Effects of Whole Grain Intake, Compared with Refined Grain, on Appetite and Energy Intake: A Systematic Review and Meta-Analysis

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ABSTRACT

Results from observational studies indicate that whole grain (WG) intake is inversely associated with BMI and risk of weight gain. WG intake may influence energy balance and body composition through effects on appetite and energy intake. To evaluate the impact of WG food consumption on appetite and energy intake, a systematic review and meta-analysis was performed of results from randomized controlled trials (RCTs) assessing WG food consumption, appetite, and energy intake in adults. A search of PubMed, Scopus, and Food Science and Technology Abstracts yielded 36 RCTs measuring subjective appetite ratings after consuming WG foods compared with refined grain (RG) controls. Thirty-two of these studies reported AUCs for subjective appetite (hunger, fullness, satiety, desire to eat, or prospective consumption) and/or energy intake and were included in the meta-analysis. Pooled estimates from meta-analyses are expressed as standardized mean differences (SMDs). Compared with RG foods, intake of WG foods resulted in significant differences in AUCs for subjective hunger (SMD: −0.34; 95% CI: −0.46, −0.22; $P < 0.001$), fullness (SMD: 0.49; 95% CI: 0.31, 0.66; $P < 0.001$), satiety (SMD: 0.33; 95% CI: 0.18, 0.47; $P < 0.001$), and desire to eat (SMD: −0.33; 95% CI: −0.46, −0.20; $P < 0.001$). There were small, nonsignificant reductions in prospective consumption ratings ($P = 0.08$) and energy intake ($P = 0.07$) with WG intake compared with RG. These results support the view that consumption of WG foods, compared with RG foods, significantly impacts subjective appetite, and might partly explain the inverse associations between WG food intake and risk of overweight, obesity, and weight gain over time. PROSPERO registration: CRD42020148217. *Adv Nutr* 2021;12:1177–1195.

Keywords: whole grain, appetite, satiety, hunger, fullness, desire to eat, prospective food consumption, energy intake, meta-analysis, randomized controlled trials

Introduction

Whole grains (WGs) are intact, ground, cracked, or flaked grain kernels that contain all 3 anatomical components— endosperm, bran, and germ—in the same relative proportions as they exist in the intact kernel (1, 2). WG foods tend

to be higher in fiber, B vitamins, iron, zinc, magnesium, and selenium compared with foods made predominantly with refined grains (RGs) (3). Accordingly, the 2015 Dietary Guidelines for Americans recommends at least half of daily grain intake to be from WGs and includes WG foods in every healthy eating pattern. However, most Americans continue to consume more RG foods (e.g., white bread, white rice) than WG foods (e.g., wholewheat bread, brown rice, oatmeal) (3).

Results from observational studies suggest that higher intake of WGs is associated with lower risk of weight gain and incident overweight or obesity (4–6), although, findings from short-term (≤16 wk), randomized controlled trials (RCTs) evaluating the effect of higher WG intake on body weight have been equivocal (4, 7). One of the potential mechanisms by which WGs could impact body weight over the long term is by suppressing appetite and, consequently, reducing energy intake. Many WG foods contain quantities of dietary

fiber that have the potential to influence glucose metabolism ([8–10]), gastrointestinal transit ([11]), and gastrointestinal hormone secretions ([12]), all of which have the potential to impact appetite. Furthermore, fermentation of fiber and other phenolic compounds in WGs by gut microbes can create secondary metabolites, such as SCFAs, that could influence appetite and energy intake ([13]).

Appetite is typically measured with a series of questions relating to subjective sensations, such as hunger, fullness, satiety or satisfaction, desire to eat, and prospective consumption ([14], [15]). Visual analog scales (VAS) with an anchor term at each end of the scale have been validated as a method for assessing changes in appetite over time after food consumption ([16]). Satiety (How satisfied are you?) and fullness ("How full are you?") are related concepts and often used interchangeably, depending on the preference of the investigator, but both questions have been validated ([14], [16]). Postprandial VAS scores often correlate with subsequent meal energy intake ([15], [16]). However, VAS scores alone can be unreliable as a proxy measure for subsequent energy intake, so, ideally, both subjective appetite sensations and energy intake should be measured ([17]).

Although many clinical trials have investigated the effect of WG consumption on subjective appetite or energy intake, due to mixed results and mostly small studies, the totality of evidence remains unclear. Therefore, the objective of this systematic review and meta-analysis was to evaluate the impact of consuming WGs, compared with RGs, on outcomes related to subjective appetite and energy intake in RCTs in adults. The primary outcome was hunger AUC and secondary outcomes were fullness AUC, desire to eat AUC, satiety AUC, prospective consumption AUC, and energy intake.

Methods

Literature searches

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed for performing the systematic review and meta-analyses ([18]). A comprehensive literature search was conducted using the PubMed database, Scopus, and Food Science & Technology Abstracts, which covered studies published from 1946 through September 2019. The search was designed to identify publications of RCTs that examined WG intake from intact WGs (e.g., rye, oats, quinoa, brown rice, etc.) or foods made with WGs (e.g., breads, ready-to-eat breakfast cereals, etc.) and outcomes related to subjective appetite (hunger, fullness, satiety, desire to eat, prospective consumption), energy intake, gastric emptying, and appetite-related hormones (e.g., ghrelin, leptin). Full search term details are provided in **Supplemental Table 1**. Prior to the data analysis, in April 2020, the literature search was performed again in PubMed only to identify relevant studies published between the initial search and data analysis. No additional studies were identified.

Inclusion and exclusion criteria

Inclusion criteria consisted of RCTs conducted in adult humans ($\geq$18 y of age), English language publications, WG foods ($\geq$51% of grains being WG) ([19], [20]) as the main intervention compared with RG foods as a control, documented (or the ability to determine) quantitative intake of WG, and a measurement of subjective appetite, energy intake, appetite-related hormones, and/or gastric emptying time. Exclusion criteria included observational studies (cross-sectional, retrospective or prospective cohorts), case-control or single-arm studies with no control condition, studies in animals or in vitro, multicomponent interventions where the effect of WGs cannot be determined (e.g., intervention with WGs and additional fiber compared with RGs without added fiber), studies comparing different types of WGs without an RG control, studies on individual grain components (e.g., bran) or dietary supplements, interventions administered via tube feeding or enteral nutrition, studies in children (<18 y of age) or pregnant/lactating women, trials using medications or supplements known to influence appetite or gastric emptying, and studies in subjects with a chronic disease, with the exception of type 2 diabetes mellitus, obesity, or metabolic syndrome.

Screening and data extraction

Publications identified in each database using the search terms were combined and duplicates were removed. First-level screening of titles and abstracts was completed independently by a member of the research team (LMS) using Abstrackr (http://abstrackr.cebm.brown.edu/). Full texts of all publications identified as potentially eligible were obtained for further review. Publications that were unclear with respect to eligibility were resolved by discussion with the research team. Reference lists from eligible publications were reviewed to determine any additional studies for inclusion. Following the full-text review, PICO (population, intervention, comparator, and outcome) data were extracted from the eligible studies into a database independently by 1 reviewer (LMS) and verified for accuracy independently by a second reviewer (MLW). All discrepancies were resolved by discussion among the reviewers and referencing the original publication. Outcomes extracted from eligible studies included subjective appetite measures, energy intake (subsequent meal in acute studies and daily intake for chronic studies), appetite-related hormones, and gastric emptying.

In studies where outcomes were reported in bar graphs, Engauge Digitizer software version 4.1 (http://markummitchell.github.io/engauge-digitizer/) was used to estimate the means and SD or SEM in the graphs for inclusion in the database. If studies reported measuring subjective appetite or energy intake but did not report the data or variability, the corresponding author was contacted by e-mail to request the quantitative data. One author responded with additional data which was included in the data extraction. Two publications ([21], [22]) did not report SDs or SEMs and the authors did not respond to e-mail requests, therefore, the SDs for the outcomes were estimated

as the maximum SD reported by other studies of the same duration.

For studies where the amount of WG in the final food was not documented, the recipes for test foods, or the label information for commercial products, was reviewed. For low-moisture foods (e.g., pasta, flakes) the percentage WG in the dry ingredients of the recipe was estimated as the percentage WG of the final food. For higher moisture foods (e.g., bread), the percentage WG in the dry ingredients of the recipe was estimated as the percentage WG of the final food after adjustment for the moisture content. If the moisture content of the final food was not provided in the publication, moisture content was estimated using Food Data Central from the USDA Agriculture Research Service (23).

Assessment of study quality
Risk of bias for each relevant outcome within a study was assessed independently by a member of the research team (LMS) with the Cochrane risk-of-bias tool for randomized trials (24). The quality of the evidence for each outcome was assessed through discussion among members of the research team using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method (25).

Statistical analysis
Meta-analyses were completed using MedCalc Statistical Software version 19.0.5 (MedCalc Software BVBA; https://medcalc.org; 2019). Subjective appetite measures were prespecified as the primary outcome, but because hunger was the most frequently measured outcome for subjective appetite, it was selected after the data extraction, but prior to completion of the meta-analysis, to be the primary outcome of the subjective appetite measures. The primary analysis for all subjective appetite measures used pooled SMD estimates (WG compared with RG control) and 95% CIs for AUCs of hunger, fullness, satiety, desire to eat, and prospective consumption. Although all studies used a VAS to measure appetite and calculate AUCs, some VAS scales differed in anchoring statements and length (i.e., not all used a 100-mm line). The use of SMDs allowed pooling of the results from studies with these different approaches. The primary analysis for energy intake measures used pooled SMD estimates (WG compared with RG control) and 95% CIs for caloric intake. Statistical significance for individual study and pooled SMDs was declared when the 95% CI did not include the null value of 0 (i.e., *P* value <0.05). Studies were weighted according to the inverse of the variance of each study's effect using random effects models. Random effects models were chosen for the primary analyses due to differences across studies in key design elements such as subject characteristics and length of test period. Fixed effects models were completed for hunger and other appetite measures in the main analysis (i.e., not for subgroups) as sensitivity analyses. Because results did not differ materially between random and fixed effects models, only results from the former are presented. The magnitude of effect sizes were interpreted as <0.40 = small, 0.40–0.70 = moderate, and >0.70 = large (26). Analyses were

not completed for gastric emptying because only 3 studies with data were available and different methodologies were used for measuring gastric emptying rate and/or time (MRI, paracetamol, and ultrasound). Analyses for appetite-related hormones were not completed due to budgetary and time constraints.

