg) and a reduction of 36% in the odds of losing waist circumference (>2 cm). The present results suggest that reducing white bread, but not whole-grain bread consumption, within a Mediterranean-style food pattern setting is associated with lower gains in weight and abdominal fat.

Key words: White bread: Whole-grain bread: Cereals: Body weight: Abdominal fat

Abbreviations: DM, diabetes mellitus; GI, glycaemic index; PREDIMED, PREvención con Dieta MEDiterránea.

* **Corresponding author:** L. Serra-Majem, email lserra@dcc.ulpgc.es

† I. B.-C. and A. S.-V. contributed equally to the present study.

The increasing rates of overweight and obesity worldwide have been attributed to social and lifestyle changes, including dietary habits and physical activity^(1,2). Dietary habits play a pivotal role in the development of overweight and obesity⁽³⁾. Because abdominal obesity is more closely associated with diabetes mellitus (DM), CVD and total mortality than adipose tissue accumulation in other regions of the body^(4,5), several epidemiological studies have investigated the relationship between diet and general or abdominal obesity with different results^(6,7). Some of these studies have specifically investigated the associations between cereal consumption and BMI or abdominal fat. They have shown inverse associations with anthropometric variables for whole-grain cereals but conflicting results for white cereals⁽⁸⁾. Factors such as postprandial insulin responses, gastric emptying after consuming a high-glycaemic index (GI) meal and other factors could be implicated in a potential differential effect of white *v.* whole-grain cereals on adiposity⁽⁹⁾.

White bread is the main staple consumed in Spain that substantially contributes to total energy intake. A higher average consumption of a food item usually reflects also a wider between-subjects variability, and this is an ideal setting to assess the health consequences of the consumption of that item. This is the case of white bread in Spain.

To address the relation between bread consumption and changes in weight or waist circumference over time, we evaluated the effect of the change in bread consumption over a 4-year period on weight or abdominal fat gain among a large sample of subjects at high risk for CVD. These participants were part of the PREvención con DIeta MEDiterránea (PREDIMED) trial, the first large randomised controlled trial for the primary prevention of CVD that allocates participants to one of three dietary patterns, namely, two Mediterranean-type diets (Med-diet) with different fat sources, mixed nuts or virgin olive oil and one low-fat diet (control group)^(10,11).

Methods

Study population

The present study has been conducted within the frame of the PREDIMED trial. The design of the PREDIMED trial has been reported in detail elsewhere^(10,11). Briefly, the PREDIMED trial is a large, parallel-group, multicentre, randomised and controlled 6-year field trial that aims to assess the effects of a Med-diet on CVD in which participants are assigned to one of three different dietary patterns: low-fat diet; Med-diet supplemented with virgin olive oil; and Med-diet supplemented with nuts⁽¹²⁾. The study population is composed of men aged between 55 and 80 years and women aged between 60 and 80 years, with no previously documented CVD, but at high cardiovascular risk. Inclusion criteria were either type 2 DM or at least three of the following risk factors: current smoking, hypertension, LDL-cholesterol > 4.110 mmol/l, HDL-cholesterol < 1.034 mmol/l, overweight/obesity or a family history of premature CHD.

The recruitment of 7447 participants in primary care centres affiliated with eleven Spanish teaching hospitals took place between October 2003 and June 2009.

The present study was designed as an observational prospective analysis in a subsample of participants of the PREDIMED trial⁽¹¹⁾, whose complete dietary information was collected at baseline and after 4 years of follow-up (*n* 3071).

Subjects with implausible data on baseline total energy intake (<3349 or 16748 kJ/d in men and <2093 or >14654 kJ/d in women)⁽¹³⁾ and those with outlier values for exposure or outcome data were excluded. Finally, 2213 participants were analysed (Fig. 1).

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki⁽¹⁴⁾ and all procedures involving human subjects/patients were approved by the institutional review boards of the participating centres.

Outcome assessment

The baseline and the 4-year follow-up examination included the assessment of weight and height measured with calibrated scales and wall-mounted stadiometers, respectively. Subjects wore indoor clothing and no shoes. Waist circumference was measured midway between the lower rib margin and the iliac crest using an anthropometric tape. BMI was calculated as weight in kg divided by the square of height in m.

The outcomes after 4 years of follow-up were: (1) change in body weight after 4 years of follow-up; (2) change in waist circumference after 4 years of follow-up; (3) risk of gaining or losing more than 2 kg of weight; and (4) risk of gaining or losing more than 2 cm of waist circumference.

Dietary exposures

All participants were also asked to complete, at baseline and every subsequent year, a 137-item semi-quantitative FFQ repeatedly validated in Spain⁽¹⁵⁾. The frequencies were registered in nine categories that ranged from 'never or almost never' to '> 6 times/d'. Energy and nutrient intake were derived using Spanish food composition tables⁽¹⁶⁾.

The consumption of total, white and whole-grain bread at baseline and in every follow-up assessment was adjusted for total energy intake using the residuals method⁽¹⁷⁾. We also determined change in bread consumption after 4 years of follow-up. These changes in consumption were categorised into quartiles. It is important to note that the first quartile of change indicates a decrease in bread consumption, whereas the highest quartile represents an increase in the consumption of all types of bread. Finally, to assess the association between change in bread consumption (categorised as decrease, no change or little change and increase in consumption) and changes in food groups, the second and third quartiles of bread consumption change were merged in an additional analysis.

