Whole grain and body weight changes in apparently healthy adults: a systematic review and meta-analysis of randomized controlled studies[1–3]

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ABSTRACT

Background: Whole grains have received increased attention for their potential role in weight regulation. A high intake has been associated with smaller weight gain in prospective cohort studies, whereas the evidence from randomized controlled studies has been less consistent.

Objective: We assessed the effects of whole-grain compared with non–whole-grain foods on changes in body weight, percentage of body fat, and waist circumference by using a meta-analytic approach.

Design: We conducted a systematic literature search in selected databases. Studies were included in the review if they were randomized controlled studies of whole-grain compared with a non–whole-grain control in adults. A total of 2516 articles were screened for eligibility, and relevant data were extracted from 26 studies. Weighted mean differences were calculated, and a metaregression analysis was performed by using the whole-grain dose (g/d).

Results: Data from 2060 participants were included. Whole-grain intake did not show any effect on body weight (weighted difference: 0.06 kg; 95% CI: −0.09, 0.20 kg; $P = 0.45$), but a small effect on the percentage of body fat was seen (weighted difference: −0.48%; 95% CI: −0.95%, −0.01%; $P = 0.04$) compared with that for a control. An examination of the impact of daily whole-grain intake could predict differences between groups, but there was no significant association ($\beta = -0.0013$ kg × g/d; 95% CI: −0.011, 0.009 kg × g/d).

Conclusions: Whole-grain consumption does not decrease body weight compared with control consumption, but a small beneficial effect on body fat may be present. The relatively short duration of intervention studies (≤16 wk) may explain the lack of difference in body weight and fat. Discrepancies between studies may be caused by differences in study design. *Am J Clin Nutr* 2013;98:872–84.

INTRODUCTION

Whole-grain foods haves gained increased attention in recent years (1) as indicated by the markedly increased number of articles published on whole grain over the last decades (from 140 hits in PubMed for "on whole-grain" in 1991–2001 to 584 hits in 2002–2012). Health benefits of whole-grain foods have been extensively investigated, and prospective cohort studies have linked a high intake of whole-grains and decreased risk of cardiovascular disease (2–6), type 2 diabetes (5, 7, 8), and overall mortality (4, 9).

According to the HEALTHGRAIN consortium, which is an association founded in May 2010 as the follow-up organization of the European Union Sixth Framework Program Integrated Project HEALTHGRAIN, whole-grains are defined as follows: "Whole grains shall consist of the intact, ground, cracked or flaked kernel after the removal of inedible parts such as the hull and husk. The principal anatomical components - the starchy endosperm, germ and bran - are present in the same relative proportions as they exist in the intact kernel." This definition resembles most of the proposed definitions to date (10), although countries apply different criteria for a food to qualify as a whole-grain food. The main whole grains consumed worldwide are wheat, rice, and maize, followed by oats, rye, barley, triticale, millet, and sorghum. In contrast to refined grain products that comprise mainly the endosperm, whole-grain foods are rich in a number of vitamins, minerals, dietary fibers, and phytochemicals, which are proposed to be responsible for health-promoting effects (11, 12). However, most of the proposed mechanisms of action linking whole grains to body weight regulation are related to the dietary fiber component (12). Dietary fiber influences food volume and energy density, and particularly viscous fibers may delay gastric emptying and suppress the glycemic response. Whole grains have also been proposed to play an important role in promoting satiety. Individuals who eat more whole-grain foods may eat less because they feel satisfied with less food; however, few studies on these products (or diets) have been able to link decreased appetite with a reduction in food intake (13).

Observational studies have consistently shown that a whole-grain intake of ∼3 servings/d is associated with lower BMI (in kg/m^2) (4, 14, 15) and decreased body weight gain (16–18) compared with nonconsumers. However, findings from a large number of randomized controlled studies published in recent

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years have been less consistent. After the present work had been initiated, a systematic review and meta-analysis was published to collate the evidence on the effect of whole-grain on a number of outcomes, including body weight, that was based on randomized controlled studies (19) in which whole grain appeared not to affect body weight changes differently compared with a control. However, this analysis only included a small number of studies. Furthermore, the studies did not include other measures of anthropometry, and, unlike in the current study, they did not attempt to differentiate between grain types or conduct a meta-regression.

The objective of the current study was to evaluate the evidence from randomized controlled studies for a role of whole grain in terms of body weight and body composition compared with a non–whole-grain or refined-grain control in apparently healthy adults. Changes in body weight were included as a primary outcome. Changes in the percentage of body fat and waist circumference (WC) were included as secondary outcomes. Furthermore, we explored whether any effect of whole-grain intake on body weight was associated with the type and dose of whole grain or whether the intervention was calorie restricted or not.

METHODS

This meta-analysis was conducted in accordance with the recommendation and criteria outlined by Moher and Tricco (20) for systematic reviews in the nutrition field and in line with the criteria outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. The respective procedures incorporated during this meta-analysis, including the identification, screening, eligibility, and criteria for inclusion, were agreed on by the authors in advance. The protocol, which was designed according to the Cochrane Collaboration guidelines was published in the Prospero database before the start of the study (http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42012002034; registration no. CRD42012002034).

Criteria for study consideration: study design and population

Randomized controlled studies, both parallel and crossover interventions, were considered eligible if they enrolled apparently healthy adults [ie, men and women >18 and <70 y of age (although initially set to 65 y of age), normal weight, overweight, or obese, and not diagnosed with diabetes mellitus or cardiovascular diseases]. There was no limit to the duration of studies, just as blinding was not an eligibility criterion. In studies with ≥3 intervention arms, of which 2 arms were eligible, only these 2 arms were included (21, 22). If a control group was included in more than one meta-analytic estimate, we inflated SEs to avoid the double counting of patients (23–26). By definition, there is no heterogeneity (ie, variation over and above chance) between comparisons within a trial with multiple comparisons. This definition means that the consideration of individual comparisons (from the same study) as if they were independent trials could potentially lead to an underestimation of the between-trial heterogeneity. Because between-group variability is a key concern in this report, this possibility was taken into account by applying a within-trial pooled approach for sensitivity to address this potential caveat.

Criteria for study consideration: intervention type and outcome

Studies were included if they examined the effect of whole-grain foods or diets high in whole-grain foods compared with the same background diet or diets without whole grains, whether calorie restricted or not. Studies were included if one or more of the following outcomes were measured: *1*) changes in body weight (kg), *2*) changes in the percentage of body fat (%), and *3*) changes in WC (cm), whether included as a primary outcome or not and whether the data were reported or not. Multiple-component interventions or interventions that incorporated factors other than whole-grain foods or diets, unless the effect of whole-grain foods or diets could be separated from the other factors, were excluded. Also, studies on foods that were based on individual grain components, such as bran or germ, were excluded. Studies that examined the effects of high fiber, dietary fiber, or cereal fiber, but in which the specific effect of whole-grain foods or diets could not be distinguished, were excluded.

Identification of potentially relevant studies

A systematic literature search followed by study selection according to defined eligibility criteria, data mining, and statistical analyses were performed on the basis of the protocol. The following 8 bibliographic databases were searched, all until March 2012: MEDLINE via PubMed from 1953 (http://ww.ncbi.nlm.nih.gov.pubmed/), Embase via Ovid from 1980 (http://www.embase.com/), AGRICOLA via Ovid from 1970 (http://agricola.nal.usda.gov/), AGRIS via Ovid from 1975 (http://agris.fao.org/), Core Agricultural Serials Abstracts via Ovid from 1910 (http://www.cabdirect.org/), Food Science and Technology Abstracts via Ovid from 1969 (www.ovid.com/site/catalog/DataBase/93.jsp/), Web of Science from 1900 (http://thomsonreuters.com/web-of-science/), and Cochrane Central Register of Controlled Trials (http://cochrane.org/). Articles that investigated the effects of whole grain on body weight were identified by using the following search terms for whole grain: "whole grain," "wholegrain," "wholemeal," "whole meal," "wholewheat," "whole wheat," "wheat," "brown rice," "rice," "barley," "maize," "corn," "rye," "oat," "millet," "sorghum," "tef," "triticale," "canary seed," "Job's tears," "fonio," "wild rice," "amaranth," "buckwheat," "quinoa," "spelt," "emmer," "faro," "einkorn," "kamut," "durum," "bread," "cereals," or "flour." These terms were combined with the following search terms for body weight: "body weight," "weight gain," "weight loss," "body weight change," "body mass index," "BMI," "waist circumference," "body fat," "fat percentage," "fat mass," "body fat distribution," "body weights and measures," or "abdominal fat" as well as with the word "controlled." No limits on language or publication type were imposed. Duplicates were removed. Reference lists of relevant studies were inspected to identify any additional published studies not identified by the literature searches. Known experts in the field were contacted and asked whether they knew about additional studies concerning this topic.