Sensitivity analyses were completed for subjective appetite measurements to assess the degree to which varying time frames for determination of AUCs could have impacted the results. This was achieved by analyzing AUC measurements <180 min and ≥180 min separately. An additional sensitivity analysis on the subset of studies requiring calculation of the WG content was also completed.

Subgroup analyses were performed on subjective appetite measures for type of WG, amount of WG consumed (less than or equal to the median, or greater than the median), feeding approach (matching available carbohydrates, matching calories and volume), and measurement timing (immediately after meal, subsequent meal). Similar subgroup analyses were performed for energy intake with the 1 difference of measurement timing (subsequent meal, third meal, or daily intake). Subgroup analyses were not possible for health status (e.g., type 2 diabetes), age, gender, or BMI due to an insufficient number of studies or combined reporting within studies (e.g., overweight and normal weight data combined) that did not allow for distinct subgroups.

Statistical heterogeneity was assessed using Cochran Q and the I^2 statistic. An I^2 value ≥40% was used to designate moderate or higher heterogeneity, in accordance with the recommendations in the Cochrane Handbook (27). The presence of publication bias was assessed visually by examining funnel plots measuring the SEM as a function of the SMD.

Results
A flow diagram summarizing the literature search process is shown in **Figure 1**. The scope of this review is limited to subjective appetite and energy intake. Therefore, of the 51 eligible articles included in the data extraction, 36 were included in the systematic review (13, 21, 22, 28–60) and 32 were included in the meta-analysis of subjective appetite and/or energy intake. The 4 studies excluded from the meta-analysis (57–60) reported measuring subjective appetite AUCs and/or energy intake, but did not show the data and authors did not respond to e-mail requests for the data.

Study characteristics are presented in **Table 1**. Thirty five (13, 21, 22, 28–47, 49–60) of the 36 studies were crossover in design, with only 1 parallel trial (48), and included data from 794 participants. Four studies included daily consumption of WGs or RGs for 3 to 8 wk (13, 48, 51, 60), whereas the remaining studies tested the response to acute intake of WGs and RGs. WG intake in longer-term feeding studies ranged from 48 to 145 g/d, and acute studies ranged from 40 g to 254 g. Subjective appetite was measured only in acute studies. The most common type of WG tested was rye in 15 publications (21, 30, 31, 34, 37, 38, 40–42, 44, 48, 49, 51, 55, 57), followed by wheat in 12 publications (22, 29, 32, 33, 36,
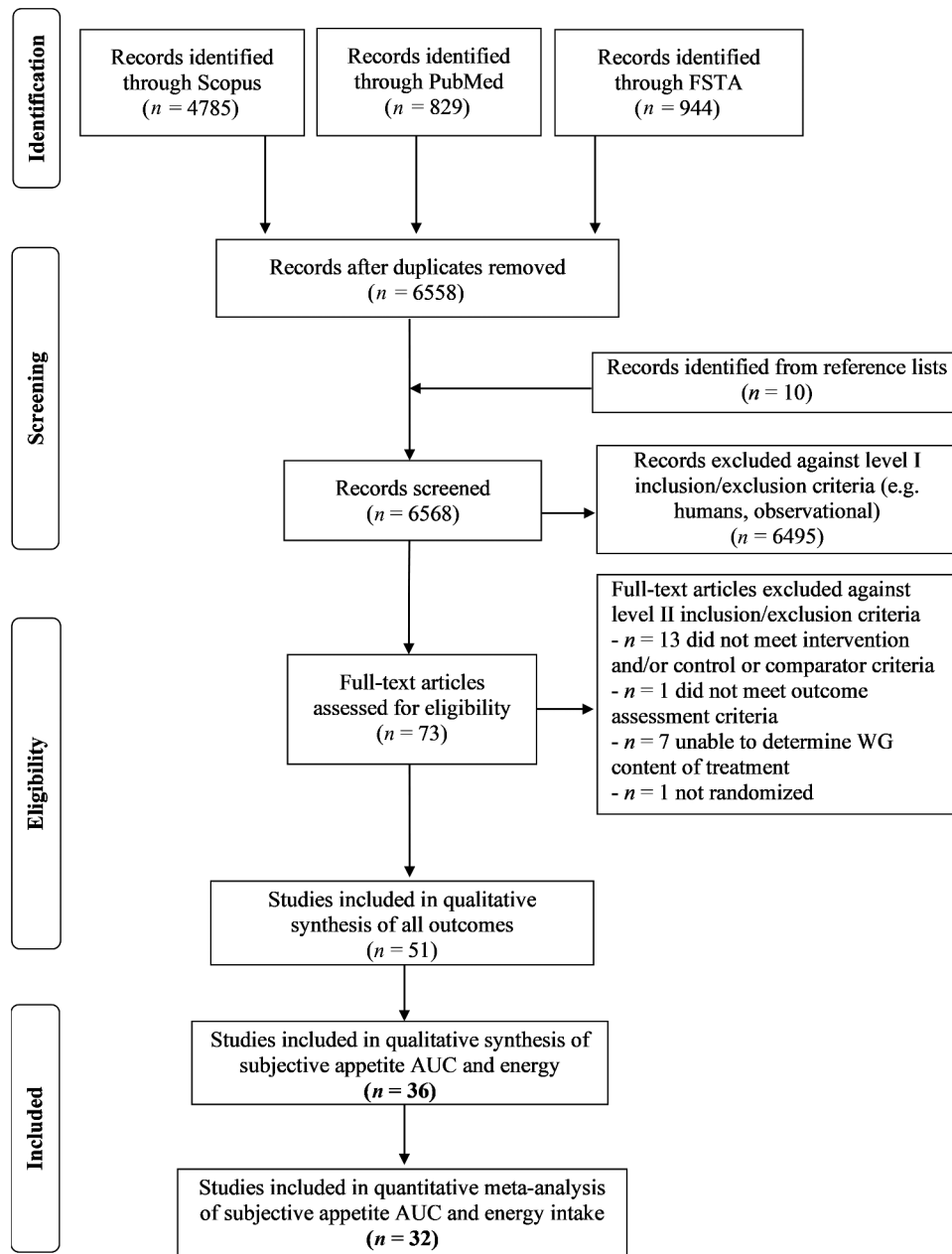
FIGURE 1 Flow diagram of literature search process for the effect of WGs on subjective appetite and energy intake in adults. FSTA, Food Science & Technology Abstracts; WG, whole grain.

43, 48, 54, 55, 57, 58, 60). Other WGs tested included barley (39, 46, 54, 59), oats (28, 35, 45, 52), corn (50, 53), rice (47), buckwheat (56), and quinoa (56).

WG intake and hunger

Overall, 35 comparisons reported in 18 different studies (21, 22, 28–43) were included in the analysis of the impact of WG on hunger AUC. Intake of WG foods resulted in significantly lower hunger AUC compared with RG foods (**Figure 2**, SMD: −0.34; 95% CI: −0.46, −0.22; $P < 0.001$) with no significant heterogeneity between studies (Q = 40.08, P = 0.22,

I^2 = 15.17%). A sensitivity analysis showed the timing of AUC measurement did not substantially impact the results, with the effect size differing slightly in studies <180 min or ≥180 min (**Supplemental Table 2**). A sensitivity analysis including the subset of studies requiring WG amounts to be calculated showed a slightly larger effect size than the analysis including all studies (SMD: −0.45); however, studies requiring calculation of WG content estimated slightly higher mean levels of WG intake (92.7 ± 5.3 g compared with 88.9 ± 4.4 g), which might contribute to this larger effect. Similar results were found for all other outcomes.

TABLE 1 Summary of studies included in the systematic review and meta-analysis of WG intake and subjective appetite AUC and/or energy intake in adults[1]

Study	Population	Health status	Study design	WG exposure[2]	RG control exposure	Outcomes measured	Length of appetite testing	Effect of WG
Wolever et al. (28)	n = 40 60% male 39.2 ± 13.1 y BMI: 26.5 ± 3.1	Healthy	Crossover Acute appetite test Matched available CHO Breakfast meal	40 g WG oats	Cream of rice in skim milk	Hunger Fullness Desire to eat Prospective consumption	180 min	NS hunger NS fullness NS desire to eat NS prospective consumption
Costabile et al. (29)	n = 14 50% male 30 ± 2 y BMI: 22 ± 1	Healthy	Crossover Acute appetite test Matched available CHO Breakfast meal Energy intake at lunch	117 g WG wheat in pasta	Wheat pasta	Hunger Satiety Desire to eat Energy intake	240 min	↓Hunger NS satiety ↓Desire to eat NS energy intake
Lee et al. (30)	n = 21 52% male 38.6 ± 11.8 y BMI: 24.9 ± 3.3	Healthy	Crossover Acute appetite test Matched calories Breakfast meal	40 g WG rye in porridge 55 g WG rye in porridge	Wheat bread (55 g portion)	Hunger Fullness Desire to eat	240 min	↓Hunger (55 g) ↑Fullness (55 g) NS desire to eat
Sandberg et al. (31)	n = 21 48% male 25.3 ± 3.9 y BMI: 22.7 ± 2.3	Healthy	Crossover Subsequent meal appetite test Matched available CHO Dinner meal Energy intake at lunch	134.5 g WG rye from rye flour bread 133.5 g WG rye from flour/kernel blend bread	Wheat bread	Hunger Satiety Desire to eat Energy intake	210 min	↓Hunger ↑Satiety (rye flour bread) ↓Desire to eat (rye flour bread) NS energy intake
Cioffi et al. (32)	n = 16 44% male 44 ± 10 y BMI: 30.1 ± 2.8	Healthy, overweight to obese	Crossover Acute appetite test Matched calories and volume Lunch meal	100 g WG wheat in pasta	Wheat pasta	Hunger Fullness Satiety Prospective consumption Energy intake	240 min	NS hunger ↑Fullness ↑Satiety ↓Prospective consumption NS energy intake
Cioffi et al. (33)	n = 8 50% male 39 ± 14 y BMI: 24.7 ± 2.7	Healthy, normal weight to overweight	Crossover Acute appetite test Matched calories and volume Lunch meal	100 g WG wheat in pasta	Wheat pasta	Hunger Fullness Satiety Prospective consumption	240 min	NS hunger NS fullness NS satiety NS prospective consumption
Sandberg et al. (34)	n = 19 45% male 25.6 ± 3.5 y BMI: 21.9 ± 1.9	Healthy	Crossover Subsequent meal appetite test Matched available CHO Dinner meal	88.8 g WG rye from bread	Wheat bread	Hunger Satiety Desire to eat	180 min	↓Hunger ↑Satiety ↓Desire to eat
Geliebter et al. (35)	n = 36 50% male 26–31 y[3] BMI normal weight: 23 ± 2 males; 22 ± 2 females BMI overweight: 33 ± 3 males; 36 ± 7 females	Healthy 50% normal weight 50% overweight	Crossover Acute appetite test Matched calories and volume Breakfast meal	93.6 g WG from oatmeal	Corn flakes	Hunger Fullness	180 min	↓Hunger ↑Fullness
Gonzalez-Anton et al. (36)	n = 23 55% male 26 ± 1 y BMI: 23.8 ± 0.5	Healthy Normal weight to overweight	Crossover Acute appetite test Matched available CHO Breakfast meal Energy intake at lunch	90.1 g WG from wheat bread	Wheat bread	Hunger Fullness Satiety Prospective consumption Energy intake	180 min	NS hunger NS fullness NS satiety NS prospective consumption NS energy intake

