



VIEWPOINT

Whole grain intake in relation to body weight: From epidemiological evidence to clinical trials

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Abstract This viewpoint aims to 1) review the available scientific literature on the relationship between whole grain consumption and body weight regulation; 2) evaluate the potential mechanisms whereby whole grain intake may help reduce overweight and 3) try to understand why epidemiological studies and clinical trials provide diverging results on this topic. All the prospective epidemiological studies demonstrate that a higher intake of whole grains is associated with lower BMI and body weight gain. However, these results do not clarify whether whole grain consumption is simply a marker of a healthier lifestyle or a factor favoring “per se” lower body weight. Habitual whole grain consumption seems to cause lower body weight by multiple mechanisms such as lower energy density of whole grain based products, lower glycemic index, fermentation of non digestible carbohydrates (satiety signals) and finally by modulating intestinal microflora. In contrast with epidemiological evidence, the results of few clinical trials do not confirm that a whole grain low-calorie diet is more effective in reducing body weight than a refined cereal diet, but their results may have been affected by small sample size or short duration of the intervention. Therefore, further intervention studies with adequate methodology are needed to clarify this question. For the time being, whole grain consumption can be recommended as one of the features of the diet that may help control body weight but also because is associated with a lower risk to develop type 2 diabetes, cardiovascular diseases and cancer.

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Introduction

A large body of evidence from observational studies has shown that the habitual consumption of whole grain foods is consistently associated with reduced risk of developing type 2 diabetes and cardiovascular diseases (CVD) [1–3]. Increased body weight is a common condition associated with insulin resistance, a precursor of type 2 diabetes (T2DM) and CVD [4,5]. Results of cohort prospective studies have reported a relationship between whole grain food consumption and lower body mass index (BMI) and/or abdominal fat, suggesting that whole grain consumption may play a role in body weight regulation, thus improving the metabolic abnormalities associated with the development of type 2 diabetes and CVD. In fact, whole grain products are less energy dense and more satiating than refined cereal products, and, if consumed regularly, seem to help reduce body weight, thus improving insulin sensitivity, blood pressure, lipid metabolism and inflammation, with overall beneficial effects on the cardiovascular risk profile [6]. Based on the evidence that dietary patterns high in whole grain foods and fiber are beneficial for human health, and considering that whole grain food intake is very low in many populations – on average one serving per day in US adults [7] and even less in British adults [8] – dietary guidelines for Americans recommend to consume at least half of the daily cereal food intake as whole grain [9]. The potential public health benefits from the inclusion of whole grains in the diet have been underlined by nutritional recommendations in the USA [10], UK and Sweden [11] as a useful tool to implement an attractive, food-based dietary strategy targeting the whole population.

In contrast with consistent epidemiological evidence associating whole grain consumption with improved health, the results of clinical trials evaluating whether the inclusion of whole grains in a restricted energy diet helps control body weight, have surprisingly failed to demonstrate a higher effectiveness of whole grain diets compared with a diet containing only refined cereals.

Therefore, the aims of this viewpoint are to 1) review the available scientific literature on the relationship between whole grain consumption and body weight regulation; 2) evaluate the potential mechanisms by which whole grain intake may help reduce overweight and 3) try to understand why results of cross-sectional and prospective epidemiological studies and of clinical trials have produced diverging evidence on this topic.

Evidence from epidemiological studies

Cross-sectional studies

The main characteristics of cross-sectional and prospective studies, the latter reporting the cross-sectional evaluation at baseline, are shown in Table 1 and the Appendix: four studies were performed in adult women, three in a group of healthy women [12–14] and one in a group of women with diabetes [15], two in healthy adult men [16,17], five in healthy adults of both genders [18–22] and one in healthy adolescents of both genders [23]. All studies show that high whole grain intake is associated with significantly lower BMI and waist circumference in both men and women. Only in

Table 1 Relationship between habitual whole grain consumption and body mass index.

