REVIEW

Whole-Grain Consumption Does Not Affect Obesity Measures: An Updated Systematic Review and Meta-analysis of Randomized Clinical Trials

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ABSTRACT

Since the release of a previous meta-analysis on the effect of whole-grain intake on obesity measures, several clinical trials have been published. Therefore, we aimed to update the previous meta-analysis on the effect of whole-grain intake on obesity measures by including recently published studies, as well as considering the main limitations in that analysis. We searched the online databases of PubMed, Scopus, Clarivate Web of Science, EmBase, and Google Scholar for relevant studies published up to February 2019, using relevant keywords. Randomized clinical trials investigating the effect of whole-grain products or diets high in whole-grain foods, compared with a control diet, on anthropometric measures [including body weight, BMI, waist circumference, and fat mass (FM)] were included. In total, 21 studies with a total sample of 1798 participants, aged ≥18 years, were considered. Based on 22 effect sizes from 19 studies on body weight, with a total sample of 1698 adults, we found no significant effect of whole-grain consumption on body weight. The same findings were obtained for BMIs, such that using 10 effect sizes from 10 clinical trials with a total sample of 769 individuals we did not find any significant effect. With regards to body fat percentage [weighted mean difference (WMD): 0.27; 95% CI: −0.05 to 0.58%; $P = 0.09$], FM (WMD: 0.45; 95% CI: −0.12 to 1.02 kg; $P = 0.12$), fat-free mass (WMD: 0.31; 95% CI: −0.67 to 0.06 kg; $P = 0.10$), and waist circumference (WMD: 0.06; 95% CI: −0.50 to 0.63 cm; $P = 0.82$), we failed to find any significant effect of whole-grain consumption. In conclusion, our findings did not support current recommendations of whole-grain intake in attempts to control obesity measures. Given the beneficial effects of whole-grain intake on other measures of human health, additional well-designed studies are required to further investigate the effect on obesity. The protocol has been registered with PROSPERO (registration number CRD42019125320). *Adv Nutr* 2020;11:280–292.

Keywords: whole grains, obesity, anthropometry, meta-analysis, clinical trials

Introduction

Whole grains are key components of healthy eating patterns (1, 2). They are rich sources of fiber, vitamins B and E, magnesium, antioxidants, and phytoestrogens (2, 3). Consumption of whole grains has been inversely associated with risks of type 2 diabetes, cardiovascular disease, colorectal cancer, and even mortality (3–5). These protective associations may be mediated through the favorable effect of whole-grain consumption on body weight and fat (6, 7).

Whole grains possess a low calorie density and satiating effect, accounting for their potential role in body weight regulation (8). Forming gel-like structures, the soluble fibers in whole grains slow gastric emptying, increase intestinal transit time, and, subsequently, decrease appetite (9). Whole-grain foods can also initiate satiety signals for a longer time through the release of gut hormones, including cholecystokinin, incretins, and peripheral peptide tyrosine-tyrosine (8, 10). In addition, the fermentation of soluble fibers by intestinal microbiota produces SCFAs that may have a benefit

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Address correspondence to AE (e-mail: a-esmaillzadeh@sina.tums.ac.ir).
Abbreviations used: FFM, fat-free mass; FM, fat mass; RCT, randomized clinical trial; WC, waist circumference; WMD, weighted mean difference.

for weight control (9). The key mechanisms by which SCFAs seem to be involved in weight management include delaying gastric emptying, palliating insulin resistance, stimulating glucagon-like peptide-1 release, and suppressing brainstem centers of appetite control (8, 11–13).

Although a large number of observational studies have shown an inverse association between whole-grain intake and the risk of obesity (14–18), findings from clinical trials are conflicting (19–39). A meta-analysis of clinical trials in 2013 revealed no significant effect of whole-grain consumption on body weight (40). However, 10 clinical trials have been published since the release of that meta-analysis (19, 23, 24, 26, 27, 29, 30, 32, 36, 39). Kikuchi et al. (41) found that consumption of whole-grain wheat bread for 12 wk resulted in a significant reduction in the visceral fat area. Reductions in body weight after 8 wk of consuming a whole grain–rich diet were also reported (26). In contrast, others found no significant effects of whole-grain consumption on anthropometric measures (23, 29, 31). Kristensen et al. (30) reported that whole-grain consumption resulted in significant increases in BMIs.

Nevertheless, data in this field are conflicting and there is a need for an updated, comprehensive meta-analysis to summarize earlier findings. The current systematic review and meta-analysis was conducted to summarize available findings on the effects of whole-grain consumption on anthropometric measures.

Methods

This study was performed based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol for reporting systematic reviews and meta-analyses (42).

Search strategy

We performed a systematic review and meta-analysis of randomized clinical trials (RCTs) that assessed the effects of whole-grain consumption on anthropometric measures. We searched PubMed, Scopus, Clarivate Web of Science, and Google Scholar databases up to February 2019, using the following search terms: ("whole grain" OR "whole-grain" OR "whole-grains" OR "oat" OR "grains" OR "cereals" OR "whole wheat" OR "brown rice" OR "barley") AND ("body weight" OR "body weight changes" OR "body mass index" OR "weight loss" OR "obesity" OR "waist circumference", OR "adipose tissue" OR "abdominal fat" OR "weight" OR "Quetelet Index" OR "body mass index" OR "BMI" OR "overweight" OR "fat mass" OR "body fat"). No restrictions were made in terms of time of publication or language. In addition, the reference lists of the relevant articles were screened to avoid missing any relevant publications. Unpublished studies were not considered. In addition, duplicate citations were removed after the search was completed.

Inclusion criteria

Studies with the following criteria were eligible for inclusion: *1*) RCTs investigating the effect of whole-grain products or diets high in whole-grain foods on anthropometric measures, including body weight, BMI, body fat percentage, fat mass (FM), fat-free mass (FFM), and waist circumference (WC); *2*) studies that had a control group in which a diet low in whole grains or a diet without whole grains, whether calorie restricted or not, was prescribed; and *3*) studies that reported means ± SDs for anthropometric measures, or any other effect sizes from which the calculation of means ± SDs was possible. If >1 publications were found for 1 data set, the more complete publication was included. Studies with 3 eligible arms were considered as 2 separate studies.

Exclusion criteria

In the current meta-analysis, we excluded letters, comments, short communications, reviews, meta-analyses, ecologic studies, and animal studies. In our initial search, we found 1129 articles, out of which 1073 were identified as unrelated after reviewing for titles and abstracts. By investigating the full texts of articles, an additional 35 articles were excluded due to the following reasons: *1*) studies that administered whole grains as a supplement (tablet or capsule; $n = 12$); *2*) studies that did not provide required data or reported only baseline values of anthropometric measures ($n = 20$); *3*) studies that were quasi-experimental, without any control group ($n = 2$) (43, 44); and *4*) an RCT that compared the effects of 2 different whole-grain foods without any control group ($n = 1$) (45). Finally, 21 studies remained for inclusion in the current systematic review and meta-analysis (**Table 1**) (19–39): 19 studies had provided data for body weight (19, 21–38), 10 for BMI (19, 20, 22, 24, 26, 29–32, 39), 8 for body fat percentage (19, 21, 27–30, 32, 36), 4 for FM (24, 27, 29, 32) and FFM (27, 30–32), and 10 for WC (19, 23, 24, 26–31, 36). A flow diagram of the study selection is shown in **Figure 1**.