We also determined alcohol intake and the energy-adjusted intake of food groups such as legumes, vegetables, fruits, fish, meat, olive oil, nuts, dairy products, cereals (sources other than bread) and sweets and nutrients such as SFA, PUFA and

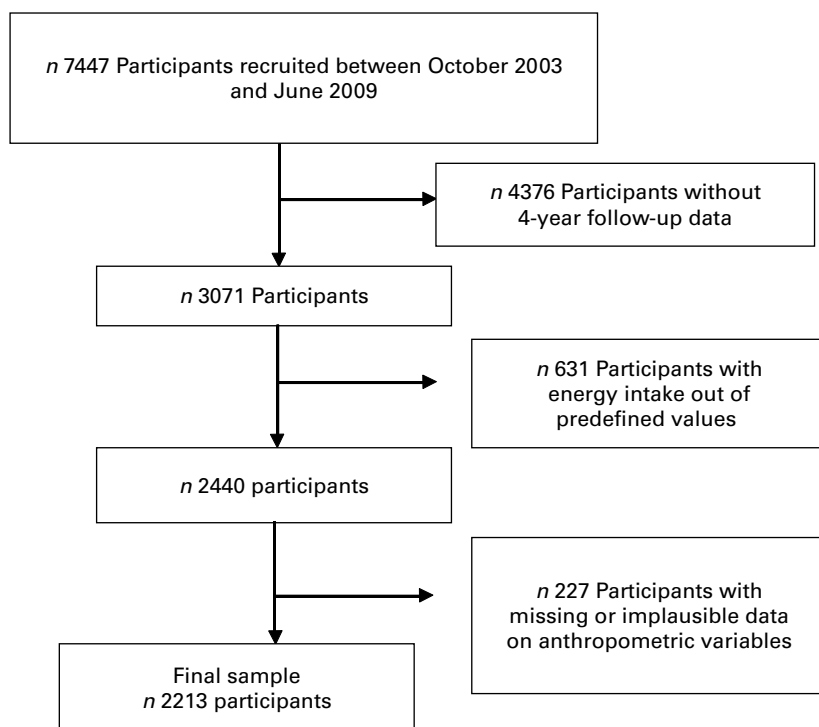


Fig. 1. Flow-chart of participants: the PREverción con Dieta MEDiterránea trial.

MUFA, proteins and dietary fibre at baseline and after 4 years of follow-up. Changes in intake were defined as the difference in intake between the two points in time.

Assessment of non-dietary variables

Physical activity was measured at baseline and during the 4-year follow-up visit using the validated Spanish version of the Minnesota Leisure Time Physical Activity Questionnaire⁽¹⁸⁾. Physical activity levels at baseline and after 4 years of follow-up were categorised into tertiles. Change in physical activity during the 4 years of follow-up was categorised into three groups: increase, decrease and no change in physical activity over time. We considered that a participant had increased his/her physical activity if the participant had moved to a higher tertile of physical activity from baseline; a participant had decreased his/her physical activity if the participant had moved to a lower tertile from baseline; and a participant had not changed the physical activity level if he/she remained in the same tertile at baseline and after 4 years of follow-up.

Lifestyle, health conditions, smoking habits and socio-demographic variables were assessed by a general questionnaire, as described in detail previously⁽¹⁰⁾.

Change in smoking status between baseline and the 4-year follow-up were categorised into two groups: no change and cessation of smoking over time.

Moreover, the baseline assessment also collected data regarding the prevalence of previous diseases such as DM or other medical conditions.

Statistical analysis

For descriptive purposes, we calculated means, standard deviations and proportions of characteristics at baseline and after 4 years of follow-up across quartiles of change in bread consumption. Moreover, we analysed the association between changes in total bread consumption and changes in different food groups through ANOVA tests.

Multivariate means and their 95% CI for anthropometric measures at baseline according to quartiles of initial consumption of total, white and whole-grain bread and increases in anthropometric measures according to quartiles of change in the consumption of total, white and whole-grain bread were calculated using generalised linear models. The lowest quartile of bread consumption at baseline and the lowest quartile of change in bread consumption were considered as the reference categories. Finally, ordinal logistic regression analyses were fit to assess the association between the change in each type of bread consumption (quartiles) and a clinically meaningful gain or loss (>2 kg) in body weight and waist circumference (>2 cm) after 4 years of follow-up. A change no higher than 2 kg or 2 cm was considered as the reference category in all the analyses.

Multivariate models included age (continuous variable), sex, intervention group, weight or waist circumference (continuous variable) and prevalence of type 2 DM at baseline, 4-year change in physical activity and smoking, and change in alcohol, energy and macronutrients intake after 4 years of follow-up (continuous variables). In additional analyses, the changes in intake of total dietary fibre and dietary fibre from



other sources than bread were also considered as possible confounders.

Finally, we repeated the multivariate analyses, adjusting the results for changes in different food groups (legumes, vegetables, fruit, fish, meat, olive oil, nuts, dairy products, cereals excluding bread and sweets) after 4 years of follow-up instead of changes in macronutrients intake.

All *P* values presented are two-tailed and statistical significance was defined *a priori* at $P < 0.05$. Data analyses were performed using SPSS 15.0 (SPSS, Inc.).

Results

The median intake of energy-adjusted total bread was 126.5 (SD 69.1) g/d, the median intake for white bread was 98.7 (SD 79.3) g/d and the median intake for whole-grain bread was 27.8 (SD 60.4) g/d. After 4 years of follow-up, the median energy-adjusted change in total bread consumption ranged from -98.72 g/d (first quartile) to 84.77 g/d (fourth quartile). The change for white bread ranged from -107.53 to 87.29 g/d and for whole-grain bread from -55.43 to 57.17 g/d.

The main characteristics of the study population at baseline and their changes over time across extreme quartiles of changes in white and whole-grain bread intake are shown in Table 1. In general, among the participants allocated to the low-fat diet group, in comparison with those allocated to the Med-Diet intervention groups, the proportion of bread consumption increased. A decrease in total energy intake and fibre intake was observed for the subjects in the highest category of change of white bread consumption, whereas an increase in total energy intake and fibre was seen for those participants in the highest category for change in whole-grain bread. Physical activity tended to decrease for participants who increased their bread consumption (for both white and whole grain).