Studies	BMI
Framingham Offspring study [18]	↓
ARIC Study [19]	↔
Minneapolis Students Study [23]	↓
Nurses' Health Study [12]	↓
Health Professionals Follow-up Study [16]	↓(?)
Swedish Mammograph Cohort [13]	↓(?)
Physicians' Health Study [17]	↓
Nurses' Health Study (Diabetic women) [15]	↓(?)
Boston MA Study [20]	↓
Baltimore Longitudinal Study of Aging [21]	↓
National Health and Nutrition Survey [14]	↓
Trial examining the effect of Vit.K [22]	↓(*)

↓ inverse relationship; ↔ no relationship; (?) statistical significance not reported; (*) of borderline statistical significance ([Methodological details in the online appendix](#)).

two studies was the association between whole grain and BMI of borderline statistical significance [22] or not significant [19]. However, in these studies individuals with the highest whole grain intake had significantly lower waist to hip ratio and percentage of fat mass and trunk fat mass, suggesting that even in the absence of a significant relationship with body weight, whole grain consumers had less central adiposity. In all studies the difference in BMI among subjects in the highest category of whole grain intake compared with those in the lowest category ranged between 1.0 and 2.5 kg/m².

Noteworthy, in these studies the adjustment for confounding factors, like dietary variables and physical activity attenuated the association between whole grain and BMI, which nevertheless remained significant. No association between refined cereals and BMI was observed in Newby's and McKeown's studies [21,22].

Thus, current data from cross-sectional studies consistently demonstrate that whole grain intake is associated with lower body weight; however, the cross-sectional nature of these studies does not allow us to infer any causality between dietary exposures and body weight regulation, which can instead be demonstrated by prospective studies.

Prospective studies

The Nurses' Health Study [12], the Health Professionals Follow-up Study [16] and the Physicians' Health Study [17] provided information regarding habitual whole grain consumption and body weight gain over a period of 8–12 years (Table 2).

In the Nurses' Health Study [12] the associations between the intakes of whole grain, fiber or refined grain based products, and weight gain over time were examined in a large number of women. In general, increases in the intake of whole grains were associated with 0.39 kg less weight gain over 12 years of follow-up (mean weight gain 4.51 kg in the lowest quintile and 4.12 kg in the highest quintile); this difference although small was statistically significant (p per trend <0.0001). Women who had the greatest increase in dietary fiber intake gained an average

Table 2 Multivariate adjusted average weight gain (kg) according to quintile (Q) or category of change in whole grain (WG) intake from baseline to follow-up in prospective epidemiological studies.

Studies	Participants sex and age (range)	Country	Dietary assessment	Follow-up (yrs)	Changes in WG intake (servings or g/d)	Average weight gain (kg)	Difference in weight gain (kg)	P for trend
Liu et al., 2003 [12]	74 091 F (38–63 yrs)	USA NHS	FFQ	12	Q1 (WG -0.59 s/d) Q5 (WG 0.90 s/d)	4.51 4.12	0.39	<0.0001
Koh-Banerjee et al., 2004 [16]	27 082 M (40–75 yrs)	USA HPFS	FFQ	8	Q1 (WG -14.2 g/d) Q5 (WG 23.8 g/d)	1.24 0.75	0.49	<0.0001
Bazzano et al., 2005 [17]	17 881 M (40–84 yrs)	USA PHS	SFFQ	8	Q1 (WG Rarely) Q4 (WG ≥ 1 s/d)	1.55 1.13	0.42	<0.003

NHS = Nurses' Health Study; HPFS = Health Professionals Follow-up Study; PHS = Physicians' Health Study; s/d = serving/day.

1.52 kg less than those who had the smallest intake, independently of body weight at baseline, age and changes in physical activity, smoking habits and alcohol consumption. After further correction for measurement errors in fiber intake variations, a 12 g increase in dietary fiber intake was associated with 3.5 kg less weight gain during the 12 year follow-up. Therefore, in this cohort of women, the highest consumption of whole grain foods or cereal fiber reduced the risk to become obese and/or to gain weight by 49%, compared to women with the lowest intake.