Compared with the meta-analysis of Pol et al. (40), which included 26 clinical trials, we included 21 RCTs in the current meta-analysis (19–39). In the current meta-analysis, unlike that of Pol et al. (40), we did not include RCTs examining the effects of individual whole grains on anthropometric measures (46–49). An individual whole grain is defined as a single type of whole-grain food item, such as brown rice, or a single type of whole-grain product, such as a whole-grain biscuit; in comparison, studies that did interventions with whole-grain diets or products administered at least 2 types of whole-grain food items. Furthermore, Pol et al. (40) included a quasi-experimental study (44) without any control group. Therefore, the number of included studies are different when comparing Pol et al.'s (40) analysis and ours.

Data extraction

We collected data on the first author's name, year of publication, mean age ± SD of participants in each group, health status of study subjects, sample size, number and sex of participants in each group, length of the intervention (week), study design (parallel, crossover), foods provided, types and amounts of whole grains, control diet, and type of intervention (feeding/semi-feeding/nonfeeding). When data

TABLE 1 Characteristics of studies included in the current systematic review and meta-analysis[1]

Author (ref)	Participants, *n*	Age,[2] y	Health condition	Design	Diet type		Duration, wk	Outcome		Adjust/matching
					Intervention	Control		Intervention[3]	Control[3]	
Ampatzoglou et al. (19)	F: 21, M: 12; WG: 33, RG: 33	48.8 ± 1.1	Healthy	RCT, crossover	WG diet; WG ≥ 80 g/d	RG diet; WG ≤ 16 g	6	BW, pre: 77.5 ± 14.3 kg, post: 77.3 ± 14.9 kg; BMI, pre: 28.1 ± 4.0 kg/m^2, post: 28.0 ± 4.0 kg/m^2; BF, pre: 32.1 ± 9.1%, post: 32.2 ± 8.6%; WC, pre: 95.6 ± 12.0 cm, post: 96.0 ± 11.4 cm	BW, pre: 77.5 ± 14.3 kg, post: 77.7 ± 14.3 kg; BMI, pre: 28.0 ± 4.0 kg/m^2, post: 28.1 ± 4.0 kg/m^2; BF, pre: 31.8 ± 8.6%, post: 31.9 ± 8.6%; WC, pre: 96.2 ± 11.4 cm, post: 95.8 ± 11.4 cm	Matched for age, sex, and BMI
Giacco et al. (24)	F: 65, M: 58; WG: 62, Cnt: 61	40–65	Metabolic syndrome	RCT, parallel	WG products	RG products	12	BW, pre: 88.6 ± 15.8 kg, post: 87.9 ± 18.3 kg; BMI, pre: 31.6 ± 4.6 kg/m^2, post: 31.0 ± 5.8 kg/m^2; FM, pre: 32.3 ± 9.3 kg, post: 32.2 ± 9.4 kg; WC, pre: 106.7 ± 13.0 cm, post: 106.4 ± 12.8 cm	BW, pre: 87.8 ± 15.8 kg, post: 87.8 ± 16.1 kg; BMI, pre: 31.3 ± 4.4 kg/m^2, post: 31.3 ± 4.5 kg/m^2; FM, pre: 30.9 ± 9.8 kg, post: 31.2 ± 10.3 kg; WC, pre: 105.8 ± 10.7 cm, post: 105.8 ± 10.8 cm	Adjusted for baseline measurements. Matched for age, sex, and BMI
Giacco et al. (23)	Both: 54; WG: 28, RG: 26	40–65	Metabolic syndrome	RCT, parallel	WG products	RG products	12	BW, pre: 87.9 ± 16.7 kg, post: 87.4 ± 15.8 kg; WC, pre: 107.3 ± 15.5 cm, post: 107.4 ± 14.6 cm	BW, pre: 85.2 ± 19.0 kg, post: 84.7 ± 19.3 kg; WC, pre: 105.7 ± 12.0 cm, post: 105.2 ± 12.3 cm	Matched for age, sex, and BMI
Harris Jackson et al. (26)	F: 25, M: 25; WG: 25, RG: 25	WG: 46.40 ± 5.90; RG: 45.80 ± 6.0	Overweight and obesity	RCT, parallel, open-label	WG products; WG: 232 g/d, hypocaloric diet	RG products; WG: 0 g/d, hypocaloric diet	12	BW, change: −5.0 ± 2.0 kg; BMI, change: −1.7 ± 0.5 kg/m^2; WC, change: −2.3 ± 3.5 cm	BW, change: −4.4 ± 2.0 kg; BMI, change: −1.5 ± 0.5 kg/m^2; WC, change: −3.9 ± 3.5 cm	Adjusted for age, sex, and baseline measurements. Matched for age, sex, and BMI
Kirwan et al. (29)	F: 27, M: 6; WG: 33, RG: 33	39.0 ± 7.0	Overweight and obesity	RCT, crossover	WG products; WG: 93 g/d	RG products; WG: 0 g/d	8	BW, change: −2.4 ± 2.8 kg; BMI, change: −0.9 ± 0.9 kg/m^2; BF, change: −1.1 ± 1.8%; FM, change: −1.8 ± 2.8 kg; FFM, change: −6.0 ± 1.2 kg; WC, change: −2.1 ± 5.0 cm	BW, change: −2.5 ± 2.8 kg; BMI, change: −0.9 ± 0.9 kg/m^2; BF, change: −1.1 ± 1.4%; FM, change: −2.2 ± 2.2 kg; FFM, change: −0.5 ± 1.1 kg; WC, change: −2.4 ± 4.7 cm	Adjusted for age, sex, baseline measurements, fiber intake, and body fat change
Kristensen et al. (30)	F: 169; WG: 81, RG: 88	WG: 36.2 ± 10.1; RG: 35.3 ± 8.7	Overweight and obesity	RCT, parallel, open-label	WG products; WG: 124 g/d	RG products; WG: 0.5 g/d	12	BW, change: 0.4 ± 2.3 kg; BMI, change: 1.8 ± 0.9 kg/m^2; BF, change: 0.4 ± 2.3%; WC, change: 0.0 ± 3.2 cm	BW, change: 0.4 ± 2.7 kg; BMI, change: 0.1 ± 1.0 kg/m^2; BF, change: −0.2 ± 2.9%; WC, change: −0.1 ± 4.2 cm	Adjusted for age and baseline measurements
Malin et al. (32)	F: 11, M: 3; WG: 14, RG: 14	37.90 ± 1.80	Obesity	RCT, crossover	WG diet; WG: 90.5 g/d	RG diet; WG: 0 g/d	8	BW, change: −2.8 ± 2.6 kg; BMI, change: −1.0 ± 0.7 kg/m^2; BF, change: −0.8 ± 0.7%; FM, change: −2.2 ± 1.8 kg; FFM, change: −1.0 ± 0.7 kg	BW, change: −2.5 ± 2.2 kg; BMI, change: −0.9 ± 0.7 kg/m^2; BF, change: −1.5 ± 1.1%; FM, change: −2.7 ± 2.0 kg; FFM, change: −0.2 ± 1.1 kg	Adjusted for age, body fat change, baseline measurements, and fiber intake
Karl et al. (27)	F: 32, M: 49; WG: 41, RG: 40	WG: 55 ± 6; RG: 54 ± 5	Normal weight, overweight, and obesity	RCT, parallel	WG diet; WG: 207 g/d	RG diet; WG: 0 g/d	6	BW, change: −0.1 ± 1.7 kg; BF, change: −0.2 ± 2.2%; FM, change: −0.1 ± 1.9 kg; FFM, change: 0.1 ± 1.9 kg; WHR, change: −0.001 ± 0.03; WC, change: −0.6 ± 2.5 cm	BW, change: −0.5 ± 1.8 kg; BF, change: −0.9 ± 2.1%; FM, change: −0.8 ± 1.8 kg; FFM, change: 0.3 ± 1.2 kg; WHR, change: −0.001 ± 0.03; WC, change: −0.2 ± 3.1 cm	Adjusted for age, sex, and baseline measurements
Vetrani et al. (39)	F: 24, M: 16; WG: 21, RG: 19	WG: 57.2 ± 1.9; RG: 58.4 ± 1.6	Metabolic syndrome	RCT, parallel	WG products	RG products	12	BMI, pre: 32.1 ± 6.4 kg/m^2, post: 31.9 ± 6.4 kg/m^2	BMI, pre: 31.5 ± 5.6 kg/m^2, post: 31.3 ± 5.6 kg/m^2	N/R
Roager et al. (36)	F: 32, M: 18; WG: 50, Cnt: 50	20–56	Overweight and obesity	RCT, crossover	WG products; WG: 158 g/d	RG products; WG: 6 g/d	8	BW, pre: 85.4 ± 13.4 kg, post: 85.2 ± 13.1 kg; BF, pre: 28.8 ± 9.1%, post: 28.6 ± 9.5%; WC, pre: 100.1 ± 8.4 cm, post: 99.4 ± 9.3 cm	BW, pre: 86.1 ± 12.6 kg, post: 87.0 ± 13.0 kg; BF, pre: 29.1 ± 9.2%, post: 29.8 ± 9.3%; WC, pre: 100.4 ± 8.6 cm, post: 100.8 ± 9.1 cm	Adjusted for age and sex