Screening and eligibility

To determine which studies were to be assessed further, 2 authors (KP and MK) independently screened titles of all records retrieved. All potentially relevant articles were investigated as abstracts, and if potentially relevant, as full texts by the same 2 authors. Where differences of opinion existed, these were resolved by a third party (IT). For studies that fulfilled the inclusion criteria, 2 investigators (KP and MK) extracted relevant population and intervention characteristics by using data-extraction templates including *1*) general information (ie, title, authors, and year of publication), *2*) trial characteristics [ie, design, duration (wk), and risk of bias], *3*) intervention [ie, dietary information and foods provided, types and amounts of whole grains (g/d), length of intervention, comparison intervention, background diet calorie restricted or not, and dietary fiber intake (g/d)], *4*) participants (ie, total number and number in comparison groups, sex, average age, and attrition and losses to follow-up), and 5) outcomes (ie, body weight (kg), body fat (% or kg), and WC (cm)].

Assessment of reviewer agreement and risk of bias for included studies

Study quality was assessed by using the Cochrane Collaboration's tool (27). Two authors (KP and MK) independently assessed whether each of the following domains would be considered adequate (ie, presumably with low risk of bias): *1*) sequence generation and allocation concealment, *2*) attention to the participants, *3*) incomplete outcome data addressed, and *4*) selective reporting. Each of these key components of methodologic quality was assessed as either adequate (A), unclear (B), or inadequate (C).

Test for heterogeneity

Heterogeneity refers to the existence of variation between studies for each main effect being evaluated. Effect sizes are presented as weighted mean differences with 95% CIs. We examined the heterogeneity between trials by using a standard Q-test statistic and present the I^2 value (28). This procedure quantifies the proportion of variability in the results that are due to a function of heterogeneity, rather than by chance. With this method, I^2ranges from 0 to 100%, where 0% reflects homogeneity and 100% indicates substantial heterogeneity (29). When heterogeneity was shown, we tried to find potential reasons behind it by examining individual study and subgroup characteristics.

Data synthesis

Whole-grain intake was not reported for all studies included because only 6 studies reported the amount of whole grains provided (in g/d) (23, 24, 30–33). Therefore, the intake was estimated on the basis of the information provided in the articles and data on the whole-grain content in products used in the different studies from an online database (http://wholegrainscouncil.org/find-whole-grains/stamped-products) where possible. This estimation was calculated in one of the following ways: *1*) from the given amount of whole-grain foods in the diet (34), *2*) from the reported total amount of whole grain added to the habitual diet (31, 35, 36), *3*) from the amount of whole-grain present in the food multiplied by the reported serving size (37–41), *4*) from the reported addition of whole grain per kilogram of body weight (42), or *5*) from the reported addition of whole grain per energy (MJ) consumed. In 8 studies, it was not possible to quantify the amount of the whole grain provided (21, 22, 25, 43–47).

Calculation of summary measures

We calculated the difference in means for all continuous outcomes extracted. In crossover trials, in which SEs for paired differences (SE_Δ) were lacking, the pooled SE was estimated by assuming a correlation at a conservative level of 0 between intervention and control periods (r = 0.0). Net changes in body weight (kg), body fat (%), and WC (cm) were calculated as the difference (whole grain minus the control) between changes (follow-up minus at baseline) in these mean values. When variances for net changes were not reported directly, they were calculated from the SD with the largest value.

Statistical analyses

To combine individual study results, we performed a meta-analysis with Review Manager software (version 5.2; Cochrane Collaboration) and applied a restricted maximum likelihood–based (ie, random-effects) metaregression analysis to answer the specific question raised by the secondary hypothesis of whether the amount of whole-grain intake could predict changes in body weight.

We performed a number of predefined stratified analyses by stratifying the available trials according to *1*) different types of individual whole grains (ie, wheat, barley, oat, rice, rye, or mixed grains) and *2*) the energy content of background diets (ie, calorie restricted or not). The metaregression analysis was performed with SAS software (PROC MIXED version 9.2; SAS Institute Inc) (48) by applying a restricted maximum likelihood method to estimate the between-study variance (49). This method corresponds to random-effects metaregression including both within-trial variances of treatment effects and the residual between-trial heterogeneity.

RESULTS

Study characteristics

A total of 26 studies met the inclusion criteria and were included in the meta-analysis. In these studies, results were reported from 57 groups, which gave rise to 31 whole-grain compared with control comparisons (**Table 1**, **Figure 1**). The publication date for included studies ranged from 1988 to 2012.

Participant characteristics

Data from 2060 participants aged 18–70 y were included in the analysis. The degree of adiposity ranged from normal weight [BMI (in kg/m^2) >18.5 to <25) to morbidly obese (BMI >35 kg/m^2) (Table 1). One study included men only (24), and some studies included women only (31, 42, 45), whereas the majority of studies included both sexes (21–23, 25, 26, 30, 32–41, 43, 44, 46, 47, 50, 51). Three studies were conducted in Asian populations (33, 42, 45), and the remaining studies were carried out in Western Europe, Australia, or North America, all in predominantly white populations.

Study design

Of the 26 studies included, 7 studies evaluated whole-grain compared with refined-grain intake in a calorie-restricted background diet (22, 31, 39, 40, 45, 47, 50). In the other 19 studies, the

TABLE 1
Characteristics of eligible studies[1]

First author, year of publication (reference) (location)	Design and duration	Subjects	Age, BMI, and TC[2]	Intervention	Products	Diet instruction	Type of WG	WG intake	DF intake	Risk of bias[3]
			y, kg/m², and mmol/L, respectively					*g/d*	*g/d*	
Andersson, 2007 (30) (Sweden)	CO	R: 34	59 ± 5	RG	Bread, crisp bread, muesli, and pasta	N-CR	Mixed	112	RG: 17.3	B/
	6 wk	N: 30 ♂: 27%	28.3 ± 2.0 5.5 ± 0.8	WG	Test foods were provided for both groups.	Habitual diet			WG: 30.0	A/ C/ B
Bird, 2008 (26) (Australia)	CO	R: 21	56 ± 9	RG wheat	Bread, crackers, muffins, and RTE cereals	N-CR	Barley, wheat	90	RG: 21	B/
	4 wk	N: 17 ♂: 56%	27.2 ± 5.1 NA	WG barley WG wheat	Test foods were provided for all groups.	Habitual diet			WG barley: 45 WG wheat: 32	B/ C/ B
Bodinham, 2011 (35) (United Kingdom)	CO 3 wk	R: 14 N: 14 ♂: 36%	26 ± 5 21.8 ± 3.0 NA	RG wheat WG wheat	Bread, rolls Test foods were provided for both groups.	N-CR Habitual diet	Wheat	48	RG wheat: 26 WG wheat: 30	B/ A/ A/ C
Brownlee, 2010 (23) (United Kingdom)	P	R: 316	46 ± 10	Control	Bread, cereals, rice, pasta, cereal bar, and crisps	N-CR	Mixed	Control: 19	Control: +0.4	A/
	16 wk	N: 266 ♂: 50%	30.1 ± 4.1 5.2 ± 0.9	WG low WG high	Test foods were provided only for WG groups.	Habitual diet		WG low: 74 WG high: 115	WG low: +5.7 WG high: 11.0	C/ B/ A
de Mello, 2011 (21) (Finland)	P	R: 87	59 ± 7	RG	Snack bars, breads, and pasta	N-CR	Mixed	NA	RG: 17.6	B/
	12 wk	N: 68 ♂: 51%	31.2 ± 3.5 5.3 ± 1.0	WG	Test foods were provided only for WG group.	WG: healthy diet RG: Habitual diet (no fish, no bilberries)			WG: 26.5	C/ C/ A
Giacco, 2010 (44) (Italy)	CO	R: 15	55 ± 8	RG wheat	Bread, pasta, rusks, and crackers	N-CR	Wheat	NA	RG: 20	B/
	3 wk	N: 15 ♂: 80%	27.4 ± 3.0 5.3 ± 1.0	WG wheat	Test foods were provided for both groups.	Habitual diet			WG: 32	A/ A/ A
Gilhooly, 2008 (40) (United States)	P	R: 34	35 ± 5	RG	RTE cereals (FiberOne[4] or no extra fiber)	CR	Wheat	18.2	RG: 20	B/
	6 wk	N: 33 ♂: 24%	27.5 ± 1.4 NA	WG	All food was provided for both groups.				WG: 32	A/ C/ A