(Continued)

TABLE 1 (*Continued*)

Study	Population	Health status	Study design	WG exposure[2]	RG control exposure	Outcomes measured	Length of appetite testing	Effect of WG
Johansson et al. (37)	n = 23 30% male 60.1 ± 12.1 y BMI: 23.8 ± 3.4	Healthy Normal weight to overweight	Crossover Acute appetite test Matched calories Breakfast meal	60 g WG from rye crisp bread	Wheat crisp bread	Hunger Fullness Desire to eat	240 min	↓Hunger ↑Fullness NS desire to eat
Forsberg et al. (21)	n = 21 47% male 39 ± 14 y BMI: 23.3 ± 3	Healthy Normal weight to overweight	Crossover Acute appetite test Matched calories Breakfast meal Energy intake at lunch	76 g WG from rye kernel crisp bread 60.8 g WG from rye kernel crisp bread	Wheat bread (soft)	Hunger Satiety Desire to eat Energy intake	240 min	↓Hunger ↑Satiety (60.8 g) ↓Desire to eat ↓Energy intake (60.8 g)
Hartvigsen et al. (38)	n = 15 47% male 62.8 ± 4.2 y BMI: 31.1 ± 3.2	Metabolic syndrome	Crossover Acute appetite test Matched available CHO Breakfast meal Energy intake at lunch	90 g WG from rye kernel bread	Wheat bread	Hunger Fullness Satiety Prospective consumption Energy intake	270 min	↓Hunger ↑Fullness ↑Satiety ↓Prospective consumption NS energy intake
Johansson et al. (39)	n = 19 32% male 24.2 ± 1.9 y BMI: 22.3 ± 2	Healthy	Crossover Subsequent meal appetite test Matched available CHO Dinner meal Energy intake at lunch	96.8 g WG from boiled barley kernels	Wheat bread	Hunger Satiety Desire to eat Energy intake	120 min	NS hunger NS satiety NS desire to eat ↓Energy intake
Rosen et al. (40)	n = 10 50% male 26 ± 1.1 y BMI: 22.6 ± 0.4	Healthy	Crossover Acute appetite test Matched available CHO Breakfast meal Energy intake at lunch	98.5 g WG from rye bread 106.6 g WG from rye kernel porridge 97.1 g WG from wheat kernel porridge	Endosperm rye bread Wheat bread	Hunger Fullness Desire to eat Energy intake	120 min[4]	↓Hunger (porridge) ↑Fullness (porridge) ↓Desire to eat (porridge) ↓Energy intake (rye porridge)
Rosen et al. (41)	n = 20 50% male 26.7 ± 0.9 y BMI: 22.2 ± 0.39	Healthy	Crossover Acute appetite test Matched available CHO Breakfast meal	84.7 g WG from commercial rye bread 83.2 g WG from Amilo rye bread 82 g WG from Evolo rye bread 82.7 g WG from Picasso rye bread 80.1 g WG from Vicello rye bread 82.8 g WG from Kaskelott rye bread	Wheat bread	Hunger Fullness Desire to eat	180 min	↓Hunger (Evolo) NS fullness NS desire to eat
Rosen et al. (42)	n = 14 50% male 23.6 ± 0.5 y BMI: 22 ± 0.5	Healthy	Crossover Acute appetite test Matched available CHO Breakfast meal	118.2 g WG from D. Zlote rye bread 125.7 g WG from H. Loire rye bread 120.7 g WG from Nikita rye bread 122.2 g WG from Rekrut rye bread 122.9 g WG from Amilo rye bread	Wheat bread	Hunger Fullness Desire to eat	180 min	↓Hunger (Nikita, Rekrut) ↑Fullness NS desire to eat

(*Continued*)

TABLE 1 (Continued)

Study	Population	Health status	Study design	WG exposure[2]	RG control exposure	Outcomes measured	Length of appetite testing	Effect of WG
Kristensen et al. (43)	n = 16 38% male 24.1 ± 3.8 y BMI: 21.7 ± 2.2	Healthy	Crossover Acute appetite test Matched available CHO and calories Breakfast meal Energy intake at lunch	83.6 g WG from wheat pasta	Wheat bread Wheat pasta	Hunger Fullness Satiety Prospective consumption Energy intake	180 min	NS hunger NS fullness NS satiety NS prospective consumption NS energy intake
Solah et al. (22)	n = 22 Gender, age, BMI not reported	Healthy	Crossover Acute appetite test Matched calories and volume Breakfast meal	53.1 g WG from boiled bulgur kernels 53.1 g WG from steamed bulgur kernels 53.1 g WG from boiled Turkish bulgur kernels	HA rice	Hunger Fullness Desire to eat Prospective consumption	240 min	NS hunger NR fullness NR desire to eat NR prospective consumption
Rosen et al. (44)	n = 12 75% male 25.3 ± 0.8 y BMI: 23.1 ± 0.6	Healthy	Crossover Acute appetite test Matched available CHO Breakfast meal	66.1 g WG from rye bread 51.1 g WG from rye porridge	Endosperm rye bread Wheat bread Endosperm rye porridge Wheat porridge	Satiety	180 min	NS satiety
Hlebowicz et al. (45)	n = 12 50% male 28 ± 4 y BMI: 22 ± 2	Healthy	Crossover Acute appetite test Matched calories and volume Breakfast meal	42.5 g WG from oat flakes	Corn flakes	Satiety	120 min	NS satiety
Granfeldt et al. (46)	n = 10 50% male 34 ± 8 y BMI: 21.2 ± 2	Healthy	Crossover Acute appetite test Matched available CHO Breakfast meal	89 g WG from hull-less barley kernel porridge 76.2 g WG from hulled barley kernel porridge 90.6 g WG from hull-less HA barley kernel porridge 87.7 g WG from hulled HA barley kernel porridge 79.1 g WG from hulled barley flour porridge 90.3 g WG from hull-less HA barley flour porridge	Wheat bread	Satiety	180 min	↑Satiety (hull-less porridge, hull-less HA porridge, hulled HA porridge)
Hamad et al. (47)	n = 20 40% male 25.4 ± 2 y male 24.7 ± 1.9 y female BMI: 23.02 ± 1.62 male, 22.39 ± 1.32 female	Healthy and type 2 diabetes	Crossover Acute appetite test Matched available CHO Breakfast meal	70 g WG from long-grain brown rice	Long-grain white rice	Hunger Fullness Desire to eat Prospective consumption	120 min	NS all outcomes (for type 2 diabetes) NR hunger NR fullness NR desire to eat NS prospective consumption

(*Continued*)

TABLE 1 (Continued)

Study	Population	Health status	Study design	WG exposure[2]	RG control exposure	Outcomes measured	Length of appetite testing	Effect of WG
Roager et al. (13)	n = 50 36% male 48.6 ± 11.1 y BMI: 28.9 ± 3.6	Overweight or obese, ≥1 of: impaired fasting glucose, dyslipidemia, hypertension	Crossover Daily consumption for 8 wk Ad libitum intake Energy intake over the day	Target ≥75 g WG/d from variety of WG foods	Target <10 g WG/d from variety of RG foods	Energy intake	NA	NS energy intake
Suhr et al. (48)	n = 24/arm WG rye: 46% male 53 ± 8.9 y BMI: 28 ± 1.9 WG wheat: 42% male; 48.2 ± 9.9 y; BMI: 27.7 ± 1.9 RG control: 50% male; 51.8 ± 9 y; BMI: 27.8 ± 2	Overweight to moderately obese	Parallel Daily consumption for 6 wk Ad libitum intake Energy intake over the day	No target intake Mean intake WG rye: 124 ± 11.8 g/d Mean intake WG wheat: 145 ± 12.1 g/d	No target intake Mean intake WG: 5.4 ± 12.6 g/d	Energy intake	NA	NS energy intake
Ibrugger et al. (49)	n = 12 100% male 25.6 ± 3.9 y BMI: 23.1 ± 1.2	Healthy	Crossover Matched available CHO and calories Dinner meal Energy intake at lunch	90 g WG from rye kernel porridge	Wheat bread	Energy intake	NA	↓Energy intake
Luhovyy et al. (50)	n = 30 100% male 22.9 ± 0.6 y BMI: 22.6 ± 0.3	Healthy	Crossover Matched calories Preload to lunch Energy intake at lunch	50 g WG from HA corn cookie	Wheat cookie	Energy intake	NA	NS energy intake
Isaksson et al. (51)	n = 24 21% male 33 ± 13 y BMI: 23.4 ± 2.2	Healthy Normal weight to moderately overweight	Crossover Daily consumption for 3 wk—breakfast meal only Breakfast meals Matched calories Energy intake over the day	55 g WG from rye porridge	Wheat bread	Energy intake	NA	NS energy intake
Zafar et al. (52)	n = 12 0% males Age, BMI not reported	Healthy	Crossover Matched available CHO Breakfast meal Energy intake at lunch	87 g WG from oatmeal	Wheat bread	Energy intake	NA	↓Energy intake
Anderson et al. (53)	Study 1: n = 17 100% males 20.2 ± 0.1 y BMI: 22.5 ± 0.3 Study 2: n = 16 100% males 20.9 ± 0.3 y BMI: 22.5 ± 0.4	Healthy	Crossover Matched calories and volume Preload to lunch Energy intake at lunch (Study 1 = 30 min; Study 2 = 120 min)	50 g WG from HA corn in soup	HA corn starch in soup	Energy intake	NA	NS energy intake (30 min) ↓Energy intake (120 min)