(*Continued*)

TABLE 1 (*Continued*)

Author (ref)	Participants, *n*	Age,[2] y	Health condition	Design	Diet type		Duration, wk	Outcome		Adjust/matching
					Intervention	Control		Intervention[3]	Control[3]	
De Mello et al. (22)	F: 27, M: 6; WG: 34, Cnt: 34	WG: 58 ± 8; Cnt: 59 ± 7	Overweight and obesity	RCT, parallel	Whole oat products	RG products	12	BW, pre: 89.2 ± 15.3 kg, post: 89.1 ± 15.3 kg; BMI, pre: 31.4 ± 3.4 kg/m^2, post: 31.4 ± 3.4 kg/m^2	BW, pre: 89.5 ± 13.2 kg, post: 89.9 ± 13.1 kg; BMI, pre: 30.9 ± 3.5 kg/m^2, post: 31.0 ± 3.6 kg/m^2	Adjusted for age, sex, and baseline measurements
Melanson et al. (34)	F: 70, M: 19; WG: 45, Cnt: 46	WG: 42.5 ± 0.9; Cnt: 41.7 ± 1.2	Healthy	RCT, parallel	Exercise plus a hypocaloric diet containing WG products	Exercise plus a hypocaloric diet without WG products	24	BW, change: −5.70 ± 4.69 kg	BW, change: −6.20 ± 4.75 kg	N/R
Brownlee et al. (21)	F: 133, M: 133; Group 1: 85, Group 2: 81; Cnt: 100	46 ± 10	Cardiovascular disease or diabetes	RCT, parallel	Group 1: WG diet containing 60 g/d WG for 16 wk; Group 2: WG diet containing 120 g/d WG for 8 wk	Habitual diet (WG ≤ 30 g/d)	8/16	Group 1: BW, pre: 86.70 ± 14.20 kg, post: 87.40 ± 14.80 kg BF, pre: 34.00 ± 8.30%, post: 35.00 ± 8.20%; Group 2: BW, pre: 86.30 ± 14.20 kg, post: 87.40 ± 14.80 kg BF, pre: 33.40 ± 9.10%, post: 33.60 ± 9.50%	BW, pre: 86.70 ± 14.00 kg, post: 86.70 ± 13.80 kg; BF, pre: 34.60 ± 9.10%, post: 34.90 ± 9.00%	Matched for age, sex, and BMI
Andersson et al. (20)	F: 22, M: 8; WG: 30, RG: 30	WG: 28.3 ± 2; Cnt: 59 ± 5	Overweight	RCT, crossover	WG products; WG: 112 g/d	RG products	6	BMI, pre: 28.50 ± 2.40 kg/m^2, post: 28.80 ± 2.50 kg/m^2	BMI, pre: 28.40 ± 2.10 kg/m^2, post: 28.60 ± 2.10 kg/m^2	Adjusted for age
Gilhooly et al. (25)	F: 25, M: 8; WG: 16, RG: 17	WG: 27.50 ± 1.40; RG: 35 ± 5	Overweight	RCT, parallel	WG diet	RG diet	6	BW, change: −2.70 ± 0.898 kg	BW, change: −2.67 ± 1.61 kg	N/R
Pereira et al. (35)	F: 6, M: 5; WG: 11, RG: 11	WG: 42 ± 9; RG: 30.2 ± 3.3	Overweight and obesity, hyperinsulinemia	RCT, crossover	WG diet; WG: 386 g/d	RG diet	6	BMI, pre: 85.62 ± 1.33 kg/m^2, post: 84.17 ± 0.99 kg/m^2	BMI, pre: 86.20 ± 1.29 kg/m^2, post: 84.90 ± 0.83 kg/m^2	Adjusted for baseline measurements
Katcher et al. (28)	F: 25, M: 25; WG: 25, RG: 25	WG: 46 ± 9; RG: 35.8 ± 4.5	Metabolic syndrome	RCT, parallel	Hypocaloric WG-rich diet	Hypocaloric RG-rich diet	12	BW, change: −3.70 ± 3.50 kg; BF, change: −1.20 ± 1.30%; WC, change: −2.50 ± 3.70 cm	BW, change: −2.30 ± 5.20 kg; BF, change: −1.00 ± 1.60%; WC, change: −4.70 ± 6.40 cm	Adjusted for baseline measurements. Matched for sex and BMI
Kristensen et al. (31)	F: 72; WG: 38, RG: 34	WG: 59.1 ± 5.6; RG: 60.3 ± 5.3	Overweight and obesity, postmenopausal	RCT, parallel, open-label	WG wheat products; WG: 105 g/d	Refined wheat products	6	BW, pre: 81.30 ± 8.01 kg, post: 77.70 ± 1.30 kg; BMI, pre: 30.00 ± 2.47 kg/m^2, post: 28.70 ± 1.40 kg/m^2; FFM, pre: 42.90 ± 4.93 kg, post: 43.20 ± 0.07 kg; WC, pre: 97.30 ± 1.20 cm, post: 93.20 ± 1.20 cm	BW, pre: 83.50 ± 11.08 kg, post: 80.80 ± 7.58 kg; BMI, pre: 30.40 ± 3.49 kg/m^2, post: 29.40 ± 9.91 kg/m^2; FFM, pre: 44.00 ± 4.08 kg, post: 44.20 ± 4.08 kg; WC, pre: 99.00 ± 8.75 cm, post: 94.90 ± 8.16 cm	Adjusted for age and baseline measurements
McIntosh et al. (33)	M: 28; WG: 28, RG: 28	30 ± 4.8	Overweight	RCT, crossover	WG rye products; WG: 88 g/d; WG wheat products; WG: 88 g/d	RG products	4	WMD for rye products, BW: 0.00 ± 2.70 kg; WMD for wheat products, BW: 0.00 ± 2.70 kg	N/R	N/R
Tighe et al. (38)	F: 102, M: 104; Group 1: 73, Group 2: 70; RG: 63	Group 1: 28 ± 0.5; Group 2: 27 ± 0.4; RG: 28 ± 0.5	Healthy	RCT, parallel	Group 1: WG wheat products; WG: 110 g/d; Group 2: WG wheat products + oats products; WG: 110 g/d	RG products	16	Group 1: BMI, pre: 28.00 ± 4.09 kg/m^2, WMD: 0 ± 2.12 kg/m^2; Group 2: BMI, pre: 27.00 ± 3.28 kg/m^2, WMD: 0 ± 2.15 kg/m^2	RGs: BMI, pre: 28.00 ± 4.09 kg/m^2	Matched for age, sex, and BMI
Ross et al. (37)	F: 11, M: 6; WG: 17, RG: 17	35 ± 4	Healthy	RCT, crossover	WG diet; WG: 151 g/d	RG diet	2	Female: BW, pre: 63.80 ± 9.89 kg; Male: BW, pre: 78.30 ± 12.36 kg; WMD for both sexes, BW: −0.50 ± 1.48 kg	Female: BW, pre: 63.40 ± 9.06 kg; Male: BW, pre: 78.20 ± 12.77 kg	Adjusted for age, sex, and baseline measurements. Matched for study center