(Continued)

TABLE 1 (*Continued*)

First author, year of publication (reference) (location)	Design and duration	Subjects	Age, BMI, and TC[2]	Intervention	Products	Diet instruction	Type of WG	WG intake	DF intake	Risk of bias[3]
Johnston, 1998 (37) (United States)	P 6 wk	R: 135 N: 124 ♂: 63%	57 NA 6.2	RG cornflakes WG Cheerios	RTE cereals (Cheerios[4]) Test foods were provided for both groups.	N-CR Step I diet	Oat	74	RG: 20 WG: 25	B/ A/ C/ A
Karmally, 2005 (38) (United States)	P 6 wk	R: 152 N: 152 ♂: 32%	49 ± 11 29.2 ± 3.8 5.3 ± 0.7	RG corn cereal WG oat	RTE cereals (Cheerios[4]) Test foods were provided for both groups.	N-CR Step I diet	Oat	74	NA	B/ A/ C/ C
Katcher, 2008 (47) (United States)	P	R: 50	46 ± 9	RG (avoid WG)	Bread, rolls, RTE cereals, rice, pasta, and snacks	CR	Mixed	NA	RG: 15.3	B/
	12 wk	N: 47 ♂: 51%	35.8 ± 4.5 4.9 ± 0.9	WG	Test foods were not provided for any group.				WG: 20.8	C/ A/ A
Kim, 2008 (45) (South Korea)	P 6 wk	R: 47 N: 40 ♂: 0%	20–35 27.4 ± 2.5 4.8 ± 0.6	RG rice (white) WG rice (brown and black)	MR powders Test foods were provided for both groups.	CR	Rice	NA	NA	B/ A/ B/ A
Kristensen, 2012 (31) (Denmark)	P	R: 79	60 ± 5	RG wheat	Bread, pasta, and biscuits	CR	Wheat	105	RG: 4.5	B/
	12 wk	N: 72 ♂: 0%	30.2 ± 3.0 5.6 ± 0.9	WG wheat	Test foods were provided for both groups.				WG: 11.0	A/ B/ A
Leinonen, 2000 (43) (Finland)	CO 4 wk	R: 43 N: 40 ♂: 45%	43 ± 8 24.5 ± 2.8 6.4 ± 0.9	RG WG	Bread and crisp bread Test foods were provided for both groups.	N-CR Habitual diet	Rye	NA	RG: 13 WG: 28	B/ A/ C/ A
Li, 2003 (42) (Japan)	CO	R: 10	20 ± 1	Control	Barley kernels and rice	N-CR	Barley	89	RG: 19	B/
	4 wk	N: 10 ♂: 0%	19.2 ± 2.0 3.6 ± 0.6	WG barley	All food was provided for both groups.				WG: 29	A/ A/ C
Maki, 2010 (39) (United States)	P	R: 204	49 ± 1	RG corn cereal	RTE cereals (Cheerios[4]), white toast, bagels, muffins, rice cakes, and snacks	CR	Oat	66	RG:13	B/
	12 wk	N: 144 ♂: 22%	32.1 ± 0.5 6.0 ± 0.6	WG Cheerios	Test foods were provided for both groups				WG: 22	B/ C/ A

(Continued)

TABLE 1 (*Continued*)

First author, year of publication (reference) (location)	Design and duration	Subjects	Age, BMI, and TC[2]	Intervention	Products	Diet instruction	Type of WG	WG intake	DF intake	Risk of bias[3]
McIntosh, 2003 (24) (Australia)	CO	R: 31	40–65	RG	Bread, crisp bread, and RTE cereals	N-CR	Rye	88	RG: 19	B/
	4 wk	N: 28 ♂: 100%	30.0 ± 4.8 NA	WG rye WG wheat	Test foods were provided for all groups.		Wheat		WG rye: 32 WG wheat: 32	A/ C/ B
Melanson, 2006 (22) (United States)	P 12 wk	R: 129 N: 91 ♂: 21%	42 ± 9 30.8 ± 16.0 NA	Control WG	RTE cereals Test foods were provided for both groups.	CR	Mixed	NA	RG: 18 WG: 21	A/ C/ C/ A
Pereira, 2002 (46) (United States)	CO	R: 11	42 ± 9	RG	RTE cereals, muffins, bread, chips, pasta, and cookies	N-CR	Mixed	NA	RG: 18	B/
	6 wk	N: 11 ♂: 45%	30.2 ± 3.3 NA	WG	All food was provided for both groups.				WG: 28	A/ A/ B
Reynolds, 2000 (41) (United States)	CO 4 wk	R: 46 N: 43 ♂: 49%	52 24.4 ± 3.9 6.0 ± 0.9	RG corn WG Cheerios	RTE cereals (Cheerios[4]) Test foods were provided for both groups.	N-CR AHA Step 1 diet	Oat	70	RG: 17 WG: 26	B/ A/ C/ A
Ross, 2011 (32) (Switzerland)	CO	R: 22	35 ± 4	RG	RTE cereals, pasta, crackers, bread, cereal bars, frozen meals, couscous, risotto, noodles, and pizza	N-CR	Mixed	150	RG: 19	B/
	2 wk	N: 17 ♂: 35%	23.7 ± 2.2 4.6 ± 0.9	WG	All food was provided for both groups.				WG: 32	A/ C/ B
Saltzman, 2001 (50) (United States)	P	R: 43	45 ± 22	Control	Quick oats as hot cereal, bread, and casseroles	CR	Oat	82	RG: 13	B/
	6 wk	N: 43 ♂: 47%	26.4 ± 3.3 4.7 ± 0.9	WG oat	All food was provided for both groups.				WG: 16	A/ A/ A
Tighe, 2010 (25) (United Kingdom)	P 16 wk	R: 233 N: 206 ♂: 50%	52 ± 7 27.7 ± 3.9 5.6 ± 1.1	RG WG wheat WG oat and wheat	Bread and RTE cereals Test foods were provided for both groups.	N-CR	Wheat Mixed	NA	RG: 11 WG wheat: 17 WG mixed: 19	B/ A/ C/ C
Tucker, 2010 (34) (Canada)	CO 6 wk	R: 28 N: 28 ♂: 71%	55 ± 7 31.1 ± 4.3 5.0 ± 0.9	RG WG	Bread Test foods were provided for both groups	N-CR Habitual diet	Mixed	53	RG: 21 WG: 30	B/ A/ C/ A

(*Continued*)

TABLE 1 (*Continued*)

First author, year of publication (reference) (location)	Design and duration	Subjects	Age, BMI, and TC[2]	Intervention	Products	Diet instruction	Type of WG	WG intake	DF intake	Risk of bias[3]
van Horn, 1988 (36) (United States)	P 8 wk	R: 256 N: 236 ♂: 36%	42 NA 5.3	Control WG oat	Oatmeal Test food was provided only for WG group.	N-CR	Oat	56	RG: 12.3 WG: 13.2	B/C/C/C
van Horn, 1991 (51) (United States)	P 8 wk	R: 111 N: 80 ♂: 50%	42 ± 13 26.2 ± 3.6 6.5 ± 0.9	Control WG oat	Instant oats Test food was provided only for WG group.	N-CR	Oat	54	RG: 15 WG: 18	B/C/C/B
Zhang, 2011 (33) (China)	P 16 wk	R: 202 N: 193 ♂: 53%	50 ± 7 25.7 ± 3.0 5.5 ± 1.3	RG rice (white) WG rice (brown)	Rice Test food was provided for both groups.	N-CR	Rice	100	RG: 10 WG: 13	B/A/A/A

[1] Where data were not accessible, the mean or the range is presented. AHA, American Heart Association; CO, crossover design; CR, calorie-restricted; DF, dietary fiber; MR, meal replacement; N, no. of subjects analyzed; NA, not available; N-CR: non–calorie restricted; P, parallel design; R, no. of subjects randomly assigned; RG, refined grain; RTE, ready-to-eat; WG, whole grain; ♂, percentage of men in the population that was analyzed.

[2] All values are means ± SDs.

[3] Risk of bias was assessed as follows: *1*) Sequence generation and allocation concealed? *2*) Received all subjects the same attention? *3*) Was analysis on an intention-to-treat population? and *4*) Was the article free of selective outcome reporting? A = adequate; B = unclear; C = inadequate.