Table 2 shows the association between changes in total bread consumption and changes in food groups after 4 years of follow-up. The participants who decreased their consumption of total bread increased their consumption of vegetables, dairy products, fish, cereals (other than bread) and sweets. Similarly, those who increased their bread consumption decreased the consumption of these groups of foods. Moreover, meat consumption decreased in the follow-up period, but this decrease was higher among those participants who increased their bread consumption.

Multivariate models

As no significant interactions between the trial intervention and changes in total, white or whole-grain bread consumption were found, all the analyses were carried out including the overall sample. In the cross-sectional analysis, we did not find a significant dose–response relationship between baseline consumption of each type of bread and anthropometric variables (Table 3).

Table 4 shows the average weight gain (in kg) and waist gain (in cm) according to quartiles of change in total, white

and whole-grain bread consumption during the 4 years of follow-up, adjusted for potential confounders.

In general, increases in total bread consumption were associated with more weight gain (mean weight change of 0.16 kg after 4 years in the lowest quartile and of 0.82 kg in the highest quartile, *P* for trend=0.019) and with more waist circumference gain (mean waist change of 1 cm after 4 years in the lowest quartile and of 2.34 cm in the highest quartile, *P* for trend <0.001). For white bread, results were very similar for weight (mean weight change of 0.14 kg after the follow-up period in the lowest quartile and of 0.90 kg in the highest quartile, *P* for trend=0.003) and for waist circumference gain (mean waist change of 1.11 cm in the lowest quartile and of 2.39 cm in the highest quartile, *P* for trend <0.001). No significant dose–response relationship was observed for change in whole-bread consumption and anthropometric measures.

The adjustment for total dietary fibre intake had little effect on these results (data not shown). Further, adjustment for dietary fibre from sources different from bread did not change the reported results (data not shown). We repeated the analyses, adjusting the results for changes in food group consumption instead of changes in macronutrients intake. We found similar results for the analysis of the association between changes in whole-grain bread and white bread consumption and changes in anthropometric variables (data not shown).

During the 4 years of follow-up, 540 subjects gained >2 kg of weight and 831 participants gained >2 cm in waist circumference. The number of participants who lost weight and decreased their waist circumference during the follow-up was 724 and 732, respectively. Multivariate OR (95% CI) for weight gain or loss (>2 kg) and for waist circumference gain or loss (>2 cm) according to quartiles of changes in bread consumption were calculated (Table 5). Changes in the consumption of any type of bread during 4 years of follow-up were not associated with the risk of gaining more than 2 cm in waist circumference or more than 2 kg in weight among the PREDIMED participants. When compared with subjects who were in the lowest quartile of change in white bread consumption, participants in the highest quartile (Q) showed a significant reduction in the odds of losing weight (>2 kg) and waist circumference (>2 cm) of 33 and 36%, respectively. Moreover, a significant inverse dose–response relationship was found for the increment in the consumption of white bread and the probability of losing weight (*P* for trend=0.021) and waist circumference (*P* for trend=0.009). The adjustment of the results for changes in food groups intake had little effect on the results regarding waist circumference gain (data not shown). However, we found an attenuation of the association between changes in white bread consumption and the possibility of losing weight (>2 kg): Q1: 1 (reference), Q2: 0.77 (0.58–1.03), Q3: 0.85 (0.63–1.16), Q4: 0.76 (0.54–1.06) (*P* for trend=0.142).

Discussion

To our knowledge, this is the first prospective cohort study to report significant associations between an increase in bread

Table 1. Main characteristics of the participants at baseline and across extreme quartiles (Q) of 4-year changes in bread consumption (Mean values and standard deviations)