[1] Abbreviations: BF, body fat; BW, body weight; Cnt, control; FFM, fat-free mass; FM, fat mass; N/R, not reported; RCT, randomized clinical trial; ref, reference; RG, refined grain; WC, waist circumference; WHR, waist-to-hip ratio; WG, whole grain; WMD, weighted mean difference.
[2] Values are means ± SDs or ranges.
[3] Values are means ± SDs.

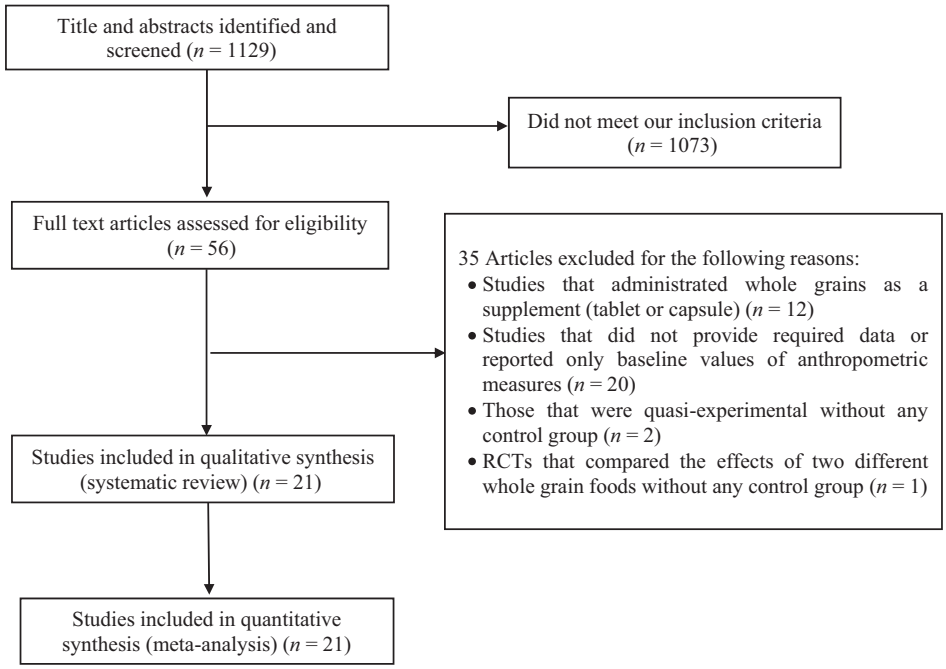

FIGURE 1 Flow diagram of study selection. RCT, randomized clinical trial.

for an anthropometric measure were reported in different units, we converted them to the most frequently used unit.

Risk of bias assessment

Each study was assessed for the risk of bias by 2 independent reviewers, using the Cochrane Risk of Bias Assessment tool (50). Domains of assessment were included, such as random sequence generation, allocation concealment, reporting bias, performance bias, detection bias, attrition bias, and other sources of bias. Each domain was scored as "high risk" if it contained methodological flaws that may have affected the results, "low risk" if the flaw was deemed inconsequential, and "unclear risk" if information was insufficient to determine the impact. Details on the scoring of each domain of the Cochrane Risk of Bias Assessment tool are presented in **Supplemental Table 1**. If a study was labeled as low risk for all domains, it was considered as a high-quality study with a total low risk of bias. We considered a study as low quality if that study was scored as high risk for at least 1 domain of the Cochrane Risk of Bias Assessment tool. Disagreements were resolved by consensus. Findings from the risk of bias assessment are shown in **Supplemental Table 2**.

Statistical analysis

Mean differences in changes of anthropometric measures, comparing whole-grain and control groups, were used to calculate the overall effect size. When mean differences were not reported, we calculated them by considering changes in each anthropometric measure throughout the study. We converted reported SEs, 95% CIs, and IQRs to SDs using relevant formulas. The overall effect size was calculated using a random-effects model, which takes between-study variations into account. Cochran's Q test and the I^2 statistic were used to assess between-study heterogeneity. In addition, we did subgroup analyses to detect probable sources of heterogeneity, with the use of a fixed-effects model. Subgroup analyses were conducted based on sex (both/females), mean baseline values of BMI ($\geq$30 vs. $<$30 kg/m^2), participants' health conditions (healthy vs. unhealthy individuals), duration of intervention ($\geq$8 vs. $<$8 wk), study design (parallel vs. crossover), administration of whole grains in the context of hypocaloric versus isocaloric diets, using a whole-grain diet versus whole-grain products for intervention, and considering anthropometric measures as primary versus accessory outcomes. Sensitivity analyses were used to explore the extent to which inferences might depend on a particular study. The possibility of a publication bias was examined by the visual inspection of funnel plots and the application of Begg's test. All statistical analyses were conducted using Stata, version 11.2 (StataCorp). P values < 0.05 were considered as statistically significant.