(Continued)

TABLE 1 (Continued)

Study	Population	Health status	Study design	WG exposure[2]	RG control exposure	Outcomes measured	Length of appetite testing	Effect of WG
Schroeder et al. (54)	$n = 50$ 26% male 31 ± 11 y BMI: 23 ± 3	Healthy Normal weight to obese	Crossover Acute appetite test Matched calories and volume Breakfast meal and mid-morning snack Energy intake at lunch	84 g WG from barley hot cereal and snack mix78.5 g WG from wheat hot cereal and snack mix	Rice hot cereal	Hunger Fullness Desire to eat Prospective consumption Energy intake	240 min	NS hunger NS fullness NS desire to eat NS prospective consumption NS energy intake
Isaksson et al. (55)	$n = 22$ 36% male 40.7 ± 14.7 y BMI: 23.2 ± 2.4	Healthy Normal weight to moderately overweight	Crossover Matched calories Breakfast and lunch meal Energy intake at dinner	162 g WG from rye porridge (breakfast) and wheat pasta (lunch) 62 g WG from rye porridge (breakfast only)	Wheat bread (breakfast) and wheat pasta (lunch)	Energy intake	NA	NS energy intake
Berti et al. (56)	Study 1: buckwheat $n = 14$ 100% males 24 ± 2.6 y BMI: 22.3 ± 2.7 Study 2: quinoa $n = 12$ 100% males 25.4 ± 2.2 y BMI: 23 ± 1.9	Healthy	Crossover Matched volume Mid-morning snack Energy intake at lunch	Study 1: 111.3 g WG from buckwheat pasta (large portion) 55.7 g WG from buckwheat pasta (small portion) Study 2: 419.8 g WG from quinoa risotto (large portion) 211.6 g WG from quinoa risotto (small portion)	Study 1: wheat pasta (large and small portions) Study 2: White rice (large and small portions)	Energy intake	NA	NS energy intake
Breen et al. (57)[5]	$n = 10$ 60% male 53.9 ± 5.5 y BMI: 35.1 ± 7.5	Type 2 diabetes	Crossover Acute appetite test Matched available CHO Breakfast meal	54.1 g WG from buttermilk wheat bread 135.4 g WG from pumpernickel rye bread	Wheat bread	Hunger Fullness Satiety Prospective consumption	270 min	NS hunger NS fullness NS satiety NS prospective consumption
Holt et al. (58)[5]	$n = 10$ 30% males 23.5 ± 6.2 y BMI: 22.1 ± 1.3	Healthy	Crossover Acute appetite test Matched calories Breakfast Meal	79.8 g WG from wheat bread	Wheat bread	Hunger Fullness	120 min	NR hunger NR fullness
Nilsson et al. (59)[5]	$n = 17$ 65% males 25.9 ± 3.2 y BMI: 22.5 ± 2.1	Healthy	Crossover Subsequent meal appetite test Matched available CHO Dinner meal	105.3 g WG from barley kernel bread 124.4 g WG from cut barley kernel bread 139.3 g WG from HA barley bread 253.9 g WG from high β-glucan barley bread 52.6 g WG from barley kernel bread	Wheat bread	Satiety	180 min	↑Satiety (high β-glucan barley bread)
Bodinham et al. (60)[5]	$n = 14$ 36% male 26 ± 1.4 y BMI: 21. 8 ± 0.8	Healthy	Crossover Daily consumption for 3 wk Energy intake over the day	48 g WG from wheat bread	Wheat bread	Energy intake	NA	NS energy intake

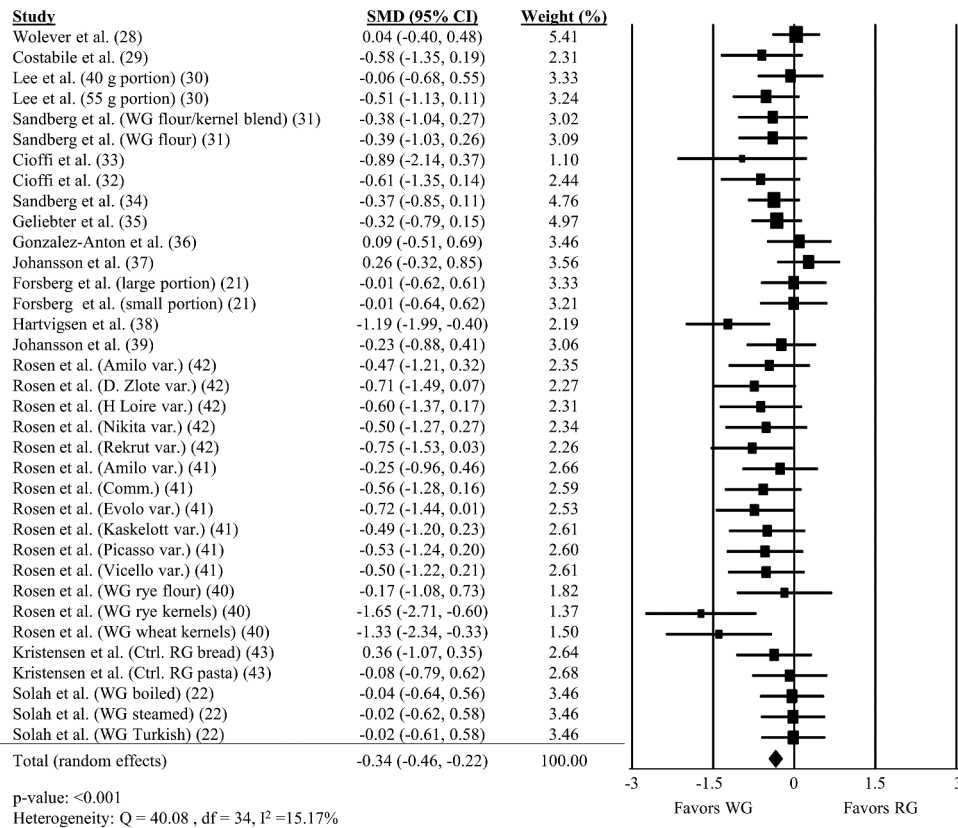[1] CHO, carbohydrate; HA, high-amylose; NA, not applicable; NR, not reported; NS, not significant ($P > 0.05$); RG, refined grain; WG, whole grain.
[2] Reported or calculated values.
[3] Range of means provided because age reported by gender and weight status.
[4] 120 min measurement = $AUC_{0-60min} + AUC_{60-120min}$
[5] Included in systematic review but data not available to include in meta-analysis.

Study	SMD (95% CI)	Weight (%)
Wolever et al. (28)	0.04 (-0.40, 0.48)	5.41
Costabile et al. (29)	-0.58 (-1.35, 0.19)	2.31
Lee et al. (40 g portion) (30)	-0.06 (-0.68, 0.55)	3.33
Lee et al. (55 g portion) (30)	-0.51 (-1.13, 0.11)	3.24
Sandberg et al. (WG flour/kernel blend) (31)	-0.38 (-1.04, 0.27)	3.02
Sandberg et al. (WG flour) (31)	-0.39 (-1.03, 0.26)	3.09
Cioffi et al. (33)	-0.89 (-2.14, 0.37)	1.10
Cioffi et al. (32)	-0.61 (-1.35, 0.14)	2.44
Sandberg et al. (34)	-0.37 (-0.85, 0.11)	4.76
Geliebter et al. (35)	-0.32 (-0.79, 0.15)	4.97
Gonzalez-Anton et al. (36)	0.09 (-0.51, 0.69)	3.46
Johansson et al. (37)	0.26 (-0.32, 0.85)	3.56
Forsberg et al. (large portion) (21)	-0.01 (-0.62, 0.61)	3.33
Forsberg et al. (small portion) (21)	-0.01 (-0.64, 0.62)	3.21
Hartvigsen et al. (38)	-1.19 (-1.99, -0.40)	2.19
Johansson et al. (39)	-0.23 (-0.88, 0.41)	3.06
Rosen et al. (Amilo var.) (42)	-0.47 (-1.21, 0.32)	2.35
Rosen et al. (D. Zlote var.) (42)	-0.71 (-1.49, 0.07)	2.27
Rosen et al. (H Loire var.) (42)	-0.60 (-1.37, 0.17)	2.31
Rosen et al. (Nikita var.) (42)	-0.50 (-1.27, 0.27)	2.34
Rosen et al. (Rekrut var.) (42)	-0.75 (-1.53, 0.03)	2.26
Rosen et al. (Amilo var.) (41)	-0.25 (-0.96, 0.46)	2.66
Rosen et al. (Comm.) (41)	-0.56 (-1.28, 0.16)	2.59
Rosen et al. (Evolo var.) (41)	-0.72 (-1.44, 0.01)	2.53
Rosen et al. (Kaskelott var.) (41)	-0.49 (-1.20, 0.23)	2.61
Rosen et al. (Picasso var.) (41)	-0.53 (-1.24, 0.20)	2.60
Rosen et al. (Vicello var.) (41)	-0.50 (-1.22, 0.21)	2.61
Rosen et al. (WG rye flour) (40)	-0.17 (-1.08, 0.73)	1.82
Rosen et al. (WG rye kernels) (40)	-1.65 (-2.71, -0.60)	1.37
Rosen et al. (WG wheat kernels) (40)	-1.33 (-2.34, -0.33)	1.50
Kristensen et al. (Ctrl. RG bread) (43)	0.36 (-1.07, 0.35)	2.64
Kristensen et al. (Ctrl. RG pasta) (43)	-0.08 (-0.79, 0.62)	2.68
Solah et al. (WG boiled) (22)	-0.04 (-0.64, 0.56)	3.46
Solah et al. (WG steamed) (22)	-0.02 (-0.62, 0.58)	3.46
Solah et al. (WG Turkish) (22)	-0.02 (-0.61, 0.58)	3.46
Total (random effects)	-0.34 (-0.46, -0.22)	100.00

p-value: <0.001

Heterogeneity: Q = 40.08 , df = 34, I^2 =15.17%

FIGURE 2 Forest plot of the meta-analysis on the effect of WG intake on hunger in adults. Values are the standardized mean differences (SMDs) for hunger AUC between WG intake and RG intake (21, 22, 28–43). Comm., commercial; Ctrl., control; RG, refined grain; var., variety; WG, whole grain.