[4] Cheerios (General Mills); FiberOne (General Mills).

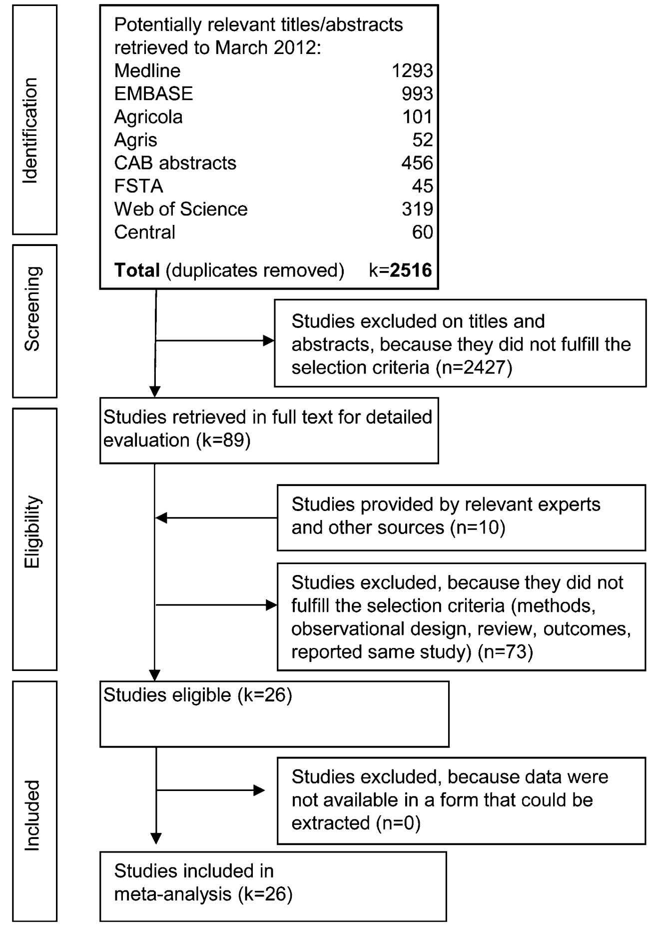

FIGURE 1. Flow diagram showing the flow of papers through the search strategy and selection of studies. CAB, Core Agricultural Serials; FSTA, Food Science and Technology Abstracts.

researchers attempted to keep body weight constant (21, 23–26, 30, 32–36, 38, 41–44, 46, 51). The duration of the intervention ranged from 2 wk (32) to 16 wk (23, 25, 33), with the majority of studies lasting 4–6 wk.

Whole-grain intervention

The whole-grain intervention varied between studies, as did the daily whole-grain dose that ranged from 18.2 g/d (40) to 150 g/d (32). Nine studies evaluated a mixed whole-grain diet [containing whole-grain products such as bread, crisp bread, rolls, muesli, ready-to-eat (RTE) cereals, pasta, rice, snack bar, crisps, muffin, and cookies] compared with a mixed refined-grain diet (containing the same products but produced of refined grain) (22, 25, 30, 32, 46, 47), or the participants' habitual diet (21, 23, 34). Seven studies included only oat (eg, oatmeal, instant oats, RTE cereal or Cheerios cereal (General Mills), hot cereal, or oat incorporated into other foods) compared with a refined-grain diet (other carbohydrate foods with the avoidance of oat, corn cereals, participants' habitual diet including wheat, cream of wheat, or nonoat RTE cereal, or low-fiber breakfast and snack foods) (36, 37, 39, 41, 50, 51). In 7 studies, whole-grain wheat (bread, crackers, muffins, RTE cereal, bread rolls, rusks, and biscuits) were compared with refined-grain wheat (containing the same products but of refined wheat or other non–whole-grain cereal) (24, 25, 31, 40), or participants' habitual diet (26, 35, 44). Two studies included only whole-grain barley (bread, crackers, muffins, other RTE cereal, and barley kernels) and used refined wheat (26) or white rice (42) as a comparison. Two studies compared whole-grain rye foods (bread, crisp bread, and RTE cereal) to refined-grain foods (white-wheat breads and low-fiber foods) (24, 43). Finally, 2 studies included only whole-grain rice; one study compared brown rice to white rice (31), and one study compared a brown- and black-rice meal replacement to a white-rice meal replacement (45).

Intervention effect

Body weight

In total, 26 pertinent studies were included in the analysis. One study investigated 2 different doses (23), one study reported results for both normoglycemic/normoinsulinemic and hyperglycemic/hyperinsulinemic individuals (34). One study investigated both whole-grain wheat and rye (24), one study investigated both whole-grain wheat and mixed whole grain (25), and one study included both a whole-grain barley and wheat arm (26), resulting in 31 comparisons.

Compared with a control, whole grain did not result in a decreased body weight change (weighted difference: 0.06 kg; 95% CI: −0.09, 0.20 kg, $P = 0.45$) (**Figure 2**). A subgroup analysis for individual grains showed that only whole-grain rice decreased body weight compared with that with a control (weighted difference: −1.10 kg; 95% CI: −20.6, −0.14 kg; $P = 0.02$) (Figure 2). This result was based on data from only 2 studies (33, 45), of which one study reported a greater weight reduction with consumption of whole-grain rice (−6.75 ± 0.40 kg) compared with white rice (−5.37 ± 0.40 kg) (45). The application of a stratified analyses according to the background diet did not change the result because a greater reduction for whole grain compared with a control was not observed when we applied calorie restriction (weighted difference: −0.35 kg; 95% CI: −0.87, 0.17 kg; $P = 0.18$) compared with non–calorie restriction (weighted difference: 0.11 kg; 95% CI: −0.04, 0.26 kg; $P = 0.17$).

Body fat

In total, 7 studies reported changes in the percentage of body fat, which resulted in 9 comparisons because one study investigated 2 different doses (23), and one study reported results for both normoglycemic/normoinsulinemic and hyperglycemic/hyperinsulinemic individuals (34). Five studies used bioelectric impedance to measure body fat (23, 34, 35, 45, 47), one study used dual-energy X-ray absorptiometry (31), and one study failed to report the method applied (50). Overall, whole grain resulted in a greater decrease in the percentage of body fat than did a control (weighted difference: −0.48%; 95% CI: −0.95%, −0.01%; $P = 0.04$) (**Figure 3**). However, one study (45) strongly influenced the analysis because removal of the study rendered the positive finding not significant (weighted difference: −0.34 kg; 95% CI: −0.86, 0.17 kg; $P = 0.19$). For subgroup analyses that were based on grain types, we showed that whole-grain rice decreased the percentage of body fat more so than a control (weighted difference: −1.20%; 95% CI: −2.36%, −0.04%; $P = 0.04$), although this result was only based on one study. On the basis of 2 studies, whole-grain wheat tended to lower the percentage of body fat more than did a control (−0.71%; 95% CI: −1.52%, 0.09%; $P = 0.08$). This result was not the case for oat or for mixed whole grain. In the subgroup of studies that applied calorie restriction, the reduction in body fat percentage with whole-grain compared with a control was greater than for all studies (weighted difference: −0.67%; 95% CI: −1.21%, −0.14%; $P = 0.01$), whereas the effect was attenuated in non–calorie-restricted studies (weighted difference: 0.16%; 95% CI: −0.82%, 1.15%; $P = 0.74$).

WC

In total, 9 studies (11 comparisons) reported changes in WC. Compared with a control, whole grain did not result in a greater decrease in WC (weighted difference: −0.10 cm; 95% CI: −0.25, 0.04 cm; $P = 0.15$) (**Figure 4**). However, on the basis of one study, whole-grain oat decreased WC more than did a control (weighted difference: –1.20 cm; 95% CI: −1.66, −0.74 cm; $P < 0.001$). This result was not the case for wheat, rice, or mixed whole grain. Subgroup analyses according to study design (not calorie restricted compared with calorie restricted) did not change the overall results.

Some evidence of heterogeneity was observed ($I^2 = 67\%$, $P < 0.001$). To explore this heterogeneity, a funnel plot was drawn. A funnel plot (not shown) indicated that the study by Maki et al (39) that reported a reduction in WC with whole-grain oat compared with a control was responsible for this heterogeneity. The omission of this study eliminated the heterogeneity ($I^2 = 0\%$) but did not change the overall pattern of results.