Results

Findings from the systematic review

Overall, 21 studies, which were published between 2002 and 2019, were included in our systematic review (19–39). Characteristics of included studies are shown in Table 1. The total population of these studies was 1798 participants, aged $\geq$18 y. Most studies included both sexes, although 2 studies were done on females only (30, 31). Out of 21 studies, 6 studies were performed in the United States (25–28, 34, 35), 1 in Australia (33), and the remaining studies

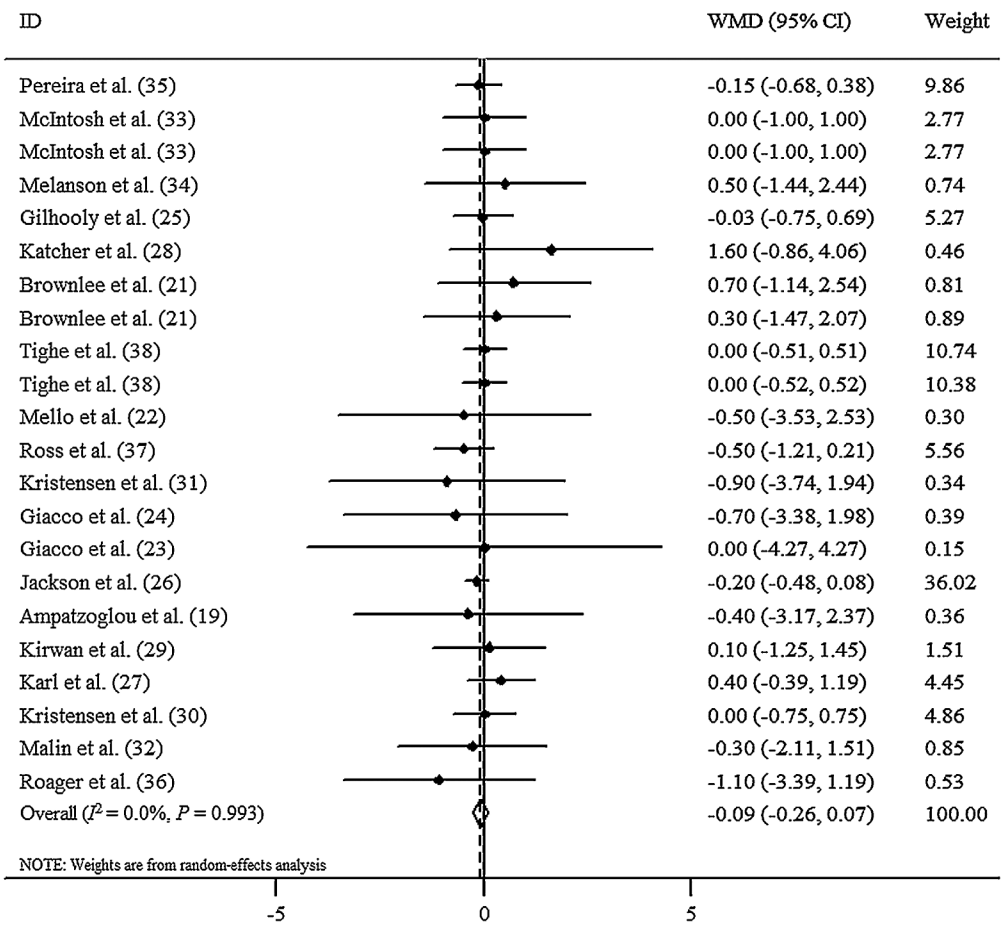

FIGURE 2 Forest plot for the effect of whole-grain consumption on body weight, expressed as mean differences between intervention and control groups. The area of each square is proportional to the inverse of the variance of the WMD. Horizontal lines represent 95% CIs. Diamonds represent pooled estimates from random-effects analysis. WMD, weighted mean difference.

on Europeans (19–24, 29–32, 36–39). There were 8 studies that had crossover designs (19, 20, 29, 32, 33, 35–37), and the others were parallel (21–28, 30, 31, 34, 38, 39).

There were 12 studies conducted with individuals who were overweight or obese (20, 22, 25–27, 29–33, 35, 36), 4 with healthy individuals (19, 34, 37, 38), 4 studies with persons who had metabolic syndrome (23, 24, 28, 39), and 1 with patients with diabetes or cardiovascular diseases (21). There were 5 RCTs that did the intervention with whole grains along with a hypocaloric diet (25, 26, 28, 31, 34), while other studies recommended energy intakes based on participants' requirements (19–24, 27, 29, 30, 32, 33, 35–39). In the current analysis, the effects of 2 different types of intervention were examined: *1*) a whole grain–containing diet (i.e., a diet containing a mix of different types of whole-grain foods); and *2*) whole-grain products (i.e., products contained a minimum of 50% whole grain per dry matter) (51, 52). There were 11 studies that compared whole grain–containing diets with control diets containing refined-grain foods (19, 21, 25–29, 32, 33, 35, 37), whereas others had compared whole-grain products with refined-grain products (20, 22–24, 30, 31, 34, 36, 38, 39). There were 16 feeding trials (19–21, 23–27, 29, 31–36, 39), and 4 were done on nonfeeding conditions (22, 28, 37, 38). In Kristensen et al.'s (30) study, participants were asked to purchase their whole- or refined-grain foods from a supermarket, which was considered as a semi-feeding trial. There were 3 studies that had a third arm (21, 33, 38); out of them, 1 had examined a different dose of whole grains in the third arm (21) and 1 had examined a different type of whole grains, with the same dosage, in the intervention arm (33, 38). These arms were considered as separate studies. Durations of intervention in the included clinical trials varied from 2 to 24 wk. There were 10 studies that controlled their analyses for baseline values of anthropometric measures (22, 24, 27–32, 35, 37). None of the studies had a low risk of bias in all domains of the Cochrane Risk of Bias Assessment tool (Supplemental Table 1).

Among 19 studies on body weight (19, 21–38), no study had reported a significant effect on weight following whole-grain intake. Only 1 study found any significant effect on BMIs: in it, whole-grain consumption resulted in a significant increase in BMIs, compared with the control group (30). None of 8 studies showed a significant effect of whole-grain consumption on body fat (19, 21, 27–30, 32, 36), and none

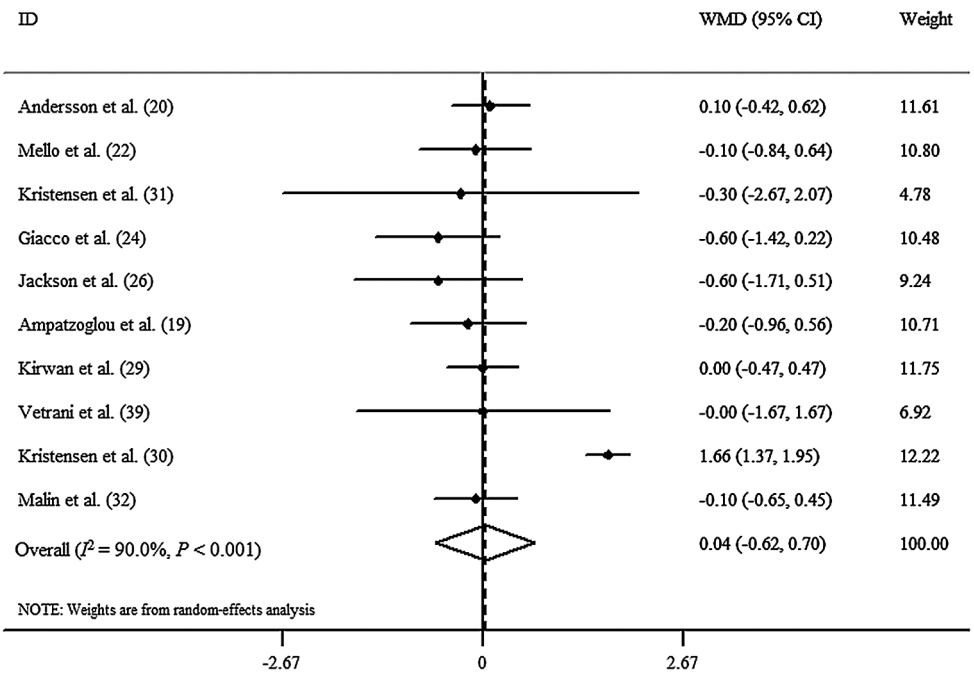

FIGURE 3 Forest plot for the effect of whole-grain consumption on BMI, expressed as mean differences between intervention and control groups. The area of each square is proportional to the inverse of the variance of the WMD. Horizontal lines represent 95% CIs. Diamonds represent pooled estimates from random-effects analysis. WMD, weighted mean difference.

had reached a beneficial effect. There were 4 studies that examined the effect of whole-grain consumption on FM (24, 27, 29, 32); all reached nonsignificant effects. Only 1 study revealed a reducing effect of whole-grain consumption on FFM (32), while others did not reach any significant effect (27, 29, 31). None of 10 studies showed a significant effect of whole-grain consumption on WC (19, 23, 24, 26–31, 36).