Findings from the subgroup analyses for hunger AUC are shown in **Table 2**. Hunger was lower in the WG group relative to the control when the test and control conditions were matched by available carbohydrate ($P < 0.001$). However, studies matched by calories or matched by calories and volume did not show a significant difference in hunger AUC between WG and RG controls.

Three studies not included in the meta-analysis measured hunger AUC but did not report the data. All of these studies (47, 54, 57) did not show a significant effect of WG on hunger AUC compared with RG.

WG intake and fullness
Twelve studies (28, 30, 32, 33, 35–38, 40–43) with 25 comparisons were included in the analysis of the effect of WG on fullness. Intake of WG foods resulted in significantly greater fullness AUC compared with RG foods (**Figure 3**; SMD: 0.49; 95% CI: 0.31, 0.66; $P < 0.001$) with moderate heterogeneity between studies (Q = 37.95, $P = 0.035$, $I^2 = 36.76$%). A sensitivity analysis showed the timing of AUC measurement impacted the effect size, with studies measuring fullness at <180 min having a greater effect size than studies measuring at ≥180 min (**Supplemental Table 2**).

Subgroup analyses' results for fullness AUC are shown in Table 2. There was a significant positive effect of WG on fullness in studies matched by available carbohydrate ($P < 0.001$), but not in studies that matched calories. There were insufficient studies matched by calories and volume to include as a subgroup. Subgroup analyses were not possible for acute compared with subsequent meal studies because all studies were acute.

Five studies (22, 47, 54, 57, 58) not included in the meta-analysis measured fullness AUC but did not report the data. Three studies (47, 54, 57) did not find a significant effect of WG on fullness AUC compared with RG. One of the studies only calculated fullness AUC to use in a satiety index (58) and thus did not statistically compare the AUC values between treatments. Solah et al. (22) did not report the statistical results for fullness AUC.

WG intake and satiety
Thirteen studies (21, 29, 31–34, 36, 38, 39, 43–46) with 24 comparisons were included in the analysis of the effect of WG on satiety. There was a significant positive effect of WG on satiety AUC (**Figure 4**, SMD: 0.33; 95% CI: 0.18, 0.47; $P < 0.001$) with no significant heterogeneity between studies (Q = 15.40, $P = 0.88$, $I^2 = 0.00$%). A sensitivity analysis showed the timing of AUC measurement did not impact the effect size although there were only 2 studies that measured satiety AUC for <180 min (**Supplemental Table 2**).

TABLE 2 Subgroup analyses for the effect of WGs on subjective appetite in adults[1]

Outcome and subgroups	Number of comparisons/studies	Subjects (WG/control)	Effect estimate SMD (95% CI)[2]	I^2 (%)	P value[2]
Hunger AUC					
Type of WG					
Rye	22/9	759 (378/381)	−0.42 (−0.57, −0.26)	12.04	<0.001
Wheat	10/7	330 (165/165)	−0.27 (−0.52, −0.02)	22.14	<0.031
Amount of WG (median split)					
≤88.8 g	18/8	748 (374/374)	−0.20 (−0.34, −0.06)	0.00	0.006
>88.6 g	17/10	531 (267/264)	−0.53 (−0.72, −0.35)	16.07	<0.001
Feeding approach					
Matched available CHO	24/11	821 (409/412)	−0.44 (−0.59, −0.30)	10.65	<0.001
Matched calories	7/4	276 (138/138)	−0.10 (−0.33, 0.14)	0.00	0.421
Matched calories and volume	6/4	246 (123/123)	−0.22 (−0.47, 0.03)	0.00	0.078
Measurement timing					
Acute appetite test	31/15	1096 (548/548)	−0.35 (−0.49, −0.21)	24.80	<0.001
Subsequent meal appetite test	4/3	183 (90/93)	−0.35 (−0.64, −0.06)	0.00	0.019
Fullness AUC					
Type of WG					
Rye	17/6	531 (265/266)	0.54 (0.32, 0.75)	35.77	<0.001
Wheat	6/5	170 (85/85)	0.53 (0.12, 0.94)	42.56	0.012
Amount of WG (median split)					
≤90.0 g	13/6	496 (248/248)	0.33 (0.12, 0.54)	28.12	0.002
>90.0 g	12/6	357 (178/179)	0.69 (0.43, 0.94)	28.72	<0.001
Feeding approach					
Matched available CHO	19/7	609 (304/305)	0.57 (0.37, 0.77)	34.09	<0.001
Matched calories	5/3	194 (97/97)	0.19 (−0.18, 0.57)	43.81	0.315
Satiety AUC					
Type of WG					
Rye	10/5	351 (173/178)	0.31 (0.07, 0.55)	22.38	0.011
Wheat	6.5	178 (89/89)	0.22 (−0.07, 0.51)	0.00	0.141
Barley	7/2	156 (77/79)	0.46 (0.15, 0.76)	0.00	0.004
Amount of WG (median split)					
≤88.3 g	12/5	323 (160/163)	0.21 (−0.004, 0.42)	0.00	0.055
>88.3 g	12/9	386 (191/195)	0.42 (0.23, 0.63)	0.00	<0.001
Feeding approach					
Matched available CHO	19/9	561 (277/284)	0.37 (0.21, 0.53)	0.00	<0.001
Matched calories	4/2	146 (73/73)	0.08 (−0.24, 0.40)	0.00	0.631
Matched calories and volume	3//3	66 (33/33)	0.36 (−0.11, 0.84)	0.00	0.132
Measurement timing					
Acute appetite test	20/10	526 (265/261)	0.31 (0.14, 0.48)	0.00	<0.001
Subsequent meal appetite test	4/3	183 (90/93)	0.38 (0.09, 0.67)	0.00	0.011
Desire to eat AUC					
Type of WG					
Rye	21/8	727 (363/364)	−0.36 (−0.50, −0.21)	0.00	<0.001
Amount of WG (median split)					
≤88.8 g	13/6	552 (276/276)	−0.23 (−0.40, −0.07)	0.00	0.006
>88.8 g	13/5	341 (170/171)	−0.50 (−0.72, −0.28)	6.56	<0.001
Feeding approach					
Matched available CHO	20/8	681 (340/341)	−0.42 (−0.57, −0.27)	0.00	<0.001
Matched calories	5/3	212 (106/106)	−0.07 (−0.33, 0.20)	0.00	0.623
Measurement timing					
Acute appetite test	21/8	711 (355/356)	−0.34 (−0.50, −0.19)	14.12	<0.001
Subsequent meal appetite test	4/3	182 (91/91)	−0.35 (−0.64, −0.06)	0.00	0.018
Prospective consumption AUC					
Type of WG					
Wheat	5/4	150 (75/75)	−0.15 (−0.51, 0.21)	19.32	0.406
Amount of WG (median split)					
≤86.8 g	4/3	184 (92/92)	−0.17 (−0.46, 0.12)	0.00	0.240
>86.8 g	4/4	116 (58/58)	−0.40 (−1.02, 0.23)	62.96	0.213
Feeding approach					
Matched avail CHO	6/5	258 (129/129)	−0.21 (−0.53, 0.11)	38.83	0.202

[1] CHO, carbohydrate; RG, refined grain; SMD, standardized mean difference; WG, whole grain.
[2] Effect estimates and P values from random effects models.

Study	SMD (95% CI)	Weight (%)
Wolever et al. (28)	0.03 (-0.42, 0.47)	6.57
Lee et al. (40 g portion) (30)	0.25 (-0.36, 0.87)	4.80
Lee et al. (55 g portion) (30)	0.51 (-0.11, 1.13)	4.73
Cioffi et al. (33)	0.84 (-0.40, 2.09)	2.02
Cioffi et al. (32)	0.43 (-0.31, 1.17)	3.91
Geliebter et al. (35)	0.35 (-0.12, 0.82)	6.25
Gonzalez-Anton et al. (36)	0.16 (-0.44, 0.76)	4.94
Johansson et al. (37)	-0.42 (-1.01, 0.17)	5.01
Hartvigsen et al. (38)	0.98 (0.21, 1.76)	3.67
Rosen et al. (Amilo var.) (42)	0.76 (-0.03, 1.54)	3.62
Rosen et al. (D. Zlote var.) (42)	1.14 (0.32, 1.95)	3.42
Rosen et al. (H Loire var.) (42)	0.47 (-0.30, 1.23)	3.73
Rosen et al. (Nikita var.) (42)	0.79 (0.004, 1.57)	3.61
Rosen et al. (Rekrut var.) (42)	0.90 (0.10, 1.69)	3.55
Rosen et al. (Amilo var.) (41)	-0.04 (-0.75, 0.66)	4.13
Rosen et al. (Comm.) (41)	0.48 (-0.24, 1.19)	4.05
Rosen et al. (Evolo var.) (41)	0.77 (0.03, 1.50)	3.94
Rosen et al. (Kaskelott var.) (41)	0.51 (-0.21, 1.22)	4.04
Rosen et al. (Picasso var.) (41)	0.46 (-0.26, 1.17)	4.06
Rosen et al. (Vicello var.) (41)	0.56 (-0.16, 1.28)	4.02
Rosen et al. (WG rye flour) (40)	0.30 (-0.63, 1.24)	2.93
Rosen et al. (WG rye kernels) (40)	1.60 (0.56, 2.65)	2.45
Rosen et al. (WG wheat kernels) (40)	1.66 (0.60, 2.71)	2.41
Kristensen et al. (Ctrl. RG bread) (43)	0.63 (-0.09, 1.36)	4.00
Kristensen et al. (Ctrl. RG pasta) (43)	0.06 (-0.64, 0.77)	4.13
Total (random effects)	0.49 (0.31, 0.66)	100.00

p-value: <0.001
Heterogeneity: Q = 37.95 , df = 24, I² =36.76%

FIGURE 3 Forest plot of the meta-analysis on the effect of WG intake on fullness in adults. Values are the standardized mean differences (SMDs) for fullness AUC between WG intake and RG intake (28, 30, 32, 33, 35, 36, 38–43). Comm., commercial; Ctrl., control; RG, refined grain; var., variety; WG, whole grain.

Findings of the subgroup analyses for satiety AUC are shown in Table 2. There was a positive effect on satiety AUC with WG rye ($P = 0.011$) and WG barley ($P = 0.004$), but not WG wheat. There was also a significant positive effect of WG when tested at amounts greater than the median (88.25 g), but not less than or equal to the median. A significant positive effect of WG on satiety was determined in studies with test and control conditions matched by available carbohydrate ($P < 0.001$), but not when matched by calories or calories and volume.