Sample characteristics	Change in white bread consumption				Change in whole-grain bread consumption					
	Q1 (n 553)		Q4 (n 553)		Q1 (n 553)		Q4 (n 553)			
Variables at baseline										
Total bread consumption (g/d)	126.5	69.1	174.2	68.9	97.7	72.4	136.7	66.4	117.9	79.0
White bread consumption (g/d)	98.7	79.3	168.9	74.9	45.3	63.5	54.7	70.2	107.3	87.0
Whole-grain bread consumption (g/d)	27.8	60.4	5.3	26.7	52.4	87.3	82.0	87.6	10.6	31.5
Sex (% men)	43.2		48.5		45.8		36.2		43.2	
Age (years)	67.2	5.8	67.2	5.7	66.9	5.7	67	5.7	67.1	5.8
BMI (kg/m ²)	29.6	3.5	29.5	3.6	29.5	3.5	29.7	3.5	29.7	3.6
Intervention group (%)		44.9		47.7		44.1		47.9		45.6
Med-diet olive oil (%)		32.6		32.9		30.6		32.9		30.4
Med-diet nuts (%)		22.5		19.3		25.3		19.2		24.4
Low-fat diet										
CVD (no CHD or stroke) (%)		4.1		4.2		2.9		4.9		3.6
Hypertension (%)		81.9		80.3		79		80.7		82.3
Hyperlipidaemia (%)		67.9		67.1		66.9		68		68.7
Diabetes mellitus (%)		48.5		47.9		53.2		53.9		48.8
Energy intake (kJ/d)	9573.4	2303.7	9979.2	2325.0	10 030.7	2318.7	8846.7	2285.2	10 434.0	2755.8
SFA (g/d)	25.5	5.6	23.8	5.5	26.7	6.0	25.2	5.1	25.7	6.1
PUFA (g/d)	16.1	5.2	14.7	4.7	17.1	5.6	16.1	4.8	16.0	6.0
MUFA (g/d)	51.0	10.8	47.1	10.3	54.4	11.2	50.7	10.3	51.0	11.6
Total fibre (g/d)	24.8	7.22	23.4	5.6	26.5	8.7	28.7	8.2	23.9	6.6
Proteins (g/d)	16.10	5.28	14.71	4.77	17.1	5.65	16.20	4.81	16.06	6.00
Carbohydrates (g/d)	234.1	40.2	220.6	43.6	261.0	35.42	235.3	51.8	232.7	37.5
Alcohol intake (g/d)	9.8	15.5	9.5	14.8	10.9	17.4	7.2	12.8	10.3	16.7
METs total (last year)										
kcal/d	253.78	236.83	253.4	214.8	265.9	270.8	240.9	239.6	257.0	236.1
kJ/d	1061.8	990.9	1060.2	898.7	1112.5	1133.0	1007.9	1002.5	1075.3	987.8
Smoking status (%)										
Smoker		12.9		15.0		12.5		10.3		11.6
Ex-smoker		24.5		25.9		25.3		19.5		25.8
Never smoker		62.6		59.1		64.2		70.2		62.6
Variables (changes at 4 years of follow-up)*										
Total energy intake (kJ/d)	-259.4	2691.9	-135.14	2795.3	-715.8	3142.6	828.8	3268.9	1377.7	3184.8
Proteins (g/d)	-2.9	22.3	-2.9	23.6	-6.2	23.6	1.4	24.8	-5.4	23.4
Carbohydrates (g/d)	-10.8	43.6	0.42	43.6	-30.8	43.5	-16.5	50.8	-9.5	40.2
SFA (g/d)	-2.1	7.6	1.2	7.4	-4.8	7.4	-0.2	7.9	-3.6	7.7
PUFA (g/d)	0.2	7.1	2.7	7.2	-1.6	7.1	1.48	7.3	-0.7	7.4
MUFA (g/d)	2.1	16.5	9	14.7	-4.1	17.3	4.2	16.7	-0.5	17
Total fibre (g/d)	0.85	9.52	5.3	9.5	-2.8	10	-2.2	10.9	4.4	10.5
Alcohol intake	-1.34	10.90	0.33	11.27	-3.40	12.25	0.30	9.88	-2.83	12.21
Smoking status (% of no change)		95.7		94.4		96.2		95.8		96.7
Physical activity (%)										
Increased		24.9		28.9		24.7		27.7		25.5
Decreased		24.8		20.6		27.6		23.9		25.7

Bread consumption and adiposity

Med-diet, Mediterranean-type diet; METs, metabolic equivalents.
 * Change from baseline is presented (e.g. negative values represent a decrease in the particular characteristic).

Table 2. Changes in food group consumption according to change in total bread consumption (Mean values, standard deviations and 95% confidence intervals)

Food groups	Baseline intake (g/d)		Change at 4 years of follow-up (g/d)		Changes in total bread consumption						P (ANOVA)
	Mean	SD	Mean	SD	Q1 (-98.72 g)*		Q2-Q3 (-8.39 g)†		Q4 (84.77 g)‡		
					Mean	95% CI	Mean	95% CI	Mean	95% CI	
Legumes	18.9	10.0	2.6	11.8	4.41	3.42, 5.40	2.43	1.78, 3.08	1.11	0.02, 2.21	<0.001
Vegetables	328.0	137.5	-3.9	154.9	38.11	25.72, 50.50	-3.82	-12.94, 5.29	-46.06	-58.64, -33.47	<0.001
Fruits	351.6	187.0	51.3	216.1	98.81	79.85, 117.78	48.74	36.44, 61.03	8.89	-8.72, 26.51	<0.001
Fish	101.2	51.0	2.3	53.8	14.80	10.95, 18.65	2.72	-0.17, 5.62	-11.05	-16.52, 5.58	<0.001
Meat	134.8	50.9	-12.7	54.0	-1.36	-5.90, 3.16	-12.00	-14.91, -9.09	-25.42	-30.42, -20.40	<0.001
Olive oil	42.7	16.7	7.0	20.6	10.07	8.33, 11.80	7.75	6.57, 8.94	2.4	0.66, 4.15	<0.001
Nuts	11.0	13.1	4.5	17.7	7.59	5.90, 9.28	4.76	3.84, 5.69	0.86	-0.67, 2.40	<0.001
Dairy products	384.4	214.5	-17.0	213.9	32.90	14.56, 51.23	-13.48	-25.35, -1.61	-73.93	-92.29, 55.57	<0.001
Cereals§	20.4	15.4	-0.7	16.7	1.84	0.54, 3.14	-1.01	-2.01, -0.02	-3.00	-4.43, -1.56	<0.001
Sweets	32.0	30.6	-5.2	33.0	3.32	0.66, 5.98	-5.55	-7.36, -3.74	-13.15	-16.21, -10.09	<0.001

Q, quartile.

* Decrease.

† No change.

‡ Increase.

§ Cereals excluding bread.

consumption (in g/d) and weight or waist circumference gains in a sample of participants at high cardiovascular risk (PRE-DIMED trial). The present results suggest a dose-response relationship between the increase in white bread consumption and weight or waist circumference gain. Moreover, gaining weight (>2 kg) and gaining waist circumference (>2 cm) during follow-up were not associated with an increase in bread consumption, but losing weight and waist circumference were associated with a decrease in white bread consumption. In addition, when changes in the consumption of whole-grain bread were assessed, we did not find any significant relationship with anthropometric changes.

The large sample size and the thorough information collected allowed us to comprehensively adjust for potential confounding, including both dietary and non-dietary confounders. Nonetheless, the present study has some limitations. The only source of information on food consumption was a self-administered FFQ. FFQ are known to contain measurement errors. Nevertheless, Fernández-Ballart *et al.* have recently published a study to assess the reproducibility and relative validity of the self-administered FFQ used in the PREDIMED study. They concluded that this FFQ had good reproducibility and a relative validity similar to those FFQ used in other prospective studies⁽¹⁵⁾. Anyway, the most likely effect of the measurement error derived from assessing dietary habits using FFQ would have been to attenuate the true association between bread consumption and adiposity, given the prospective nature of the present study.