Findings from the meta-analysis

In total, 21 studies assessed in the systematic review were included in the current meta-analysis. These studies included 1798 participants, aged ≥18 y.

The effect of whole grains on body weight

Overall, 22 effect sizes from 19 studies with a total sample of 1698 adults were included in the analysis of the impact of whole grains on body weight (19, 21–38). Combining these effect sizes revealed no significant effect of whole grains on body weight [weighted mean difference (WMD): −0.09, 95% CI: −0.26 to 0.07 kg; $P = 0.26$; **Figure 2**], without a significant between-study heterogeneity (I^2, 0; $P = 0.99$). A sensitivity analysis revealed that the overall estimate did not depend on a single study. According to the Begg test ($P = 0.82$), and based on a visual inspection of the funnel plot, no evidence of a publication bias was found.

The effect of whole grains on BMI

Overall, 10 effect sizes from 10 clinical trials with a total population of 769 individuals were included in the analysis of the impact of whole grains on BMI (19, 20, 22, 24, 26, 29–32, 39). Pooling these effect sizes, we found no significant effect of whole-grain consumption on BMI (WMD: −0.04; 95% CI: −0.62 to 0.70 kg/m^2; $P = 0.91$; **Figure 3**). However, the between-study heterogeneity was significant (I^2, 90.0; $P < 0.001$). To find the source of heterogeneity, we did subgroup analyses based on sex, mean baseline values of BMI (≥30 vs. <30 kg/m^2), participants' health conditions (healthy vs. unhealthy individuals), durations of interventions (≥8 vs. <8 wk), study designs (parallel vs. crossover), the administration of whole grains in the context of hypocaloric versus isocaloric diets, the use of a whole-grain diet versus whole-grain products for an intervention, and considering anthropometric measures as primary versus accessory outcomes (**Table 2**). In this analysis, RCTs that were conducted on individuals with diagnoses of diabetes, metabolic syndrome, being overweight, and obesity were considered as the "unhealthy" subgroup. We found that between-study heterogeneity was explained by all the above-mentioned variables. Whole-grain intake resulted in a significant increase in BMIs after combining 8 effect sizes from studies done on individuals with baseline mean BMIs of ≥30 kg/m^2 (WMD: 0.74; 95% CI: 0.54–0.95 kg/m^2; $P < 0.001$), 6 effect sizes from RCTs that used whole-grain products for interventions (WMD: 0.98; 95% CI: 0.71–1.21 kg/m^2; $P < 0.001$), 9 effect sizes from studies that were performed on unhealthy individuals (WMD: 0.66; 95% CI: 0.47–0.85 kg/m^2; $P < 0.001$), 7 effect sizes from studies that had intervention durations of ≥8 wk (WMD: 0.75; 95% CI: 0.55–0.85 kg/m^2; $P < 0.001$), 6 effect sizes from RCTs

TABLE 2 Subgroup analysis on the effects of whole-grain consumption on BMI

	Effect sizes, *n*	Mean (95% CI)	*P*: within[1]	I^2,[2] %	*P*: between
Overall	10	0.61 (0.54, 0.95)	<0.001	90.0	
Sex					<0.001
Both	8	−0.11 (−0.34 to 0.13)	0.38	0	
Females	2	1.63 (1.35–1.92)	<0.001	61.4	
Baseline mean of BMI					0.002
Nonobese (<30 kg/m^2)	2	0.01 (−0.42 to 0.43)	0.98	0	
Obese (≥30 kg/m^2)	8	0.74 (0.54–0.95)	<0.001	91.3	
Health condition					<0.001
Healthy	1	−0.20 (−0.96 to 0.56)	0.60	0	
Unhealthy	9	0.66 (0.47–0.85)	<0.001	90.6	
Duration of intervention					0.002
<8 wk	3	−0.00 (−0.43 to 0.42)	0.98	0	
≥8 wk	7	0.75 (0.55–0.95)	<0.001	92.4	
Study design					<0.001
Parallel	6	1.10 (0.86–1.35)	<0.001	90.6	
Crossover	4	−0.02 (−0.30 to 0.25)	0.87	0	
Calorie restriction					0.02
Hypocaloric diet	2	−0.55 (−1.55 to 0.46)	0.28	0	
Isocaloric diet	8	0.65 (0.46–0.84)	<0.001	91.7	
Intervention type					<0.001
Whole-grain diet	4	−0.11 (−0.43 to 0.20)	0.47	0	
Whole-grain products	6	0.98 (0.76–1.21)	<0.001	91.3	
Anthropometric measures as:					<0.001
Primary outcome variables	5	1.00 (0.77–1.23)	<0.001	92.9	
Secondary outcome variables	5	−0.10 (−0.40 to 0.21)	0.53	0	

[1] Refers to the mean (95% CI).
[2] Inconsistency, percentage of variation across studies due to heterogeneity.

with parallel designs (WMD: 1.10; 95% CI: 0.86–1.35 kg/m^2; $P < 0.001$), 8 effect sizes from RCTs that administered whole grains along with an isocaloric diet (WMD: 0.65; 95% CI: 0.46–0.84 kg/m^2; $P < 0.001$), 2 effect sizes from those studies that were conducted on females only (WMD: 1.63; 95% CI: 1.35–1.92 kg/m^2; $P < 0.001$), and 5 effect sizes from studies that considered BMI as the primary outcome variable (WMD: 1.00; 95% CI: 0.75–1.23 kg/m^2; $P < 0.001$).

The sensitivity analysis revealed that the exclusion of any single study did not alter the overall effect size. We found no evidence of a substantial publication bias based on the visual inspection of the funnel plot and a formal Begg test.

The effect of whole grains on body fat percentage

Combining 9 effect sizes from 8 studies (19, 21, 27–30, 32, 36) with a total population of 853 individuals, no significant effect of whole-grain consumption on body fat percentage was seen (WMD: 0.26; 95% CI: −0.08 to 0.59%; $P = 0.12$; **Figure 4**). The between-study heterogeneity was not significant (I^2, 9.5; $P = 0.35$). Sensitivity analyses and funnel plots provided no further information.

The effect of whole grains on fat mass and fat-free mass

Considering 4 effect sizes for FM and 4 effect sizes for FFM, obtained from 5 studies (24, 27, 29, 31, 32) (a total sample of 298 participants for FM and 247 subjects for FFM), we found no significant effect of whole-grain consumption on FM (WMD: 0.45; 95% CI: −0.12 to 1.02 kg; $P = 0.12$) or FFM (WMD: 0.31; 95% CI: −0.67 to 0.06 kg; $P = 0.10$; **Figure 5**). In both analyses, no evidence of between-study heterogeneity was found (I^2, 0). Based on findings from sensitivity analyses, overall estimates obtained for FM and FFM did not depend on a particular study. No evidence of a publication bias was found.