Two studies (57, 59) not included in the meta-analysis measured satiety AUC but did not report the data. Breen

Study	SMD (95% CI)	Weight (%)
Costabile et al. (29)	0.40 (-0.36, 1.16)	3.98
Sandberg et al. (WG flour/kernel blend) (31)	0.40 (-0.26, 1.07)	5.14
Sandberg et al. (WG flour) (31)	0.48 (-0.16, 1.12)	5.53
Cioffi et al. (33)	0.38 (-0.82, 1.58)	1.89
Cioffi et al. (32)	0.23 (-0.50, 0.96)	4.30
Sandberg et al. (34)	0.39 (-0.09, 0.88)	9.33
Gonzalez-Anton et al. (36)	0.11 (-0.49, 0.71)	6.23
Forsberg et al. (large portion) (21)	0.001 (-0.61, 0.61)	5.96
Forsberg et al. (small portion) (21)	0.01 (-0.62, 0.63)	5.69
Hartvigsen et al. (38)	1.16 (0.37, 1.94)	3.68
Johansson et al. (39)	0.23 (-0.42, 0.87)	5.38
Kristensen et al. (Ctrl. RG bread) (43)	0.35 (-0.36, 1.06)	4.53
Kristensen et al. (Ctrl. RG pasta) (43)	0.001 (-0.70, 0.71)	4.60
Rosen et al. (bread, ctrl. RG rye) (44)	-0.32 (-1.17, 0.52)	3.33
Rosen et al. (bread, ctrl. RG wheat) (44)	0.34 (-0.51, 1.18)	3.33
Rosen et al. (porridge, ctrl. RG rye) (44)	0.004 (-0.81, 0.82)	3.52
Rosen et al. (porridge, ctrl. RG wheat) (44)	0.76 (-0.09, 1.61)	3.27
Hlebowicz et al. (45)	0.53 (-0.30, 1.37)	3.39
Granfeldt et al. (WG bread) (46)	0.30 (-0.63, 1.23)	2.80
Granfeldt et al. (HAWG bread) (46)	0.76 (-0.20, 1.73)	2.63
Granfeldt et al. (hulled HAWG porridge) (46)	0.49 (-0.43, 1.40)	2.89
Granfeldt et al. (hull-less HAWG porridge) (46)	0.47 (-0.45, 1.38)	2.90
Granfeldt et al. (hulled WG porridge) (46)	0.51 (-0.41, 1.43)	2.88
Granfeldt et al (hull-less WG porridge) (46)	0.66 (-0.27, 1.58)	2.81
Total (random effects)	0.33 (0.18, 0.47)	100.00

p-value: <0.001
Heterogeneity: Q = 15.39, df = 23, I² = 0.00%

FIGURE 4 Forest plot of the meta-analysis on the effect of WG intake on satiety in adults. Values are the standardized mean differences (SMDs) for satiety AUC between WG intake and RG intake (21, 29, 31–34, 36, 38, 39, 43–46). Ctrl., control; HAWG, high-amylose whole grain; RG, refined grain; var., variety; WG, whole grain.

Study	SMD (95% CI)	Weight (%)
Wolever et al. (28)	0.02 (-0.43, 0.46)	8.98
Costabile et al. (29)	-0.40 (-1.17, 0.36)	3.20
Lee et al. (40 g portion) (30)	0.06 (-0.55, 0.67)	4.80
Lee et al. (55 g portion) (30)	-0.41 (-1.03, 0.21)	4.70
Sandberg et al. (WG flour/kernel blend) (31)	-0.34 (-0.99, 0.32)	4.19
Sandberg et al. (WG flour) (31)	-0.50 (-1.41, 0.15)	4.33
Sandberg et al. (34)	-0.40 (-0.88, 0.09)	7.51
Johansson et al. (37)	0.02 (-0.56, 0.61)	5.24
Forsberg et al. (large portion) (21)	-0.01(-0.62, 0.61)	4.80
Forsberg et al. (small portion) (21)	-0.01 (-0.64, 0.62)	4.58
Johansson et al. (39)	-0.14 (-0.79, 0.50)	4.35
Rosen et al. (Amilo var.) (42)	-0.24 (-1.000, 0.51)	3.24
Rosen et al. (D. Zlote var.) (42)	-0.52 (-1.28, 0.25)	3.16
Rosen et al. (H Loire var.) (42)	-0.49 (-1.26, 0.27)	3.17
Rosen et al. (Nikita var.) (42)	-0.49 (-1.25, 0.28)	3.17
Rosen et al. (Rekrut var.) (42)	-0.78 (-1.56, 0.004)	3.03
Rosen et al. (Amilo var.) (41)	-0.23 (-0.93, 0.48)	3.68
Rosen et al. (Comm.) (41)	-0.64 (-1.36, 0.09)	3.52
Rosen et al. (Evolo var.) (41)	-0.55 (-1.27, 0.17)	3.56
Rosen et al. (Kaskelott var.) (41)	-0.43 (-1.14, 0.28)	3.62
Rosen et al. (Picasso var.) (41)	-0.40 (-1.11, 0.28)	3.63
Rosen et al. (Vicello var.) (41)	-0.57 (-1.29, 0.15)	3.55
Rosen et al. (WG rye flour) (40)	-0.04 (-0.96, 0.89)	2.29
Rosen et al. (WG rye kernels) (40)	-1.65 (-2.70, -0.59)	1.75
Rosen et al. (WG wheat kernels) (40)	-1.30 (-2.30, -0.30)	1.95
Total (random effects)	-0.33 (-0.46, -0.20)	100.00

p-value: <0.001
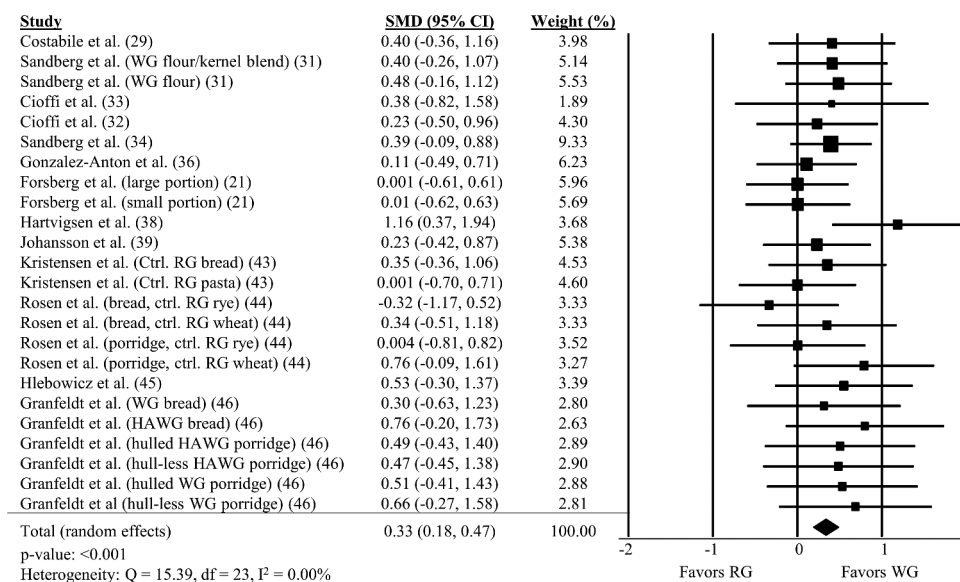Heterogeneity: Q = 23.97 , df = 24, I^2 = 0.00%

FIGURE 5 Forest plot of the meta-analysis on the effect of WG intake on desire to eat in adults. Values are the standardized mean differences (SMDs) for desire to eat AUC between WG intake and RG intake (21, 28–31, 34, 37, 39–42). Comm., commercial; Ctrl., control; RG, refined grain; var., variety; WG, whole grain.
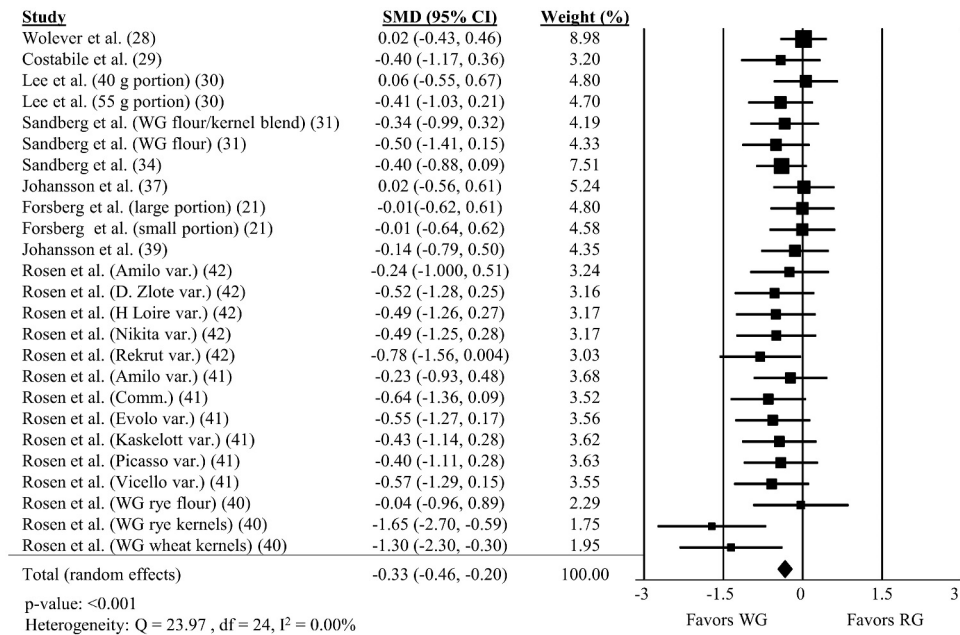
et al. (57) did not find a significant effect of WG wheat bread or WG rye bread on satiety AUC compared with RG wheat bread in a study of subjects with type 2 diabetes. Nilsson et al. (59) found a high–β-glucan WG barley variety had a significantly positive effect on satiety AUC compared with RG wheat; however, other WG barley treatments were not significantly different from RG wheat.