Similar results were reported in two studies performed in men [16,17]. In the Health Professionals Follow-up Study, which lasted over 8 years, a lower weight gain by 0.49 kg was associated with every 40g/day increment in whole grain intake, and after correction for measurement error, it was lower by 1.1 kg [16]. Dietary fiber was inversely related to weight gain independent of whole grain. The men in the lowest quintile of fiber change gained 1.40 kg, whereas those in the highest quintile of change gained only 0.39 kg (p per trend $p < 0.0001$). For every 20 g/d increase in dietary fiber, weight gain was reduced by 1.18 kg; however, considering only cereal fiber, weight gain was reduced by 0.81 kg for every 20 g/d increment in cereal fiber. Similar results in the reduction of body weight gain over 8 years of follow-up were achieved in men participating in the Physicians' Health Study who consumed ≥ 1 serving per day of whole grain breakfast cereals compared to those who consumed it rarely [17]. Therefore, the analysis of data from prospective studies clearly highlights that an increase in whole grain consumption is associated, on average, with a reduction in body weight gain ranging between 0.39 and 0.49 kg over 8–12 years of follow-up. How can such a small effect be explained? First of all, this information takes into account the impact on body weight reduction only of whole grain intake and does not consider the contribution of fiber deriving from sources such as fruit and vegetables. Second, this effect has been evaluated in the general population, including also lean individuals; whole grain consumption has a greater impact on body weight reduction when consumed by overweight individuals. However, body weight reduction induced by whole grain consumption seems too small to explain the benefits on the risk of developing type 2 diabetes and cardiovascular diseases. In this perspective, it seems reasonable to suggest that the beneficial influence of whole grain on body weight regulation represents one of

the multiple mechanisms working synergistically to beneficially influence insulin sensitivity [23].

Although data linking changes in whole grain consumption to weight gain are few, the consistency of the findings support causal relation between whole grain intake and body weight.

However, these results need to be interpreted cautiously, since in most studies people who consume more whole grains are less likely to consume an unhealthy diet and more likely to engage in physical activity. For this reason, whole grain consumption could be simply a marker of a healthier lifestyle rather than a factor favoring lower body weight in an independent way. However, the Framingham Offspring Cohort Study supports a mechanistic role of whole grain in body weight regulation. In this study, when data were adjusted for potential confounders and other dietary factors, the association between whole grain intake and BMI or WHR was attenuated but nevertheless significant [18]. Further support to this thesis comes from the Nurses' Health Study, where, taking into account numerous dietary and lifestyle indicators like change in exercise, smoking and hormone replacement therapy [12], women with the highest whole grain intake had lower body weight and a trend to gain less weight over time than those who ate less whole grain. Therefore, results from prospective studies consistently suggest that whole grain intake has beneficial effects on body weight regulation; however, only results of randomized controlled intervention studies can provide the evidence of a cause/effect relationship between whole grain intake and body weight.

Hypotheses on the mechanism of action whereby whole-grains influence body weight

There is a wealth of very different mechanisms underlying the potential role of whole grain cereals on body weight regulation [24] (Fig. 1). The lower energy density of products based on whole grain cereals compared to those based on refined cereals, as well as the satiating effect of the former—which favors a lower energy intake per eating occasion, could both play an important role in body weight regulation. However, this hypothesis is not supported by the results of epidemiological studies where the daily energy intake between whole grain consumers and non

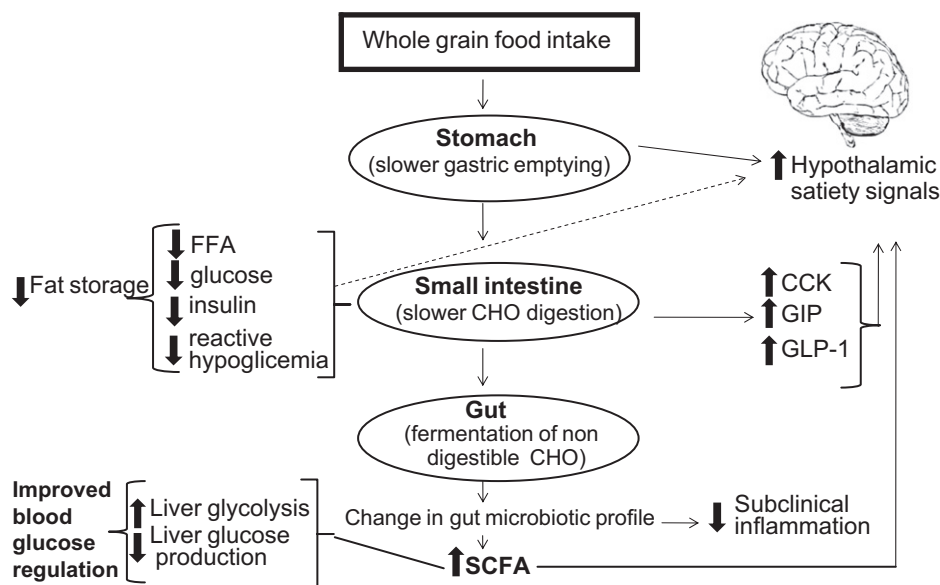


Figure 1 Possible mechanisms of action whereby whole grain influences body weight regulation and related body functions.

consumers was otherwise similar. However, it has to be underlined that methods used to assess food and energy intake are not very accurate and can miss the small differences in daily energy intake that could have a significant impact on body weight in the long term.