The effect of whole-grain intake on waist circumference

There were 10 studies (19, 23, 24, 26–31, 36), providing 10 effect sizes, with a total sample of 823 individuals, included in the analysis of the impact of whole grains on WC. Based on them, no significant effect of whole-grain intake on WC was observed (WMD: 0.06; 95% CI: −0.50 to 0.63 cm; $P = 0.82$; **Figure 6**). No significant between-study heterogeneity was seen (I^2, 0; $P = 0.56$). A sensitivity analysis revealed that the summary effect size was not influenced by a particular study. No evidence of a substantial publication bias was seen based on the Begg test and a visual inspection of the funnel plot ($P = 0.09$).

Discussion

Unlike earlier reports from observational studies, we found no beneficial effects of whole-grain consumption on anthropometric measures, including body weight, BMI, body fat percentage, FM, FFM, and WC. However, subgroup analyses revealed a significant effect of whole-grain consumption on increased BMIs in some subgroups. Although a previous meta-analysis in 2013 had reported the effects of whole

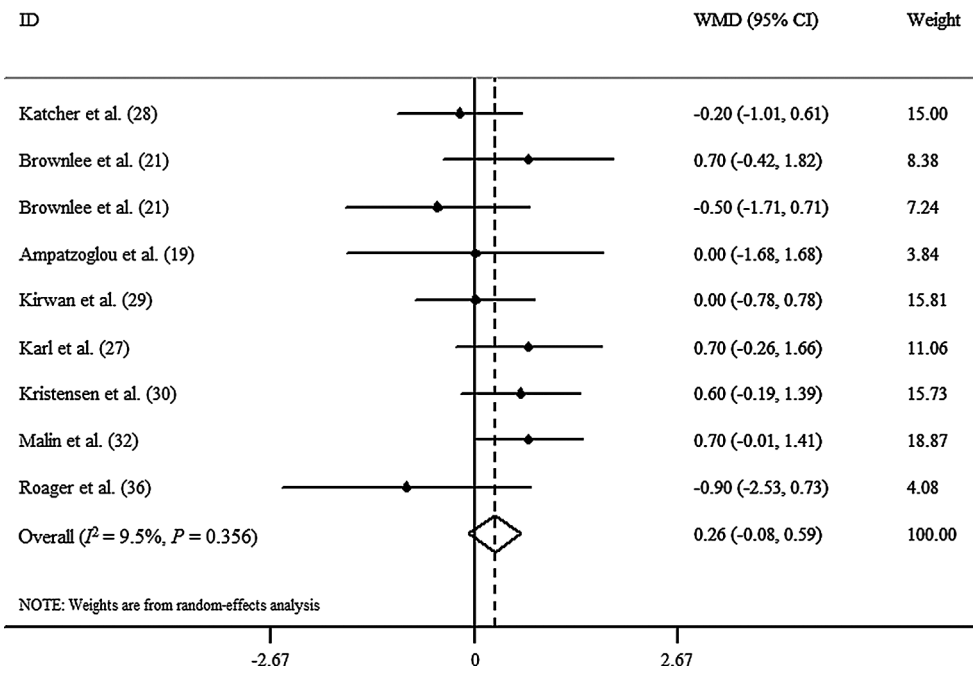

FIGURE 4 Forest plot for the effect of whole-grain consumption on body fat percentage, expressed as mean differences between intervention and control groups. The area of each square is proportional to the inverse of the variance of the WMD. Horizontal lines represent 95% CIs. Diamonds represent pooled estimates from random-effects analysis. WMD, weighted mean difference.

grains on body weight and BMI (40), this is the first study summarizing earlier publications on the effects of whole grains on FM and FFM.

Whole grains contain high amounts of fiber, which has been proposed to be effective in weight-loss programs (53–55). Findings from a large number of observational studies have also suggested protective associations between whole-grain intake and risks of obesity and weight gain (8–12). However, we observed no significant effects of whole-grain intake on body weight, BMI, body fat percentage, FM, and FFM. A meta-analysis in 2013 (40) revealed no significant effects of whole-grain intake on body weight and BMI; however, the authors in that meta-analysis (40) found a significant effect of whole grains on reduced body fat percentage. That meta-analysis had some limitations which might have distorted the findings. For example, the investigators in that study included a quasi-experimental study without any control group (44). We did not include quasi-experimental studies in this analysis. Furthermore, effect sizes from RCTs that administered individual, whole-grain foods were combined with those that prescribed diets rich in whole grains in that meta-analysis in 2013, while we did not include studies that administered individual, whole-grain foods in the current analysis because people do not consume individual foods in their usual diet; rather, they adhere to dietary patterns that are rich in several whole-grain foods and products. In addition, the effect of individual whole-grain foods on body fat might be negligible and undetectable, while the consumption of whole-grain products in the framework of a whole grain–rich dietary pattern, which consists of several whole-grain foods and products, can easily be detected.

These differences might explain the discrepant findings. In addition to the effect of whole grains on obesity measures, previous meta-analyses on clinical trials revealed a beneficial effect of whole-grain consumption on obesity-related conditions, including hyperlipidemia, diabetes, hypertension, and cardiovascular diseases (56, 57). Therefore, whole grains might have beneficial effects on human health, but the recommendations to increase these foods in an effort to control body weight and fat require further conclusive evidence.

When we did subgroup analyses, we found that whole-grain consumption resulted in a significant increase in BMIs in studies done on individuals with baseline mean BMIs of $\geq$30 kg/m^2 (number of effect sizes = 8), those that used whole-grain products for interventions (number of effect sizes = 6), those that were performed on unhealthy individuals (number of effect sizes = 9), and those that had an intervention duration of $\geq$8 wk (number of effect sizes = 7). Our findings on the effects of whole grains on BMIs in these subgroups might be explained by several reasons. Most of the studies in these subgroups added whole-grain foods to the diet, rather than substituting them for nonwhole-grain foods. The addition of whole-grain foods to the diet would result in increased energy intake, which can, in turn, lead to an increased BMI. In addition, out of 10 studies examining the effect of whole grains on BMI (19, 20,