WG intake and desire to eat

Twenty-five comparisons reported in 11 different studies (21, 28–31, 34, 37, 39–42) were included in the analysis of the impact of WGs on desire to eat AUC. Intake of WG foods resulted in a significantly lower desire to eat AUC compared with RG foods (**Figure 5**; SMD: −0.33; 95% CI: −0.47, −0.20; $P < 0.001$) with no significant heterogeneity between studies (Q = 23.97, $P = 0.46$, $I^2 = 0.00\%$). A sensitivity analysis showed the timing of AUC measurement did not substantially impact the results, with the effect size differing slightly in studies <180 min or ≥180 min (**Supplemental Table 2**).
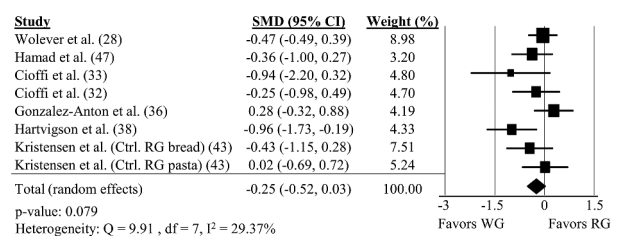
Results of subgroup analyses for desire to eat AUC are shown in Table 2. Desire to eat was lower in the WG group relative to the control when the test and control conditions matched by available carbohydrate ($P < 0.001$), but not when matched by calories.

Three studies (22, 47, 54) not included in the meta-analysis measured desire to eat AUC but did not report the data. Two studies (47, 54) did not find a significant effect of WGs on desire to eat AUC compared with RGs. The other study (22) did not report the statistical results for desire to eat AUC.

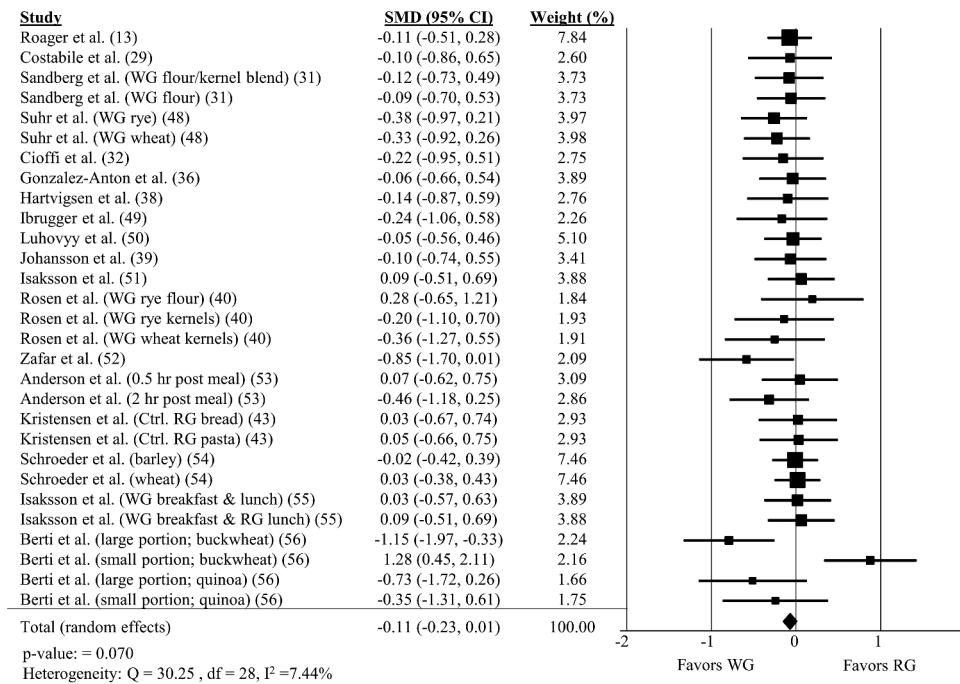### WG intake and prospective consumption

Eight comparisons reported in 7 different studies (28, 32, 33, 36, 38, 43, 47) were included in the analysis of the impact of WG on prospective consumption AUC. There was no effect of WG on prospective consumption AUC (**Figure 6**; SMD: −0.25; 95% CI: −0.52, 0.03) with no significant heterogeneity between studies (Q = 9.91, $P = 0.19$, $I^2 = 29.37\%$). Sensitivity analyses could not be performed because all studies measured prospective consumption at a time frame ≥180 min. There were no significant effects of WGs on prospective consumption AUC in any of the subgroups (Table 2).

Two studies (54, 57) not included in the meta-analysis measured prospective consumption AUC but did not report the data. One study (57) in subjects with type 2 diabetes

Study	SMD (95% CI)	Weight (%)
Wolever et al. (28)	-0.47 (-0.49, 0.39)	8.98
Hamad et al. (47)	-0.36 (-1.00, 0.27)	3.20
Cioffi et al. (33)	-0.94 (-2.20, 0.32)	4.80
Cioffi et al. (32)	-0.25 (-0.98, 0.49)	4.70
Gonzalez-Anton et al. (36)	0.28 (-0.32, 0.88)	4.19
Hartvigson et al. (38)	-0.96 (-1.73, -0.19)	4.33
Kristensen et al. (Ctrl. RG bread) (43)	-0.43 (-1.15, 0.28)	7.51
Kristensen et al. (Ctrl. RG pasta) (43)	0.02 (-0.69, 0.72)	5.24
Total (random effects)	-0.25 (-0.52, 0.03)	100.00

p-value: 0.079
Heterogeneity: Q = 9.91 , df = 7, I^2 = 29.37%

FIGURE 6 Forest plot of the meta-analysis on the effect of WG intake on prospective consumption in adults. Values are the standardized mean differences (SMDs) for prospective consumption AUC between WG intake and RG intake (32, 33, 36, 38, 43, 47, 61). Ctrl., control; RG, refined grain; var. variety; WG, whole grain.

Study	SMD (95% CI)	Weight (%)
Roager et al. (13)	-0.11 (-0.51, 0.28)	7.84
Costabile et al. (29)	-0.10 (-0.86, 0.65)	2.60
Sandberg et al. (WG flour/kernel blend) (31)	-0.12 (-0.73, 0.49)	3.73
Sandberg et al. (WG flour) (31)	-0.09 (-0.70, 0.53)	3.73
Suhr et al. (WG rye) (48)	-0.38 (-0.97, 0.21)	3.97
Suhr et al. (WG wheat) (48)	-0.33 (-0.92, 0.26)	3.98
Cioffi et al. (32)	-0.22 (-0.95, 0.51)	2.75
Gonzalez-Anton et al. (36)	-0.06 (-0.66, 0.54)	3.89
Hartvigsen et al. (38)	-0.14 (-0.87, 0.59)	2.76
Ibrugger et al. (49)	-0.24 (-1.06, 0.58)	2.26
Luhovyy et al. (50)	-0.05 (-0.56, 0.46)	5.10
Johansson et al. (39)	-0.10 (-0.74, 0.55)	3.41
Isaksson et al. (51)	0.09 (-0.51, 0.69)	3.88
Rosen et al. (WG rye flour) (40)	0.28 (-0.65, 1.21)	1.84
Rosen et al. (WG rye kernels) (40)	-0.20 (-1.10, 0.70)	1.93
Rosen et al. (WG wheat kernels) (40)	-0.36 (-1.27, 0.55)	1.91
Zafar et al. (52)	-0.85 (-1.70, 0.01)	2.09
Anderson et al. (0.5 hr post meal) (53)	0.07 (-0.62, 0.75)	3.09
Anderson et al. (2 hr post meal) (53)	-0.46 (-1.18, 0.25)	2.86
Kristensen et al. (Ctrl. RG bread) (43)	0.03 (-0.67, 0.74)	2.93
Kristensen et al. (Ctrl. RG pasta) (43)	0.05 (-0.66, 0.75)	2.93
Schroeder et al. (barley) (54)	-0.02 (-0.42, 0.39)	7.46
Schroeder et al. (wheat) (54)	0.03 (-0.38, 0.44)	7.46
Isaksson et al. (WG breakfast & lunch) (55)	0.03 (-0.57, 0.63)	3.89
Isaksson et al. (WG breakfast & RG lunch) (55)	0.09 (-0.51, 0.69)	3.88
Berti et al. (large portion; buckwheat) (56)	-1.15 (-1.97, -0.33)	2.24
Berti et al. (small portion; buckwheat) (56)	1.28 (0.45, 2.11)	2.16
Berti et al. (large portion; quinoa) (56)	-0.73 (-1.72, 0.26)	1.66
Berti et al. (small portion; quinoa) (56)	-0.35 (-1.31, 0.61)	1.75
Total (random effects)	-0.11 (-0.23, 0.01)	100.00

p-value: = 0.070
Heterogeneity: Q = 30.25 , df = 28, I^2 =7.44%

Favors WG   Favors RG

FIGURE 7 Forest plot of the meta-analysis on the effect of WG intake on energy intake in adults. Values are the standardized mean differences (SMDs) for caloric intake between WG intake and RG intake (13, 29, 31, 32, 36, 38–40, 43, 48–56). Ctrl., control; RG, refined grain; WG, whole grain.

WG intake and energy intake

The impact of WGs on energy intake included 29 comparisons from 17 different studies (13, 29, 31, 32, 36, 38–40, 43, 48–56). There was a small, nonsignificant reduction in energy intake following WG consumption (**Figure 7**; SMD: −0.11; 95% CI: −0.23, 0.01; $P = 0.070$) and no significant heterogeneity between studies (Q = 30.25, $P = 0.35$, $I^2 = 7.44\%$). There was a significant effect of WGs on energy intake when the amount of WGs fed was >90.1 g ($P = 0.006$), the median amount among all studies, but this effect was not observed with amounts ≤90.1 g. No other subgroup analyses showed a significant effect on energy intake (**Table 3**).

Two studies (21, 60) not included in the meta-analysis measured energy intake but did not report the data. One study reported no significant effect of WGs compared with RGs on energy intake at a subsequent meal (60). Forsberg et al. (21) also reported no significant difference between WGs and RGs in energy intake at a subsequent meal with a large breakfast (∼600 kcal), but a significant effect of WGs on energy intake with a smaller breakfast (∼375 kcal).

Quality of evidence

The quality of evidence as assessed by GRADE criteria is summarized in **Table 4**. Overall, the evidence for subjective measures of appetite and energy intake was rated as moderate (low for prospective consumption). The evidence rating was downgraded due to concerns about risk of bias in the studies and possible publication bias. Sources of bias in the studies were typically inadequate description of randomization procedures or allocation concealment and inability to blind the treatments. There was also an indication of possible publication bias suggesting that smaller studies with results that did not confirm the main study hypothesis were not as likely to be published. Risk-of-bias assessment on the outcomes of individual studies and funnel plots for the main outcomes are shown in **Supplemental Table 3** and **Supplemental Figures 1–6**.