Lower plasma glucose and insulin responses to whole grain cereals intake can also contribute to body weight regulation. Whole grain foods prepared with barley, rice, rye, oats, maize or wheat have glycemic indices (GI) ranging from 36 to 81, barley and oats having the lowest [25]. Lower plasma glucose and insulin responses have been observed in diabetic and non diabetic subjects after the ingestion of a low GI diet containing pumpernickel bread, pasta and legumes, compared with a high GI diet containing white bread and potatoes. In fact, several studies have shown that the consumption of foods or meals with low GI has a higher satiating effect than those with high GI, irrespective of the evaluation method utilised (direct or indirect) and the possible contribution of some confounders (palatability, fiber content) [26]. In fact, the lower rate of nutrient digestion and absorption, typical of low GI foods, seems to stimulate the gastrointestinal receptors that trigger satiety signals for a longer time, thus protracting the effects on hunger/satiety centers. Therefore, the intact food structure that confers to whole grain cereals their lower GI can contribute to body weight regulation.

A further mechanism by which whole grains can regulate body weight depends on their content in non digestible carbohydrates like dietary fiber, resistant starch (RS) and oligosaccharides.

Cereal fiber influences body weight by multiple mechanisms depending on intrinsic properties, hormonal effects and intestinal fermentation. Specifically, intrinsic properties concern the ability of soluble fiber to bind to water and form a viscous solution that delays gastric emptying and intestinal transit, and limits glucose absorption thus leading to a lower blood glucose response [27]. The hormonal effects of fiber are mediated by insulin and gastrointestinal

hormones. Fiber decreases insulin secretion and consequently reduces the risk of reactive hypoglycemia during the post-absorption period, thus promoting satiety, increasing fat oxidation and decreasing fat storage. Fiber also influences gut hormones secretion which, independently of plasma glucose response, acts on satiety or by modifying glucose homeostasis. Cholecystokinin, secreted by small bowel cells, stimulates pancreatic secretion, modulates gastric emptying and stimulates the hypothalamic center of satiety. There is clear evidence that the consumption of a fiber-rich meal compared with one low in fiber (similar for nutrient composition and energy content) induces higher plasma cholecystokinin levels and a longer action time [28,29]. Gastric Inhibitor Peptide (GIP) and Glucagon like peptide-1 (GLP-1), two incretins secreted in the small intestine, increase insulin secretion in the postprandial period. In addition, GLP-1 also regulates postprandial satiety and glucose availability [30]. In animal models, dietary fiber improved glucose homeostasis through the effects of incretin [31,32]. Another important mechanism whereby whole grain intake can influence body weight is via the production of short chain fatty acids (SCFA). In fact, fiber, resistant starch and oligosaccharides are fermented in the colon by intestinal bacteria with the production of acetic, propionic and butyric acids. These molecules may influence body weight regulation by at least three processes: 1) by decreasing gastric emptying rate by SCFA, as demonstrated in animals and humans [33], thus increasing the satiating effect of the meal; moreover increased polypeptide YY plasma levels are induced by SCFA, which may lead to a reduced glucose concentration in the bloodstream; 2) by using the ability of propionate and acetate to reduce non esterified fatty acids (NEFA) plasma levels, responsible for peripheral and hepatic insulin resistance [34,35]; and finally, 3) by exploiting the ability of propionate to modulate glucose metabolism by increasing hepatic glycolysis and decreasing hepatic glucose production, as shown in isolated rat hepatocytes [36], as well as by stimulating GLP-1 secretion [37].

The latter mechanism is confirmed by the results of an intervention study performed on healthy subjects, in which the consumption of a meal rich in non digestible carbohydrates in the evening improved glucose response to the subsequent morning meal. The amelioration of glucose tolerance was associated with lower NEFA and higher propionate plasma levels (from colon fermentation) and with an increase in satiety after a subsequent standardized breakfast [38]. Therefore, the preservation of food structure, the fermentation of non digestible carbohydrates and the lesser energy density and palatability of products based on whole grain cereals are all important factors in preventing body weight gain.