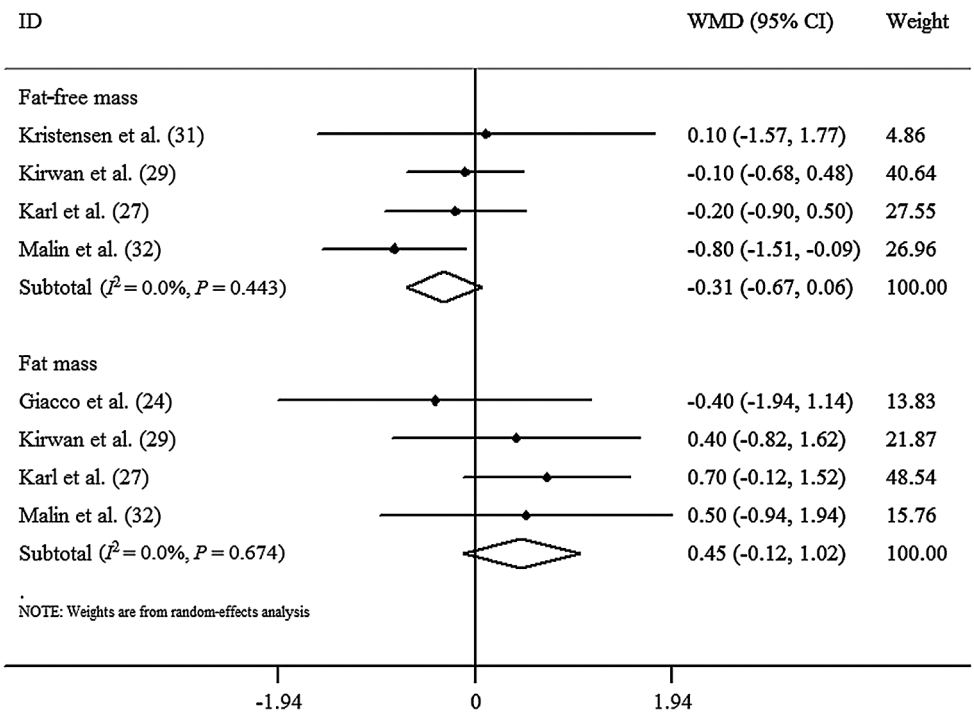

FIGURE 5 Forest plots for the effect of whole-grain consumption on fat mass and fat-free mass, expressed as mean differences between intervention and control groups. The area of each square is proportional to the inverse of the variance of the WMD. Horizontal lines represent 95% CIs. Diamonds represent pooled estimates from random-effects analysis. WMD, weighted mean difference.

22, 24, 26, 29–32, 39), only 1 recorded the physical activity of participants during the intervention period (26). Lower levels of physical activity in whole-grain groups, compared with controls, might explain increased BMIs. Another reason might be the low compliance of participants. For example, in the study by Kristensen et al. (30), in which whole-grain consumption resulted in a significant increase in BMIs, the compliance of participants to the intervention was low. Finally, differences in the consumption of other foods and nutrients between the whole-grain and control groups might also provide a reason. Overall, it seems that additional RCTs that consider these important factors are needed to further examine the effects of whole-grain consumption on BMIs.

In the current meta-analysis, we found that whole-grain consumption had no significant effect on WC. This finding was in agreement with the previous meta-analysis in 2013, in which Pol et al. (40) failed to find any significant effect of whole-grain intake on WC. However, unlike in our analysis, findings from a meta-analysis of observational studies revealed a significant, inverse association between whole-grain consumption and the risk of abdominal obesity (58). In the Multi-Ethnic Study of Atherosclerosis, whole grain consumption was inversely associated with risk of obesity (59). In another prospective cohort study, such an inverse association was reported in middle-aged women who were followed for 12 y (60). In contrast, in the Australian Longitudinal Study on Women's Health, the consumption of whole grains in the breakfast meal was not associated with the risk of obesity during 12 y of follow-up (61). The same finding was reported in another short-term cohort study (62). A meta-analysis of cohort studies in 2019 revealed a significant, inverse association between whole-grain consumption and the risk of obesity (63). In cohort studies, free-living people who consume different amounts of whole grains are followed for a long time. Therefore, their findings might be comparable to those obtained from clinical trials. However, the duration of follow-up among clinical trials included in the current study was short—varying from 6 to 24 wk—compared with cohort studies. Nevertheless, summarizing previous findings from clinical trials, we observed different findings than those reported from cohort studies. It should be noted that findings from prospective cohort studies are subject to bias due to residual confounding, while clinical trials are less subject to such a bias.

Although we found no significant effect of whole-grain consumption on anthropometric measures, some mechanisms have been proposed in the literature for the beneficial effects of whole grains on obesity. Mostly, these mechanisms have been based on the effects on insulin and glucose responses that favor lipolysis and lipid oxidation rather than fat storage (64–66). Whole grains are rich in fiber or indigestible components, which might help reduce the absorption of energy-containing dietary components in the gut (67).

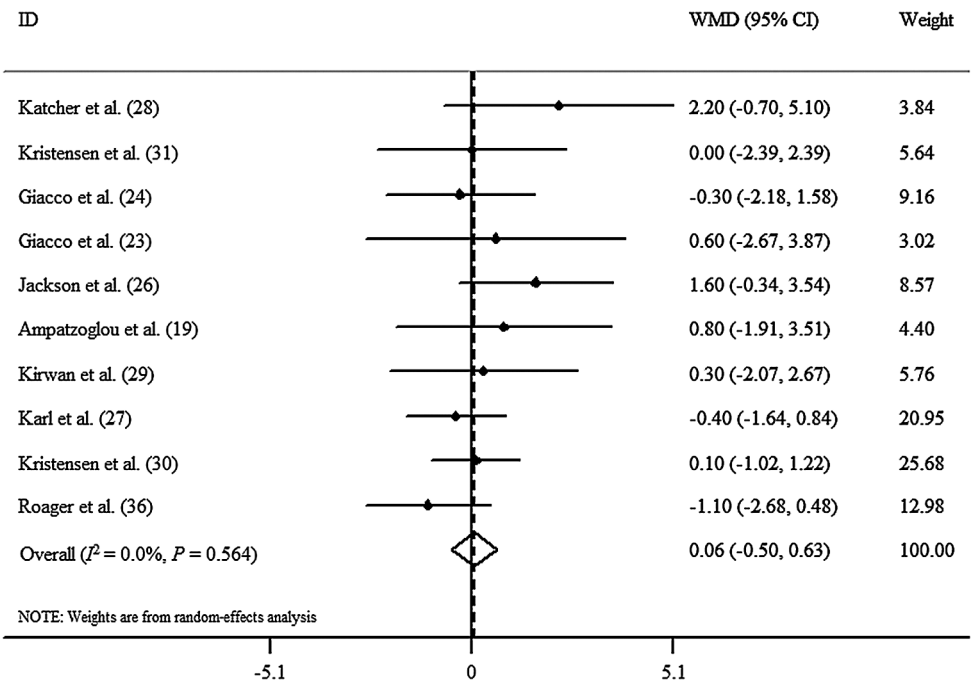

FIGURE 6 Forest plot for the effect of whole-grain consumption on waist circumference expressed as mean differences between intervention and control groups. The area of each square is proportional to the inverse of the variance of the WMD. Horizontal lines represent 95% CIs. Diamonds represent pooled estimates from random-effects analysis. WMD, weighted mean difference.

The strengths of this study include the consideration of all published clinical trials reporting the effects of whole grains on different anthropometric measures. In addition, we considered all obesity-related anthropometric measures, including body weight, BMI, body fat percentage, FM, FFM, and WC. Moreover, no between-study heterogeneity was found. However, some limitations should be considered. For instance, different methods of whole-grains prescriptions, calorie restrictions in a number of studies, considering anthropometric measures as the secondary outcome variables in some included studies, the lack of controlling for baseline measures in some others, and different study designs should be taken into account.

Overall, we found no significant beneficial effect of whole-grain consumption on anthropometric measures. The lack of considering physical activity throughout the trials, the low compliance of participants, and the differences in dietary intakes of other foods between the intervention and control groups should be taken into account in future investigations. Additional, well-designed, longitudinal RCTs recruiting homogenous groups of participants with respect to anthropometric measures are required to further examine this issue. Despite the significant effect of whole-grain consumption on increased BMIs in studies of ≥8 wk, we still recommend longitudinal, well-designed interventions, because previously published longitudinal studies did not consider several above-mentioned factors. Additional studies investigating the effects of different types and doses of whole grains are also needed in future.

Acknowledgments

The authors' responsibilities were as follows—OS, MS: contributed equally to the current study; SR, VM: conducted the research; OS, BL: analyzed the data; MS, AE: wrote the manuscript; AE: had primary responsibility for the final content; and all authors: designed the research and read and approved the final manuscript.

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