Because many dietary factors may induce metabolic alterations within a relatively short latency period, we assessed changes in bread that were concurrent with weight or waist circumference gain^(13,17). The present study design may limit the drawing of causal inferences. Confounding also poses a challenge in the study of bread consumption, as increased consumption may be a marker for changes in other health behaviours. However, we adjusted the regression models for changes in several other lifestyle and dietary behaviours, including smoking, physical activity and fat consumption, with only a modest attenuation of the relation between bread consumption change and weight and waist circumference gains.

In the present study, the adjustment for total dietary fibre or for fibre from sources different from bread did not change the results. Thus, the difference between white and whole-grain bread would not be attributed to the increased fibre content of whole-grain bread. Nevertheless, Estruch *et al.*⁽¹⁰⁾ assessed the effects of a 3-month change in dietary fibre intake on cardiovascular risk factors in 772 subjects from the PREDIMED study, observing that body weight, waist circumference and mean systolic and diastolic blood pressure decreased across quintiles of fibre intake ($P < 0.005$; all).

We considered it interesting to investigate by which food groups bread consumption was replaced. It is really remarkable that individuals who decreased their bread consumption increased their fruit, vegetable, fish and olive oil consumption. Also, individuals who increased their bread consumption decreased their dairy intake. These changes in consumption could also be a consequence of the

Table 3. Baseline weight, waist circumference and BMI according to quartiles (Q) of initial bread consumption* (Mean values and 95 % confidence intervals)

	Q1		Q2		Q3		Q4		P for trend
	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	
Energy-adjusted total bread consumption									
n		553		553		554		553	
Median		54.54		99.31		139.65		200.34	
Weight (kg)	76.34	75.37, 77.30	76.38	75.49, 77.27	76.62	75.73, 77.51	75.69	74.75, 76.64	0.378
Waist (cm)	100.07	99.17, 100.96	100.26	99.44, 101.09	99.52	98.69, 100.35	99.58	98.70, 100.46	0.291
BMI (kg/m ²)	29.65	29.35, 30.03	29.61	29.30, 29.92	29.46	29.14, 29.77	29.25	28.92, 29.58	0.071
Energy-adjusted white bread consumption									
n		553		553		554		553	
Median		13.18		70.48		115.45		187.38	
Weight (kg)	76.45	75.43, 77.48	75.54	75.65, 77.44	75.95	75.04, 76.85	76.02	75.03, 77.01	0.882
Waist (cm)	99.28	98.43, 100.13	100.55	99.72, 101.38	99.65	98.82, 100.48	99.90	99.03, 100.76	0.538
BMI (kg/m ²)	29.36	29.04, 29.68	29.64	29.33, 29.95	29.50	29.19, 29.81	29.45	28.13, 29.78	0.793
Energy-adjusted whole-grain bread consumption									
n		553		553		554		553	
Median		0		0.47		5.13		78.45	
Weight (kg)	76.60	75.47, 77.73	75.88	75.00, 76.75	76.31	75.25, 77.38	76.21	75.30, 77.11	0.964
Waist (cm)	100.16	99.11, 101.21	99.89	99.08, 100.71	100.20	99.21, 101.19	99.17	98.33, 100.01	0.050
BMI (kg/m ²)	29.53	29.14, 29.93	29.39	29.08, 29.69	29.80	29.43, 30.17	29.25	28.94, 29.57	0.063

* Multivariate means calculated using generalised linear models. The means were adjusted for age, sex, intervention group, prevalence of diabetes mellitus at baseline, energy, alcohol, proteins, SFA, PUFA, MUFA, smoking and physical activity.

intervention with the Mediterranean diet (more olive oil, fruits, vegetables and fish) or with the low-fat diet (more bread). Although these associations could suggest that changes in weight would be explained by dairy product and vegetable consumption changes, the additional adjustment for these kinds of foods, using the same analysis carried out by Mozaffarian *et al.*⁽¹⁹⁾, did not modify the reported results. Only the results for the association between the change in white bread consumption and the possibility of losing weight (>2 kg) were attenuated after adjusting the results

for food groups instead of macronutrients. Although it seems to be an interesting result, we can not exclude the possibility of a statistical overadjustment of the present results.

To our knowledge, only one other prospective study, the European Prospective Investigation into Cancer and Nutrition study, has analysed the relationship between changes in bread consumption and waist circumference gain. Similar results to those found in the present analysis were observed. Whereas the authors failed to find a significant association for the change in whole-grain bread consumption, they reported a

Table 4. Changes in weight and waist circumference according to quartiles (Q) of change in bread consumption (Mean values and 95 % confidence intervals)

	Q1		Q2		Q3		Q4		P for trend
	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	Mean	95 % CI	
Change in total bread consumption									
n		553		553		554		553	
Median		-98.72		-29.98		13.53		84.77	
Weight change (kg)*	0.16	-1.56, 1.89	0.61	-1.12, 2.34	0.58	-1.14, 2.31	0.82	-0.91, 2.55	0.019
Waist change (cm)†	1.00	-1.27, 3.28	1.90	-0.38, 4.20	1.93	-0.34, 4.22	2.34	-0.05, 4.64	<0.001
Change in white bread consumption									
n		553		553		554		553	
Median		-107.53		-31.05		15.72		87.29	
Weight change (kg)*	0.14	-1.57, 1.87	0.46	-1.26, 2.19	0.54	-1.17, 2.27	0.90	-0.82, 2.63	0.003
Waist change (cm)†	1.11	-1.17, 3.40	1.69	-0.59, 3.98	1.73	-0.54, 4.02	2.39	-0.09, 4.68	<0.001
Change in whole-grain bread consumption									
n		553		553		554		553	
Median		-55.43		-2.60		2.51		57.17	
Weight change (kg)*	0.75	-0.98, 2.48	0.74	-0.98, 2.48	0.18	-1.53, 1.90	0.62	-1.10, 2.35	0.738
Waist change (cm)†	1.98	-0.31, 4.29	1.88	-0.41, 4.18	1.26	-1.01, 3.54	2.14	-0.14, 4.44	0.846

* Multivariate means calculated using generalised linear models. The means were adjusted for age, sex, intervention group, weight at baseline, prevalence of diabetes mellitus at baseline, change in energy, alcohol, proteins, SFA, PUFA and MUFA and change in smoking and physical activity.