A further mechanism by which whole grain may influence body weight regulation is via a probiotic effect modulating the intestinal flora. Available evidence, primarily from investigations in animal models, suggests that the gut microbiota affects nutrient acquisition and energy regulation. Microbiota composition has also been shown to differ in lean vs obese animals and humans [39]. Among the possible mechanisms of this relation, of particular interest is the hypothesis that the metabolic activities of the gut microbiota facilitate the extraction of calories from ingested dietary substances and help store these calories in host adipose tissue for later use. As a matter of fact, the gut bacterial flora of obese mice and humans include fewer Bacteroidetes and correspondingly more Firmicutes than that of their lean counterparts, suggesting that differences in caloric extraction of ingested food substances may be due to the composition of the gut microbiota [39]. It is not known whether the habitual intake of whole grain products is able to influence the composition of gut microbiota in humans; however, available data in humans show that a diet rich in whole wheat cereals compared with a diet based on bran wheat is able to increase the number of fecal bifidobacteria and lactobacilli, the target genera for prebiotic intake [40].

Clinical trials

Few clinical trials have investigated the efficacy of a whole grain cereals/calorie restrict diet on body weight loss (Table 3). Rave et al., in a randomized two-way cross-over study with two 4-week treatment periods, evaluated the effect of a low calorie diet containing whole grain products in comparison to a control diet on body weight [41]. The results showed that body weight and waist to hip ratio decreased to a similar extent after the low calorie/whole grain diet as well as after the control treatment, even if insulin resistance adjusted for the extent of body weight loss improved more after whole grain than after the control diet (Table 3). The substantial weight loss observed in this study was attributed primarily to energy restriction rather than to an effect of whole grain cereals per se; however the short duration of the intervention, only 4-weeks for each treatment, and the small sample size could account for the lack of differences in body weight between interventions. Melanson et al. [42], in a randomized controlled study in obese subjects of both genders, compared the effect of a low calorie diet (reduced by 500 kcal/day), rich in whole grain cereals, with a conventional low calorie diet, low in cereals, on body weight loss in association with exercise, for a period of twenty-four weeks. The study design was composed of two phases: an initial 12-week phase, aimed to monitor the intervention, and the second 12-week phase, designed to assess the sustainability of the intervention. In the whole grain diet group, subjects were advised to eat two meals containing whole grain cereals per day in the first 12 weeks, and one meal rich in whole grain per day in the second 12 weeks; in the conventional diet subjects were recommended to avoid whole grain cereal. At the end of the intervention, the magnitude of weight loss was similar between the whole grain and the conventional low calorie diets (5.7 and 6.2 kg, respectively), even if energy restriction, evaluated by 3-day food records, was

Table 3 Effects of low calorie diet based on whole grain products on body weight loss in clinical trials.

	Participants (n), Sex, mean age and BMI	Study Design	Treatment period (weeks)	Diet	Δ in Body Weight (kg) in WG diet	Δ in Body Weight (kg) in Control diet	ΔWG vs ΔCD p value
Rave et al., 2007	31 M/F obese subjects, 51 yrs, BMI 33.9 kg/m ²	Randomized, Controlled, Cross-over	4 wks separated by a 2 wks wash-out	Low calorie WG diet vs low calorie MR [^]	-2.5	-3.2	ns
Melanson et al., 2006	45 M/F obese subjects, 42.5 yrs, BMI 31.1 kg/m ²	Randomized, Controlled, Parallel Group	12 wks of intervention followed by 12wks of monitoring	Low calorie diet: WG vs Control diet	-4.7 (12 wks) -5.7 (24 wks)	-5.0 (12 wks) -6.2 (24 wks)	ns
Katcher et al., 2008	50 M/F obese subjects, 20–65 yrs, BMI ≥30 kg/m ²	Randomized, Controlled, Parallel Group	12 wks	Low calorie diet: WG vs Refined G diet	-3.7	-5.3	ns

MR = nutrient-dense meal replacement product; °CD = Control Diet; ΔWG = Change with Whole Grain Diet; ΔCD = Change with Control Diet.