Sensitivity analysis

A sensitivity analysis was performed to determine whether the results concerning changes in body weight depended on the attention given to the whole grain compared with control groups (ie, if the products were provided to both groups or only to the whole-grain group). The difference in attention was interpreted as an indicator of whether a supplementation or replacement of habitual cereal consumption occurred. This was done by excluding studies with risk of bias assessed as either B or C for this specific question (Table 1). For body weight, this method resulted in the exclusion of 7 comparisons, but the overall result was not changed (weighted mean difference: 0.05 kg; 95% CI: −10, 0.19 kg; $P = 0.50$). For body fat, only the study by Brownlee et al (23) was excluded, and the results were unchanged (weighted difference: −0.52%; 95% CI: −1.00%, −0.04%; $P = 0.03$). For WC, only the study by de Mello et al (21) was removed, and again the results were unchanged (weighted difference: −0.10 cm; 95% CI: −0.25, 0.04 cm; $P = 0.15$). Thus, overall, there was no indication that the effect on any outcome depended on whether participants in both control and whole-grain groups were given equal attention.

Metaregression analysis of dose-response effect

An examination of the impact of whether daily whole-grain intake could predict differences between groups (**Figure 5**), showed no significant association [$\beta = -0.0013$ kg × g/d (95% CI: −0.011–0.009 kg × g/d); $z = 0.245$, $P = 0.81$]. There was no linear dose-response effect of the whole-grain dose on the mean difference in body weight change compared with that of the control. In other words, the mean difference in weight change

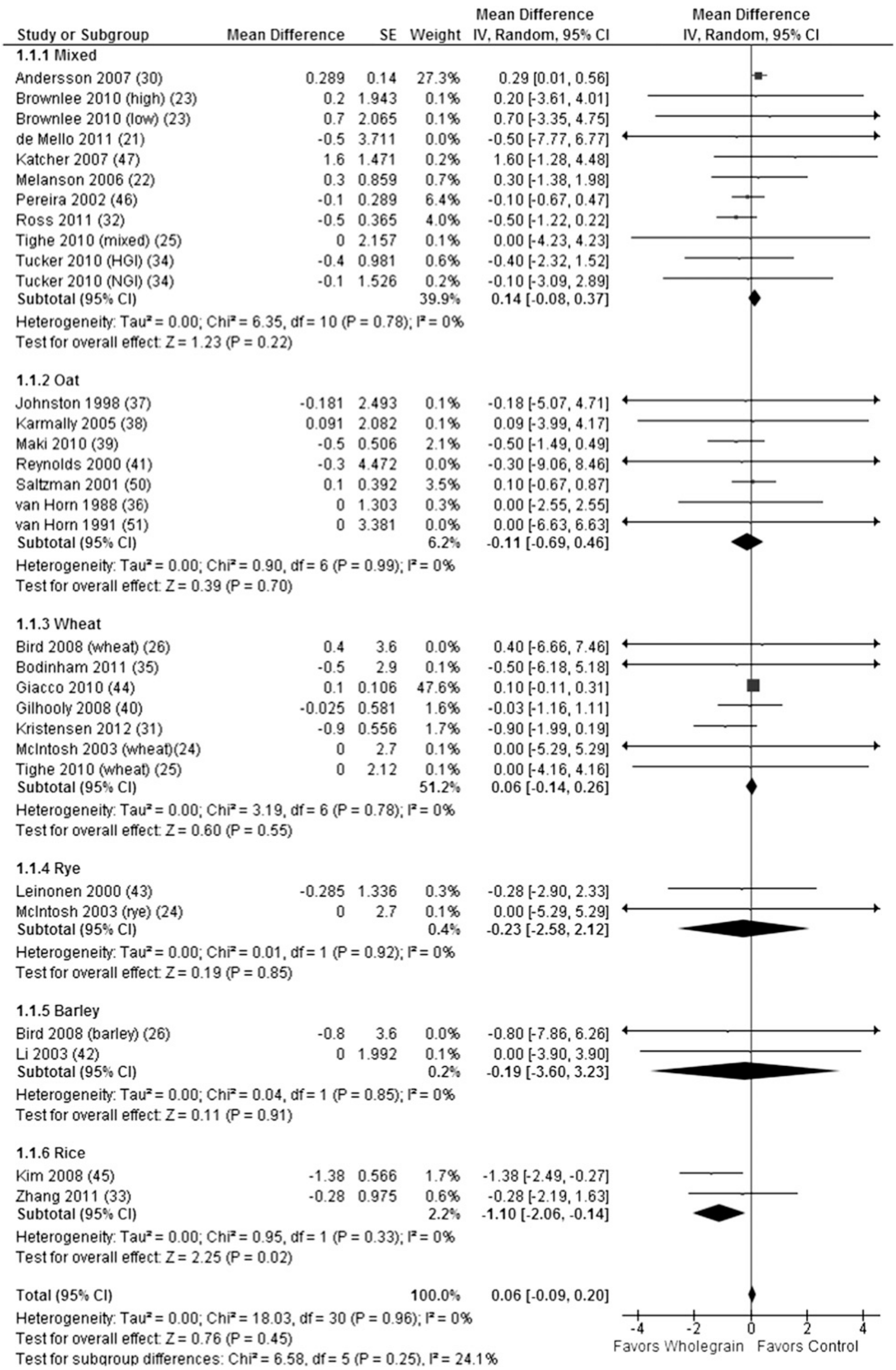

FIGURE 2. Forest plot of the results of the fixed-effects meta-analysis of change in body weight according to grain type shown as pooled mean differences with 95% CIs. For each study, the square represents the point estimate of the intervention effect. Horizontal lines join lower and upper limits of the 95% CI of this effect. The area of shaded squares reflects the relative weight of the study in the meta-analysis. Diamonds represent the subgroup mean difference and pooled mean differences. HGI, hyperglycemic/insulinemic; high, high whole-grain dose (115 g/d); IV, inverse variance; low, low whole-grain dose (74 g/d); NGI, normoglycemic/insulinemic.

was invariant across the range of whole-grain dose used in the studies (18.2 to 150 g/d).

DISCUSSION

This meta-analysis reviewed the effect of whole-grain on body weight and composition in adults on the basis of randomized, controlled, intervention studies. Pooled estimates showed that whole-grain consumption did not result in a difference in the change in body weight compared with control consumption. However, it appeared that whole grain had a small beneficial effect on the percentage of body fat but not WC.

Observational studies consistently showed that a high intake of whole-grain foods is associated with decreased body weight gain (16–19). However, when it comes to randomized controlled

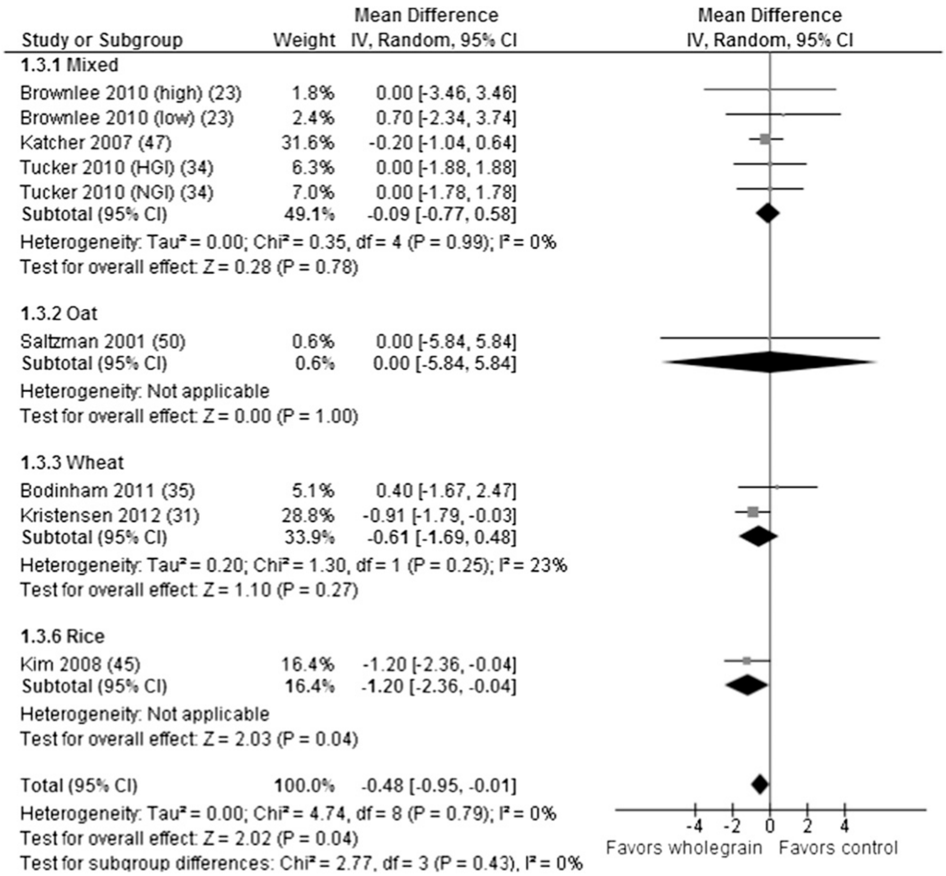

FIGURE 3. Forest plot of the results of the fixed-effects meta-analysis of change in the percentage of body fat according to grain type shown as pooled mean differences with 95% CIs. For each study, the square represents the point estimate of the intervention effect. Horizontal lines join the lower and upper limits of the 95% CI of this effect. The area of the shaded squares reflects the relative weight of the study in the meta-analysis. Diamonds represent the subgroup mean difference and pooled mean differences. HGI, hyperglycemic/insulinemic; high, high whole-grain dose (115 g/d); IV, inverse variance; low, low whole-grain dose (74 g/d); NGI, normoglycemic/insulinemic.