† Multivariate means calculated using generalised linear models. The means were adjusted for age, sex, intervention group, waist circumference at baseline, prevalence of diabetes mellitus at baseline, change in energy, alcohol, proteins, SFA, PUFA and MUFA and change in smoking and physical activity.

Table 5. Risk of gaining or losing >2 kg in weight or 2 cm in waist circumference (Odds ratios and 95 % confidence intervals)

	Q1	Q2	Q3	Q4	<i>P</i> for trend
Change in white bread consumption					
Weight gain*					0.295
<i>n</i>	352	379	372	386	
Cases	126	132	139	143	
OR*	1	0.98	1.11	1.16	
95 % CI	Ref.	0.71, 1.35	0.80, 1.54	0.83, 1.62	
Waist circumference gain†					0.780
<i>n</i>	344	372	375	390	
Cases	193	209	198	231	
OR	1	0.96	0.81	1.07	
95 % CI	Ref.	0.71, 1.31	0.59, 1.11	0.77, 1.48	
Weight lost*					0.021
<i>n</i>	427	421	415	410	
Cases	201	174	182	167	
OR	1	0.71	0.77	0.67	
95 % CI	Ref.	0.53, 0.94	0.57, 1.03	0.49, 0.91	
Waist circumference lost†					0.009
<i>n</i>	360	344	356	322	
Cases	209	181	179	163	
OR	1	0.74	0.66	0.64	
95 % CI	Ref.	0.53, 1.02	0.47, 0.91	0.45, 0.90	
Change in whole-grain bread consumption					
Weight gain*					0.724
<i>n</i>	380	382	354	373	
Cases	138	147	114	141	
OR	1	1.08	0.79	1.03	
95 % CI	Ref.	0.80, 1.45	0.56, 1.10	0.75, 1.42	
Waist circumference gain†					0.692
<i>n</i>	372	375	355	379	
Cases	233	210	162	226	
OR	1	0.78	0.53	0.90	
95 % CI	Ref.	0.58, 1.06	0.38, 0.73	0.65, 1.23	
Weight lost*					0.436
<i>n</i>	415	406	440	412	
Cases	173	171	200	180	
OR	1	1.06	1.22	1.13	
95 % CI	Ref.	0.80, 1.41	0.90, 1.64	0.84, 1.53	
Waist circumference lost†					0.493
<i>n</i>	320	343	392	327	
Cases	181	178	199	174	
OR	1	0.87	0.79	0.87	
95 % CI	Ref.	0.63, 1.129	0.57, 1.09	0.62, 1.23	

Q, quartile; Ref., reference.

* Multivariate OR and 95 % CI calculated using ordinal logistic regressions. The OR were adjusted for age, sex, intervention group, weight at baseline, prevalence of diabetes mellitus at baseline, change in energy, alcohol, proteins, SFA, PUFA and MUFA intake and change in smoking and physical activity.

† Multivariate OR and 95 % CI calculated using ordinal logistic regressions. The OR were adjusted for age, sex, intervention group, waist circumference at baseline, prevalence of diabetes mellitus at baseline, change in energy, alcohol, proteins, SFA, PUFA and MUFA intake and change in smoking and physical activity.

direct association between the increase in white bread consumption and annual visceral adiposity gain, independent from BMI⁽²⁰⁾. Moreover, we have recently reviewed this relationship by groups of foods in which bread consumption was also included⁽²¹⁾. There are twelve prospective studies^(22–33) that studied several groups of food items in which bread consumption was also included. Thus, we cannot know in what proportion the bread consumption (and not just cereals) influenced weight gain. In four of the mentioned prospective studies^(22,27,32,33), the group of food items that included bread did not differentiate between the effects of bread type, while the other eight studies^(23–26,28–31) observed differences between groups that included white or whole-grain bread.

No unfavourable effects on ponderal status were found in the studies that analysed groups of food items that included whole-grain bread^(23,26,30). Only four studies observed an unfavourable relationship for groups that included white bread: three in waist circumference alone^(25,28,31) and one in weight gain in which the group that included whole-grain bread demonstrated the contrary effect⁽²⁴⁾.

The rest of the studies did not find any significant association between the type of bread consumed and changes in anthropometric measures^(22,29) or they found a favourable influence in groups that included both types of bread^(27,32,33).

There are some controlled intervention studies^(34–37) examining the effect of diets (in which bread consumption was also

included) on the reduction of weight or weight maintenance over the long term. The study of McAuley *et al.*⁽³⁶⁾ showed that diets high in fats and high in proteins produce greater weight loss and reduction in waist circumference than diets high in carbohydrates (rich in bread), although other intervention studies indicated that the bread content of the diet did not influence variation in body weight^(34,35,37).

Similar to other mentioned studies, the present results also suggest that the different compositions of whole-grain and white bread have different influences on body weight and abdominal fat. Perhaps, factors such as postprandial insulin responses, gastric emptying after consuming a high-GI meal and other factors could be implicated in the potential variations in effects of different cereal types on adiposity⁽⁹⁾. The present study population has a high prevalence of CVD risk factors, like type 2 DM, hypertension, hyperlipidaemia, overweight/obesity and low levels of HDL-cholesterol⁽¹¹⁾, which suggests an increased insulin resistance status in most of the participants in the PREDIMED trial. Thus, the high GI of white bread, compared with whole-grain bread, could be implicated in the different postprandial insulin responses and their different effects on body composition.