higher in the whole grain than in the conventional diet (Table 3). This study did not show a higher ability of the whole grain diet to reduce body weight, notwithstanding the duration of the intervention, which was longer than in Rave's study. A possible explanation for this negative finding could be that subjects assigned to the whole grain diet, during the second phase compared with first phase of the intervention, decreased their fiber intake from 25 g/day to about 21 g/d—only a little bit higher than that in the conventional diet (about 17 g/day). Noteworthy, although a difference in fiber intake by only 4 g/day could not have significant impact on body weight loss in six-month's time, it could provide better results in a longer time. No difference in body weight change was observed in a more recent randomized, controlled trial (12-weeks duration) performed in obese individuals with the metabolic syndrome [43]. In this study, participants were assigned to two low calorie diets (reduced by 500 kcal/day), one based on whole grain products (about 5 servings/day whole grain food), whereas the other had a reduced whole grain food intake (<0.2 servings/day). In the absence of differences in body weight loss between the two treatments, the whole grain group showed a higher percentage of abdominal fat loss and a decrease in plasma C-reactive protein (CRP) levels than the refined cereal diet group.

The results of the few clinical trials available on whole grain and body weight demonstrate that whole grain consumption within a low calorie diet is unable to reduce body weight more than a diet without whole grain cereals. However, independently of the effects on body weight, habitual whole grain consumption seems effective in reducing abdominal fat and improving inflammation, with clear advantages regarding the cardiovascular risk.

How can the inconsistent results of epidemiological and nutritional clinical trials be explained, with respect to the effects of whole grain consumption on body weight?

As mentioned before, the inadequate duration of the interventions as well as the study design could have played an important role. In fact, up to now all the studies evaluating the effect of low calorie diets with different nutrient composition on body weight loss for up to one year have failed to demonstrate a higher effectiveness of one type of diet over another (i.e. low-carbohydrate vs traditional low-fat or high-protein diets) [44]. Only one study has demonstrated that either a Mediterranean restricted-calorie diet or a low-carbohydrate non restricted-calorie diet can induce a higher body weight loss after two years of intervention compared to a low-fat restricted-calorie diet [45]. In addition, the sample size in this study was significantly higher than that utilised in the trials reported above (more than 100 subjects for each treatment).

These results suggest that calorie restriction protracted for a short period of time, rather than the quality of a diet, can play a relevant role in achieving weight loss; on the contrary, the quality of a diet can help sustain weight loss in the long term. This opinion is supported indirectly by results of Freeland's study which showed that in hyperinsulinemic subjects the consumption of a high cereal fiber diet compared with a control diet increased SCFA and GLP-1 levels after 9–12 months of treatment [46]. Since whole grain foods seem to regulate body weight also by intestinal SCFA production and GLP-1 secretion, the duration of

a dietary intervention is relevant in order to show a significant effect on body weight loss and/or maintenance of a whole grain diet, and explain the negative findings of the clinical trials above reported.

Larsen et al. [47] have adopted a study design that could represent an alternative to a long-dietary intervention trial. In this study, the authors evaluated the effect of diets with different protein contents and glycemic indices on weight maintenance. In particular, overweight adults, who had lost at least 8% of their initial body weight with a low calorie diet (800 kcal), were enrolled and, in random order, assigned to one of two ad libitum experimental diets aimed to prevent weight regain over a 26 week period. The results obtained demonstrated that the diet with a modest increase in protein and a low GI could be more useful for body weight loss maintenance.

Conclusions

All the studies reviewed in this manuscript demonstrate that a higher intake of whole grains is associated with lower BMI in epidemiological studies. However, so far, the results from a few intervention trials investigating whether a whole grain-low calorie diet is able to reduce body weight, have failed to demonstrate a cause/effect relation. For this reason, further intervention studies with adequate methodology are necessary to answer this question.

On the basis of the scientific evidence so far available, the characteristics of a satisfactory study can be summarized in three points. The first two are the sample size—which should be adequate, and the duration of the intervention—which should be sufficiently long (probably at least two years). The last point is the model of the study, which should consider two steps: a first one, in which the participants are treated with a low calorie diet able to achieve at least 5–10% of body weight loss, and a second step, during which subjects are treated with a whole grain diet ad libitum, in order to evaluate body weight loss maintenance. For the time being, however, whole grain consumption can be recommended as one of the features of the diet that may help control body weight, based on consistent epidemiological evidence which compared regular whole grain consumption vs. refined cereals, with respect to a lower risk of developing overweight, and other major diseases of affluent societies, like type 2 diabetes, cardiovascular diseases and cancer.

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Appendix A Supplementary data

Supplementary data associated with this article can be found in the online version at doi: [10.1016/j.numecd.2011.07.003](https://doi.org/10.1016/j.numecd.2011.07.003).

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