studies, there is much discrepancy in the literature. This discrepancy is very likely attributed to differences in study designs, selected population, and the type and amount of whole-grain foods consumed. This meta-analysis has addressed some of these issues. When we addressed body weight changes, it was of great importance to which extent this outcome was included in the study as a primary outcome or not because this inclusion may have determined whether measures were taken to keep body weight stable during the intervention or not. In addition, we assessed whether calorie restriction was applied because this application may have indicated that body weight was a primary outcome. These subgroup analyses indicated that calorie-restricted studies tended to induce reductions in body weight and fat compared with a control. This finding suggests that studies designed to detect differences in anthropometric measures were more successful or that whole-grain foods may aid adherence to a calorie-restricted diet rather than induce spontaneous weight loss. However, one study (45) strongly influenced the analysis on the percentage of body fat as well as body weight. This study conducted in Korean overweight women reported a very low daily energy intake of 260 kJ/d, which did not resemble a normal diet even under calorie-restricted conditions, and furthermore, the whole-grain rice was provided in a powdered form as meal replacements in a relatively low dose. Thus, the results of this study should be interpreted cautiously.

The health benefits of body weight loss are usually linked to the benefits of losing body fat mass. The percentage of body fat may be a more-sensitive measure than body weight because total body weight reflects both the amount of fat and fat-free mass as well as height, which is not the case for the percentage of body fat. Our meta-analysis including 7 studies with body fat measurements suggested that whole-grain consumption beneficially affects the percentage of body fat, although the effect was modest in magnitude. Few studies have considered how dietary modification may alter body composition independent of changes in overall body weight. In two 12-wk calorie-restricted intervention studies in overweight and obese adults (31, 47), similar changes in body weight and WC were observed, whereas the percentage of total body fat (31) and percentage of abdominal fat (47) measured by using dual-energy X-ray absorptiometry decreased significantly more in whole-grain than refined-grain groups. Theories have been put forward that the mechanisms behind these effects could be mediated by decreased insulin and glucose responses that favor lipolysis and lipid oxidation rather than fat storage (52–54). However, insulin sensitivity was not improved in either of the 2 studies (31, 47). Katcher et al (47) suggested that decreased abdominal fat mass may be mediated by a decreased inflammatory response. Thus, a potential effect of whole grain on adiposity likely derives from multiple components affecting metabolism through many different pathways.

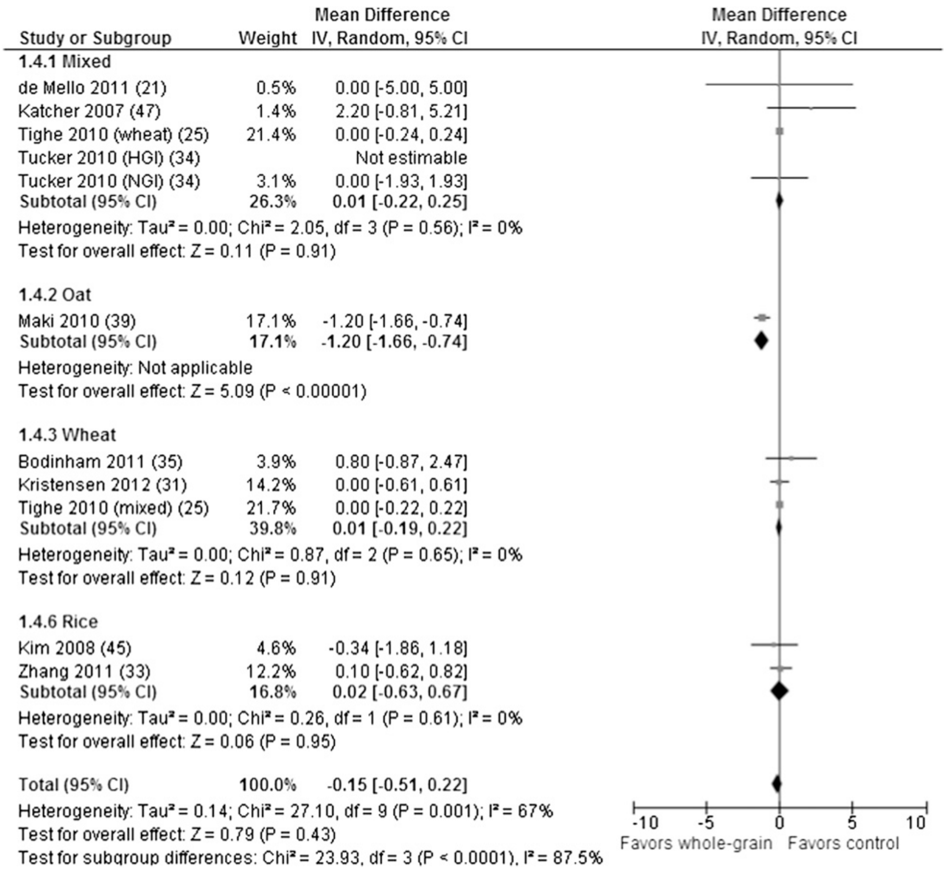

FIGURE 4. Forest plot of the results of the fixed effects meta-analysis of change in waist circumference according to grain type shown as pooled mean differences with 95% CIs. For each study, the square represents the point estimate of the intervention effect. Horizontal lines join the lower and upper limits of the 95% CI of this effect. The area of the shaded squares reflects the relative weight of the study in the meta-analysis. Diamonds represent the subgroup mean difference and pooled mean differences. HGI, hyperglycemic/insulinemic; IV, inverse variance; NGI, normoglycemic/insulinemic.

The study duration may be important because subtle differences in body weight changes may require a long time span to become evident. However, we did not conduct subgroup analyses according to the study duration because none of the studies included were

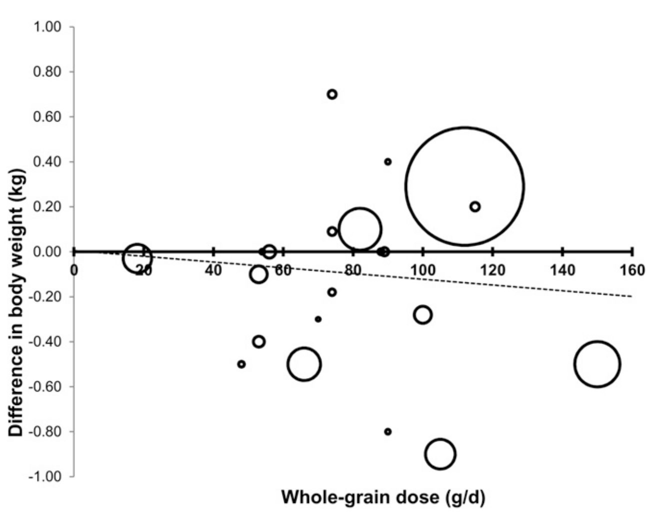

FIGURE 5. Mean differences in body weight change by whole-grain dose. In the metaregression analysis, the size of the circles is proportional to the precision of the estimate used in the metaregression. The line indicates the predicted effects (regression line). There was no significant association [$\beta = -0.0013$ 0013 kg $\times$ g/d (95% CI: -0.011, 0.009 kg $\times$ g/d); $z = 0.245$, $P = 0.81$].

conducted over a period >16 wk, with the average study length being 4–6 wk. In observational studies, the magnitude of effect was limited with an average of an ∼0.5-kg difference in body weight changes between individuals consuming no or little whole-grain compared with those consuming 3 servings/d (14, 16, 17). These effect sizes may be too subtle to detect in controlled intervention studies or may require considerable larger populations as well as studies that last 6–24 mo. However, there may be differential compliance with the protocol between short- and long-term studies. Furthermore, all but one of the studies included in this meta-analysis used doses of whole grain exceeding that of the quintile of the population consuming the greatest amount of whole grain. This was an inherent characteristic of most dietary intervention studies, in which the dose was increased as a compensation for the short duration. However, it is unknown how this may affect the outcome of the studies. The metaregression did not reveal the existence of a dose-response relation between whole-grain intake and the difference in body weight changes. Because the range of whole-grain dose (18.2–150 g/d) was markedly larger than that observed in observational studies, this should have increase the chance of detecting such a dose-response relation if present. However, in most studies, intake was not measured through diaries or food questionnaires, and thus, the doses reflected the amounts intended for consumption.