Romaguera *et al.*⁽³⁸⁾ suggested that a diet low in GI and energy density may prevent visceral adiposity, defined as prospective changes in waist circumference/BMI. A study⁽³⁹⁾ performed on a sample of 3734 Italian children showed that dietary GI is an independent determinant of body fat distribution and of total adiposity in children. Other studies have suggested that a food pattern with a high GI may promote the development of both general and abdominal obesity⁽⁴⁰⁾.

Finally, it is important to remark that the consumption of bread, which has been part of the traditional Spanish diet, has continued to fall in Spain and in the rest of the world⁽⁴¹⁾. However, although bread consumption has been decreasing over the past decades, the world epidemic of obesity has been increasing⁽¹⁾.

To generalise the results of the present study to the general population, the special characteristics of the subjects in the study, a high cardiovascular risk and a high percentage of excess of weight, should be taken into account. A weakness of the study could be to have excluded the variable of dieting as a confounder. However, as adjustments for energy intake were made, in principle, the confounding effect of dieting may be clearly attenuated⁽⁴²⁾.

Although the number of participants analysed in the present study is lower than the number of participants recruited in the PREDIMED trial, we consider that a selection bias is highly improbable. The main characteristics of the excluded participants did not significantly differ from those of the participants followed up for the 4-year period.

In summary, the results of the present study show that decreasing total and white bread and maintaining whole-grain bread consumption in the setting of a Mediterranean-style diet could help in reducing weight and abdominal fat gain.

The Mediterranean diet is characterised by high consumption of whole-grain bread, fruits, vegetables or legumes with high fibre content. Thus, if white bread consumption has to be reduced, it should be replaced by these Mediterranean

components. However, the study also suggests that clinically relevant increases in weight and abdominal fat are not attributed to an increase in bread consumption. Other studies are needed to be carried out in other population groups and countries.

Acknowledgements

The authors thank the participants of the trial for their enthusiastic collaboration and the PREDIMED personnel for excellent assistance with all aspects of the trial. RETIC PREDIMED RD06/0045 and CIBEROBN are an initiative of the Instituto de Salud Carlos III. The authors are also grateful for grant support by the Spanish Minister of Science and Innovation (FI070473) and Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC06-2007) and Agencia Canaria de Investigación, Innovación y Sociedad de la de la Información (Gobierno de Canarias; PI 2007/050). All authors have read and agreed with the present version of the manuscript and no author has any conflict of interest to declare. Authors' contributions to the paper: I. B.-C. and A. S.-V. prepared the manuscript and wrote the paper with important input and feedback from all co-authors; A. S.-V. conducted the analysis; L. S.-M. had the primary responsibility for the final content; I. B.-C., A. S.-V., R. E., M. A. M.-G., D. C., J. S.-S., M. I. C., H. S., J. A.-P., J. Q., R. M. L.-R., E. R., F. A., M. F., J. L., M. A. M., E. G.-G., J. T., X. P., V. R.-G., M. P. P.-B. and L. S.-M. participated in the design and execution of the study and contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

References

1. WHO (2000) *Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation. WHO Technical Report Series* no. 894. Geneva: WHO.
2. Swinburn BA, Caterson I, Seidel JC, *et al.* (2004) Diet, nutrition and the prevention of excess weight gain and obesity. *Pub Health Nutr* **7**, 123–146.
3. Beunza JJ, Toledo E, Hu FB, *et al.* (2010) Adherence, the Mediterranean diet, long-term weight change, and incident overweight or obesity: the Seguimiento Universidad de Navarra (SUN) cohort. *Am J Clin Nutr* **92**, 1–8.
4. Seidell JC, Perusse L, Despres JP, *et al.* (2001) Waist and hip circumferences have independent and opposite effects on cardiovascular disease risk factors: the Quebec Family Study. *Am J Clin Nutr* **74**, 315–321.
5. Janssen I, Katzmarzyk PT & Ross R (2004) Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* **79**, 379–384.
6. Gaesser GA (2007) Carbohydrate quantity and quality in relation, body mass index. *J Am Diet Assoc* **107**, 1768–1780.
7. Bradlee ML, Singer MR, Qureshi MM, *et al.* (2010) Food group intake and central obesity among children and adolescents in the Third National Health and Nutrition Examination Survey (NHANES III). *Public Health Nutr* **13**, 797–805.
8. Williams PG, Grafenauer SJ & O'Shea JE (2008) Cereal grains, legumes, and weight management: a comprehensive review of the scientific evidence. *Nut Rev* **66**, 171–182.