Whole-grain varieties differ in their contents and types of dietary fibers as well as in other nutrients. Therefore, it may be speculated that whole-grain varieties exert different physiologic responses. It may further be hypothesized that oat, rye, and barley should exert greater effects on anthropometric measures because of their greater total and soluble fiber content compared with that of wheat and rice, which may affect satiety and glucose and insulin responses. On the basis of this hypothesis, we performed subgroup analyses according to grain types; the results of these analyses did not support the mentioned hypothesis. However, only mixed grain, wheat, and oat were the grain type in >2 studies, and thus, the subgroup analyses on rye, rice, and barley should be interpreted with some caution. In addition to grain type, the difference in product characteristics, which is closely linked to cultural practices, may have also affected outcomes. Rye breads consumed in Nordic countries often contain a large proportion of intact kernels, whereas wheat in bread, pasta, and RTE cereals are finely ground. Differences in particle sizes in foods and, potentially, also food preparation may influence variables such as starch digestibility and satiety. However, this was not addressed in the current study.

We did not find that the results depended on the degree to which participants were given the same amount of attention (or intervention products) in whole-grain and control groups. Brownlee et al (23) reported that an increased amount of energy was consumed when whole-grain foods were added to the diet compared with in the control group who consumed their habitual diets. This influence could mask a potential effect on body weight. Furthermore, in many cases, it is unclear whether participants successfully managed to substitute for habitual grain products rather than add whole-grain foods. The proportion of whole grain in the diet relative to refined grain may be of importance as indicated by the finding that a high intake of whole-grain did not offset the negative association between refined-grain consumption and visceral adipose tissue in a cross-sectional study (55). A strictly controlled diet in which all foods are provided would eliminate the problem with potential insufficient substitution. However, unless consumed ad libitum, such a diet would not give evidence to the potential impact of whole-grain on body weight and fat if the mechanism of action is an effect on satiety and, thus, energy intake. The far majority of studies included in the meta-analysis did not include changes in body weight and fat as primary endpoints and may, therefore, have not been designed for this purpose. We believe that this approach is valid because of the increased data used, which was not the case in a recent meta-analysis (19) in which a smaller number of studies were included; however, the study-selection criteria applied in the meta-analysis were not clear.

In conclusion, the current meta-analysis does not lend credence to a role for whole grain in body weight management. However, we did show that whole grain beneficially affected the percentage of body fat. Studies were of 2–16-wk duration, and most studies lasted only 4–6 wk. Thus, longer-term studies should be conducted to clarify the role of whole grain on body weight changes. Furthermore, additional investigations are needed to look at whether numerical differences with a greater reduction for whole grain compared with a control when applying calorie restriction may infer modest benefits of including whole grains as part of a calorie-restricted diet.

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The authors' responsibilities were as follows—KP and MK: provided study oversight and wrote and took final responsibility for the content of the manuscript; KP, EMB, and MK: performed the data collection; MK and RC: performed statistical analyses; and all authors: designed the research and assisted in the interpretation of analyses and revision of the manuscript. None of the authors had a conflict of interest.

REFERENCES

1. Whole Grains Council. Whole grain statistics. Whole Grains Council 2012. Available from: http://wholegrainscouncil.org/newsroom/whole-grain-statistics (cited 8 January 2012).
2. Jacobs DR Jr, Meyer KA, Kushi LH, Folsom AR. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: the Iowa Women's Health Study. Am J Clin Nutr 1998;68:248–57.
3. Liu S, Stampfer MJ, Hu FB, Giovannucci E, Rimm E, Manson JE, Hennekens CH, Willett WC. Whole-grain consumption and risk of coronary heart disease: results from the Nurses' Health Study. Am J Clin Nutr 1999;70:412–9.
4. Sahyoun NR, Jacques PF, Zhang XL, Juan W, McKeown NM. Whole-grain intake is inversely associated with the metabolic syndrome and mortality in older adults. Am J Clin Nutr 2006;83:124–31.
5. McKeown NM, Meigs JB, Liu S, Wilson PW, Jacques PF. Whole-grain intake is favorably associated with metabolic risk factors for type 2 diabetes and cardiovascular disease in the Framingham Offspring Study. Am J Clin Nutr 2002;76:390–8.
6. Mellen PB, Walsh TF, Herrington DM. Whole grain intake and cardiovascular disease: a meta-analysis. Nutr Metab Cardiovasc Dis 2008;18:283–90.
7. Esmaillzadeh A, Mirmiran P, Azizi F. Whole-grain consumption and the metabolic syndrome: a favorable association in Tehranian adults. Eur J Clin Nutr 2005;59:353–62.
8. Montonen J, Knekt P, Järvinen R, Aromaa A, Reunanen A. Whole-grain and fiber intake and the incidence of type 2 diabetes. Am J Clin Nutr 2003;77:622–9.
9. Jacobs DR Jr, Andersen LF, Blomhoff R. Whole-grain consumption is associated with a reduced risk of noncardiovascular, noncancer death attributed to inflammatory diseases in the Iowa Women's Health Study. Am J Clin Nutr 2007;85:1606–14.
10. Heathgrain Consortium. Whole grain definition. 2013. Available from: http://www.healthgrain.org/webfm_send/601.
11. Fardet A. New hypotheses for the health-protective mechanisms of whole-grain cereals: what is beyond fibre? Nutr Res Rev 2010;23:65–134.
12. Jonnalagadda SS, Harnack L, Hai Liu R, McKeown N, Seal C, Liu S, Fahey GC. Putting the whole grain puzzle together: health benefits associated with whole grains–summary of American Society for Nutrition 2010 Satellite Symposium. J Nutr 2011;141:1011S–22S.
13. Wanders AJ, van den Borne JJ, de Graaf C, Hulshof T, Jonathan MC, Kristensen M, Mars M, Schols HA, Feskens EJ. Effects of dietary fibre on subjective appetite, energy intake and body weight: a systematic review of randomized controlled trials. Obes Rev 2011;12:724–39.
14. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G. 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 2003;78:920–7.
15. McKeown NM, Yoshida M, Shea MK, Jacques PF, Lichtenstein AH, Rogers G, Booth SL, Saltzman E. Whole-grain intake and cereal fiber are associated with lower abdominal adiposity in older adults. J Nutr 2009;139:1950–5.
16. Bazzano LA, Song Y, Bubes V, Good CK, Manson JE, Liu S. Dietary intake of whole and refined grain breakfast cereals and weight gain in men. Obes Res 2005;13:1952–60.
17. Koh-Banerjee P, Franz M, Sampson L, Liu S, Jacobs DR Jr, Spiegelman D, Willett W, Rimm E. Changes in whole-grain, bran, and cereal fiber consumption in relation to 8-y weight gain among men. Am J Clin Nutr 2004;80:1237–45.
18. Newby PK, Maras J, Bakun P, Muller D, Ferrucci L, Tucker KL. Intake of whole grains, refined grains, and cereal fiber measured with 7-d diet records and associations with risk factors for chronic disease. Am J Clin Nutr 2007;86:1745–53.
19. Ye EQ, Chacko SA, Chou EL, Kugizaki M, Liu S. Greater whole-grain intake is associated with lower risk of type 2 diabetes, cardiovascular disease, and weight gain. J Nutr 2012;142:1304–13.
20. Moher D, Tricco AC. Issues related to the conduct of systematic reviews: a focus on the nutrition field. Am J Clin Nutr 2008;88:1191–9.