9. Juntunen KS, Niskanen LK, Liukkonen KH, *et al.* (2002) Postprandial glucose, insulin, and incretin responses, grain products in healthy subjects. *Am J Clin Nutr* **75**, 254–262.
10. Estruch R, Martínez-González MA, Corella D, *et al.* (2006) PREDIMED study investigators effects of a Mediterranean-style diet on cardiovascular risk factors: a randomised trial. *Ann Intern Med* **145**, 1–11.
11. Martínez-González MA, Corella D, Salas-Salvadó J, *et al.* (2012) Cohort profile: design and methods of the PREDIMED study. *Int J Epidemiol* **41**, 377–385.
12. Fito M, Guxens M, Corella D, *et al.* (2007) Effect of a traditional Mediterranean diet on lipoprotein oxidation: a randomized controlled trial. *Arch Intern Med* **167**, 1195–1203.
13. Willett WC (1998) Issues in analysis and presentation of dietary data. In *Nutritional Epidemiology*. New York: Oxford University Press.
14. WMA (2004) World Medical Association Declaration of Helsinki, Tokyo.
15. Fernández-Ballart JD, Piñol JL, Zazpe I, *et al.* (2010) Relative validity of a semi-quantitative food-frequency questionnaire in an elderly Mediterranean population of Spain. *Br J Nutr* **103**, 1808–1816.
16. Moreiras O, Carvajal A & Cabrera L (2005) *Tablas de composición de alimentos (Food Composition Tables)*, 9th ed. Madrid: Ediciones Piramide.
17. Willett WC, Howe GR & Kushi LH (1997) Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr* **65**, 1220S–1228S, discussion 1229S–1231S.
18. Elosua R, Garcia M, Aguilar A, *et al.* (2000) Validation of the Minnesota leisure time physical activity questionnaire in Spanish women. Investigators of the MARATDON Group. *Med Sci Sports Exerc* **32**, 1431–1437.
19. Mozaffarian D, Hao T, Rimm EB, *et al.* (2011) Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med* **364**, 25, 2392–2404.
20. Romaguera D, Ångquist L, Du H, *et al.* (2011) Food composition of the diet in relation, changes in waist circumference adjusted for body mass index. *PLoS One* **6**, e23384.
21. Bautista I & Serra L (2012) Bread consumption and weight management: evidence from epidemiological studies. *Nutr Rev* **70**, 218–233.
22. Schulz M, Kroke A, Liese AD, *et al.* (2002) Food groups as predictors for short-term weight changes in men and women of the EPIC-Potsdam cohort. *J Nutr* **132**, 1335–1340.
23. Schulz M, Nöthlings U, Hoffmann K, *et al.* (2005) Identification of a food pattern characterized by high-fiber and low-fat food choices associated with low prospective weight change in the EPIC-Potsdam Cohort. *J Nutr* **135**, 1183–1189.
24. Liu S, Willett WC, Manson JE, *et al.* (2003) Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. *Am J Clin Nutr* **78**, 920–927.
25. Newby PK, Muller D, Hallfrisch J, *et al.* (2003) Dietary patterns and changes in body mass index and waist circumference in adults. *Am J Clin Nutr* **77**, 1417–1425.
26. Newby PK, Muller D, Hallfrisch J, *et al.* (2004) Food patterns measured by factor analysis and anthropometric changes in adults. *Am J Clin Nutr* **80**, 504–513.
27. Newby PK, Peterson KE, Berkey CS, *et al.* (2003) Dietary composition and weight change among low-income pre-school children. *Arch Pediatr Adolesc Med* **157**, 759–764.
28. Halkjaer J, Sørensen TI, Tjønneland A, *et al.* (2004) Food and drinking patterns as predictors of 6-year BMI-adjusted changes in waist circumference. *Br J Nutr* **92**, 735–748.
29. Togo P, Osler M, Sørensen TIA, *et al.* (2004) A longitudinal study of food intake patterns and obesity in adult Danish men and women. *Int J Obes Relat Metab Disord* **28**, 583–593.
30. Koh-Banerjee P, Franz M, Sampson L, *et al.* (2004) Changes in whole-grain, bran, and cereal fiber consumption in relation, 8-y weight gain among men. *Am J Clin Nutr* **80**, 1237–1245.
31. Halkjaer J, Tjønneland A, Thomsen BL, *et al.* (2006) Intake of macronutrients as predictors of 5-y changes in waist circumference. *Am J Clin Nutr* **84**, 789–797.
32. Mendez MA, Popkin BM, Jakszyn P, *et al.* (2006) Adherence, a Mediterranean diet is associated with reduced 3-year incidence of obesity. *J Nutr* **136**, 2934–2938.
33. Stamler J & Dolecek TA (1997) Relation of food and nutrient intakes, body mass in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. *Am J Clin Nutr* **65**, 1 Suppl., 366S–373S.
34. Mickelsen O, Makdani DD, Cotton RH, *et al.* (1979) Effects of a high fiber bread diet on weight loss in college-age males. *Am J Clin Nutr* **32**, 1703–1709.
35. Lean ME, Han TS, Prvan T, *et al.* (1997) Weight loss with high and low carbohydrate 1200 kcal diets in free living women. *Eur J Clin Nutr* **51**, 243–248.
36. McAuley KA, Hopkins CM, Smith KJ, *et al.* (2005) Comparison of high-fat and high-protein diets with a high-carbohydrate diet in insulin-resistant obese women. *Diabetologia* **48**, 8–16.
37. Aston LM, Stokes CS & Jebb SA (2008) No effect of a diet with a reduced glycaemic index on satiety, energy intake and body weight in overweight and obese women. *Int J Obes (Lond)* **32**, 160–165.
38. Romaguera D, Ångquist L, Du H, *et al.* (2010) Dietary determinants of changes in waist circumference adjusted for body mass index – a proxy measure of visceral adiposity. *PLoS One* **5**, e11588.
39. Barba G, Sieri S, Dello-Russo M, *et al.* on behalf of the ARCA Project Study Group (2012) Glycemic index and body fat distribution in children: the results of the ARCA project. *Nutr Metab Cardiovasc Dis* **22**, 28–34.
40. Ebbeling CB & Ludwig DS (2001) Treating obesity in youth: should dietary glycemic load be a consideration? *Adv Pediatr* **48**, 179–212.
41. Serra-Majem L & Raido Quintana B (2010) Consumo de pan en el mundo y en España (Bread consumption in the world and in Spain). In *Libro Blanco del Pan (Bread's White Book)*, pp. 63–77 [A Gil and L Serra-Majem, editors]. Madrid: Ed Med Panamericana.
42. Savage JS, Hoffman L & Birch LL (2009) Dieting, restraint, and disinhibition predict women's weight change over 6y. *Am J Clin Nutr* **90**, 33–40.