21. de Mello VD, Schwab U, Kolehmainen M, Koenig W, Siloaho M, Poutanen K, Mykkänen H, Uusitupa M. A diet high in fatty fish, bilberries and wholegrain products improves markers of endothelial function and inflammation in individuals with impaired glucose metabolism in a randomised controlled trial: the Sysdimet study. Diabetologia 2011;54:2755–67.
22. Melanson KJ, Angelopoulos TJ, Nguyen VT, Martini M, Zukley L, Lowndes J, Dube TJ, Fiutem JJ, Yount BW, Rippe JM. Consumption of whole-grain cereals during weight loss: effects on dietary quality, dietary fiber, magnesium, vitamin B-6, and obesity. J Am Diet Assoc 2006;106:1380–8.
23. Brownlee IA, Moore C, Chatfield M, Richardson DP, Ashby P, Kuznesof SA, Jebb SA, Seal CJ. Markers of cardiovascular risk are not changed by increased whole-grain intake: the WHOLEheart study, a randomised, controlled dietary intervention. Br J Nutr 2010;104:125–34.
24. McIntosh GH, Noakes M, Royle PJ, Foster PR. Whole-grain rye and wheat foods and markers of bowel health in overweight middle-aged men. Am J Clin Nutr 2003;77:967–74.
25. Tighe P, Duthie G, Vaughan N, Brittenden J, Simpson WG, Duthie S, Mutch W, Wahle K, Horgan G, Thies F. Effect of increased consumption of whole-grain foods on blood pressure and other cardiovascular risk markers in healthy middle-aged persons: a randomized controlled trial. Am J Clin Nutr 2010;92:733–40.
26. Bird AR, Vuaran MS, King RA, Noakes M, Keogh J, Morell MK, Topping DL. Wholegrain foods made from a novel high-amylose barley variety (Himalaya 292) improve indices of bowel health in human subjects. Br J Nutr 2008;99:1032–40.
27. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
28. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21;1539–58.
29. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327:557–60.
30. Andersson A, Tengblad S, Karlstrom B, Kamal-Eldin A, Landberg R, Basu S, Aman P, Vessby B. Whole-grain foods do not affect insulin sensitivity or markers of lipid peroxidation and inflammation in healthy, moderately overweight subjects. J Nutr 2007;137:1401–7.
31. Kristensen M, Toubro S, Jensen MG, Ross AB, Riboldi G, Petronio M, Bügel S, Tetens I, Astrup A. Whole grain compared with refined wheat decreases the percentage of body fat following a 12-week, energy-restricted dietary intervention in postmenopausal women. J Nutr 2012;142:710–6.
32. Ross AB, Bruce SJ, Blondel-Lubrano A, Oguey-Araymon S, Beaumont M, Bourgeois A, Nielsen-Moennoz C, Vigo M, Fay LB, Kochhar S, et al. A wholegrain cereal-rich diet increases plasma betaine, and tends to decrease total and LDL-cholesterol compared to a refined grain diet in healthy subjects. Br J Nutr 2011;105:1492–502.
33. Zhang G, Pan A, Zong G, Yu Z, Wu H, Chen X, Tang L, Feng Y, Zhou H, Chen X, et al. Substituting white rice with brown rice for 16 weeks does not substantially affect metabolic risk factors in middle-aged Chinese men and women with diabetes or a high risk for diabetes. J Nutr 2011; 141:1685–90.
34. Tucker AJ, MacKay K, Robinson L, Graham T, Bakovic M, Duncan A. The effect of whole grain wheat sourdough bread consumption on serum lipids in healthy normoglycemic/normoinsulinemic and hyperglycemic/hyperinsulinemic adults depends on presence of the APOE E3/E3 genotype: a randomized controlled trial. Nutr Metab 2010;7:37.
35. Bodinham CL, Hitchen KL, Youngman PJ, Frost GS, Robertson MD. Short-term effects of whole-grain wheat on appetite and food intake in healthy adults: a pilot study. Br J Nutr 2011;106:327–30.
36. Van Horn L, Emidy LA, Liu KA, Liao YL, Ballew C, King J, Stamler J. Serum lipid response to a fat-modified, oatmeal-enhanced diet. Prev Med 1988;17:377–86.
37. Johnston L, Reynolds HR, Hunninghake DB, Schultz K, Westereng B. Cholesterol-lowering benefits of a whole grain oat ready-to-eat cereal. Nutr Clin Care 1998;1:6–12.
38. Karmally W, Montez MG, Palmas W, Martinez W, Branstetter A, Ramakrishnan R, Holleran SF, Haffner SM, Ginsberg HN. Cholesterol-lowering benefits of oat-containing cereal in Hispanic americans. J Am Diet Assoc 2005;105:967–70.
39. Maki KC, Beiseigel JM, Jonnalagadda SS, Gugger CK, Reeves MS, Farmer MV, Kaden VN, Rains TM. Whole-grain ready-to-eat oat cereal, as part of a dietary program for weight loss, reduces low-density lipoprotein cholesterol in adults with overweight and obesity more than a dietary program including low-fiber control foods. J Am Diet Assoc 2010;110:205–14.
40. Gilhooly CH, Das SK, Golden JK, McCrory MA, Rochon J, DeLany JP, Freed AM, Fuss PJ, Dallal GE, Saltzman E, et al. Use of cereal fiber to facilitate adherence to a human caloric restriction program. Aging Clin Exp Res 2008;20:513–20.
41. Reynolds HR, Quiter E, Hunninghake DB. Whole grain oat cereal lowers serum lipids. Topics Clin Nutr 2000;15:74–83.
42. Li J, Kaneko T, Qin LQ, Wang J, Wang Y. Effects of barley intake on glucose tolerance, lipid metabolism, and bowel function in women. Nutrition 2003;19:926–9.
43. Leinonen KS, Poutanen KS, Mykkanen HM. Rye bread decreases serum total and LDL cholesterol in men with moderately elevated serum cholesterol. J Nutr 2000;130:164–70.
44. Giacco R, Clemente G, Cipriano D, Luongo D, Viscovo D, Patti L, Di Marino L, Giacco A, Naviglio D, Bianchi MA, et al. Effects of the regular consumption of wholemeal wheat foods on cardiovascular risk factors in healthy people. Nutr Metab Cardiovasc Dis 2010;20:186–94.
45. Kim JY, Kim JH, Lee dH, Kim SH, Lee SS. Meal replacement with mixed rice is more effective than white rice in weight control, while improving antioxidant enzyme activity in obese women. Nutr Res 2008;28:66–71.
46. Pereira MA, Jacobs DR Jr, Pins JJ, Raatz SK, Gross MD, Slavin JL, Seaquist ER. Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults. Am J Clin Nutr 2002;75:848–55.
47. Katcher HI, Legro RS, Kunselman AR, Gillies PJ, Demers LM, Bagshaw DM, Kris-Etherton PM. The effects of a whole grain enriched hypocaloric diet on cardiovascular disease risk factors in men and women with metabolic syndrome. Am J Clin Nutr 2008;87:79–90.
48. van Houwelingen HC, Arends LR, Stijnen T. Advanced methods in meta-analysis: multivariate approach and meta-regression. Stat Med 2002;21:589–624.
49. Normand SL. Meta-analysis: formulating, evaluating, combining, and reporting. Stat Med 1999;18:321–59.
50. Saltzman E, Das SK, Lichtenstein AH, Corrales A, Fuss P, Greenberg AS, Roberts SB. An oat-containing hypocaloric diet reduces systolic blood pressure and improves lipid profile beyond effects of weight loss in men and women. J Nutr 2001;131:1465–70.
51. Van Horn L, Moag-Stahlberg A, Liu KA, Ballew C, Ruth K, Hughes R, Stamler J. Effects on serum lipids of adding instant oats to usual American diets. Am J Public Health 1991;81:183–8.
52. Williams PG, Grafenauer SJ, O'Shea JE. Cereal grains, legumes, and weight management: a comprehensive review of the scientific evidence. Nutr Rev 2008;66:171–82.
53. Wong JM, Jenkins DJ. Carbohydrate digestibility and metabolic effects. J Nutr 2007;137:2539S–46S.
54. Koh-Banerjee P, Rimm EB. Whole grain consumption and weight gain: a review of the epidemiological evidence, potential mechanisms and opportunities for future research. Proc Nutr Soc 2003;62:25–9.
55. McKeown NM, Troy LM, Jacques PF, Hoffmann U, O'Donnell CJ, Fox CS. Whole- and refined-grain intakes are differentially associated with abdominal visceral and subcutaneous adiposity in healthy adults: the Framingham Heart Study. Am J Clin Nutr 2010;92:1165–71.