Discussion

The results of this meta-analysis of RCTs suggest that intake of WG foods reduces hunger and desire to eat and increases fullness and satiety compared with RG foods. There was no significant effect of WGs on energy intake at subsequent meals or across the day compared with RG foods from the subgroup analyses, although there was a small, nonsignificant reduction in energy intake in the main analysis when data were pooled ($P = 0.07$). To our knowledge, this is the first systematic review and meta-analysis to evaluate the effect of WG intake compared with RG intake on subjective appetite measures and energy intake. Several meta-analyses have evaluated the relation of WG intake to body weight, and observational data tend to support an inverse relation (4–6). However, RCTs with intervention periods of a few weeks up to a few months have shown

The other study (54) found no significant

did not find a significant effect of WG wheat bread or WG rye bread on prospective consumption AUC compared with RG wheat bread. The other study (54) found no significant difference in prospective consumption between WG barley or WG wheat and RG rice.

TABLE 3 Subgroup analyses for the effect of WGs on energy intake in adults[1]

Outcome and subgroups	Number of comparisons/studies	Subjects (WG/control)	Effect estimate SMD (95% CI)[2]	I^2 (%)	P value[2]
Energy intake					
Type of WG					
Rye	9/7	311 (156/155)	− 0.09 (−0.30, 0.13)	0.00	0.440
Wheat	8/7	326 (162/162)	− 0.09 (−0.30, 0.12)	0.00	0.407
Other[3]	12/8	518 (259/259)	− 0.17 (−0.45, 0.11)	57.00	0.227
Amount of WG (median split)					
≤90.1 g	15/11	660 (330/330)	− 0.01 (−0.18, 0.16)	16.94	0.928
>90.1 g	12/7	411 (207/204)	− 0.27 (−0.46, −0.08)	0.00	0.006
Feeding approach					
Matched available CHO	13/9	395 (197/198)	− 0.13 (−0.32, 0.07)	0.00	0.196
Matched calories	9/6	372 (188/184)	− 0.08 (−0.28, 0.12)	0.00	0.435
Measurement timing					
Daily intake	4/3	236 (120/116)	− 0.17 (−0.42, 0.09)	0.00	0.191
Subsequent meal intake	21/14	811 (405/406)	− 0.10 (−0.26, 0.06)	25.32	0.228
Third meal intake[4]	3/2	108 (54/54)	− 0.13 (−0.51, 0.24)	0.00	0.478

[1]CHO, carbohydrate; SMD, standardized mean difference; WG, whole grain.
[2]Effect estimates and P values from random effects models.
[3]Other category includes barley, buckwheat, corn, oat, and quinoa. There were not enough studies in individual grains to run a separate subgroup analysis.
[4]Third meal refers to the next meal consumed after the subsequent meal (e.g., breakfast = test meal, lunch = subsequent meal, dinner = third meal).

mixed effects of WG intake on body weight change (4, 7, 13, 62, 63).

WG intake was associated with significant reductions in appetite ratings, with effects that were small to moderate in magnitude. There was also a small, nonsignificant reduction in energy intake that only became significant at high levels of WG intake (above the median level of 90.1 g). Taken together, these results suggest that WGs are able to reduce subjective appetite following a meal, but not enough to significantly impact acute energy intake at a subsequent meal or across the day. Also, considering the possible publication bias favoring studies that show beneficial effects of WGs on energy intake, it is likely that WGs have little impact on short-term energy intake, except perhaps at high levels of WG intake. Studies

that assessed chronic consumption of WGs on energy intake were few and only 3 to 8 wk in duration (13, 48, 51). The longest RCT (13) did not find a significant impact of WGs on daily energy intake compared with an RG diet, but there was a significant change in body weight and body composition in the WG diet that correlated with a change in energy intake. Longer-term studies (>16 wk) might be able to determine whether small changes in energy intake associated with WG consumption can have cumulative long-term effects that explain differences in body weight reported in observational studies.

The diversity in studies allowed for several subgroup analyses. Firstly, the type of WG tested in the studies often varied, with WG rye and WG wheat being the most

TABLE 4 Quality of evidence included in the systematic review and meta-analysis of WGs on subjective appetite measures and energy intake in adults, based on GRADE approach[1]

Outcome	Risk of bias[2]	Inconsistency[3]	Indirectness	Imprecision	Publication bias[4]	Decision[5]
Hunger	Some concerns	Consistent	No serious indirectness	No serious imprecision	Possible	⊕⊕⊕∅ Moderate
Fullness	Some concerns	Moderate	No serious indirectness	No serious imprecision	Possible	⊕⊕⊕∅ Moderate
Satiety	Some concerns	Consistent	No serious indirectness	No serious imprecision	Undetected	⊕⊕⊕∅ Moderate
Desire to eat	Some concerns	Consistent	No serious indirectness	No serious imprecision	Possible	⊕⊕⊕∅ Moderate
Prospective consumption	Some concerns	Moderate	No serious indirectness	Moderate imprecision	Unable to determine[6]	⊕⊕∅∅ Low
Energy intake	Low	Consistent	No serious indirectness	Moderate imprecision	Possible	⊕⊕⊕∅ Moderate

[1]GRADE, Grading of Recommendations Assessment, Development and Evaluation; WG, whole grain.
[2]Ranked down primarily for inadequate description of allocation concealment and lack of blinding.
[3]Based on I^2 using thresholds in Cochrane Handbook for Systematic Reviews of Interventions, Version 6. The Cochrane Collaboration, 2019. Available at: https://training.cochrane.org/handbook/current.
[4]Based on visual analysis of funnel plots.
[5]Symbols are suggested representations of quality of evidence from GRADE Handbook (https://gdt.gradepro.org/app/handbook/handbook.html).
[6]Only 8 studies and a minimum of 10 studies are generally needed to evaluate a funnel plot.

frequently tested and both significantly reducing hunger and desire to eat and increasing fullness compared with RGs. Interestingly, there were fewer studies on WGs such as oat and barley, which are rich in the viscous, fermentable fiber β-glucan and may impact appetite and energy intake differently from wheat and rye with primarily nonviscous and poorly fermentable fibers. Fermentation of fiber and other phenolic compounds in WGs by gut microbes can produce metabolites, such as SCFAs, that could influence appetite and energy intake beyond the subsequent meal (13). Furthermore, viscous fibers have been shown to slow gastric emptying and prolong the release of cholecystokinin in response to a fat-containing meal, possibly contributing to enhanced feelings of satiety (35, 64). The studies on oat and barley in this meta-analysis had mixed results regarding subjective appetite and energy intake so more studies in these WGs are needed.

Using a median split to create a dichotomy of "higher" and "lower" WG intake, the results suggest small effect sizes with lower levels of WGs and moderate effect sizes with higher levels of WGs. Of note, the quantities of WGs fed in most studies were relatively high, with medians in the range of 85 to 90 g. This is higher than typical consumption and recommendations for intake. Daily WG consumption in the United States is typically ≤ 16 g, and recommendations suggest 48 g/d (3, 65). Intake is somewhat higher in Europe, ranging from 23 to 36 g/d, but even populations in northern Europe with the highest intake (37–58 g/d) are still on the low end of the levels tested in these studies (65). Several studies included these high levels to achieve 50 g of available carbohydrate from the test food. One study fed >200 g WGs in a test food and noted it was necessary to achieve 50 g of available carbohydrate, but also acknowledged that >25% of the subjects were unable to finish consuming the entire test product (59). Thus, more studies are needed at lower, realistic levels of WGs recommended for a healthy diet.

The subgroup analyses also showed differences in appetite responses based on the feeding design. When interventions were matched for available carbohydrate, WGs were significantly different from RGs for hunger, fullness, and desire to eat. However, when studies were matched for calories or calories and volume (none were matched for volume alone), there was not a significant difference between WG and RG conditions. Because calories and volume both impact subjective appetite (66), this shows the importance of considering both factors in studies on food ingredients and appetite. WG foods have less available carbohydrates than RG foods due to their fiber content; therefore, studies that match available carbohydrates often fed a greater volume of food in the WG condition than the RG condition, which could contribute to greater feelings of fullness or lower feelings of hunger. Indeed, several of the investigators commented on the difference in portion size and calories potentially contributing to the findings (29, 36, 38, 42, 56). Although matching available carbohydrate might yield a more mechanistic understanding of the influence of glycemic response on appetite, it does not reflect typical consumption patterns or recommendations,

which suggest substitutions, such as exchanging a slice of white bread for a slice of whole wheat bread. Substitution of foods containing WGs for similar foods made with RGs often results in increased dietary fiber intake and reduced energy density, both of which have been associated with lower daily energy consumption and less weight gain over time (66). Almost half (14 of 32) of studies in the current meta-analysis matched available carbohydrates and did not match conditions for calories or volume. Accordingly, there is a need for more studies matching calories and volume between WG and RG conditions to provide greater clarity regarding drivers of differences in indicators of appetite associated with WG food consumption.

Interestingly, studies that measured appetite at a subsequent meal fed ≥ 11 h after WG consumption showed significant effects on hunger, satiety, and desire to eat, similar in magnitude to differences observed in acute meal studies. The levels of WGs fed were also similar to acute meal studies, suggesting a potential long-term effect of WGs on appetite that could be mediated by slowing digestion or the fermentation of fibers from WGs in the colon. Nilsson et al. (59) showed that an evening meal with WGs significantly reduced the gastric emptying rate at a subsequent standardized breakfast meal, which could have contributed to the greater feelings of satiety after breakfast. Fermentation metabolites, such as SCFAs, have been shown to stimulate the production of appetite-related hormones, such as glucagon-like peptide-1 and peptide YY (67, 61, 68). A meta-analysis has shown glucagon-like peptide-1 to increase feelings of fullness and reduce energy intake in humans (69). These potential mechanisms by which WGs might impact long-term appetite and energy intake should be further investigated.

The strengths of the current systematic review and meta-analysis include a comprehensive search of 3 databases to ensure broad coverage of the literature and the inclusion of a number of subgroup and sensitivity analyses that have helped identify hypotheses for additional research and gaps in the available evidence. However, the systematic review and meta-analysis was also limited by poor reporting of the amount of WGs in the studies, which resulted in the exclusion of several studies and 17 of 36 studies requiring calculations to estimate WG content based on recipes. Additional studies were excluded that measured subjective appetite but did not calculate the AUC. The present analysis also only included studies that provided WG foods where $\geq 51\%$ of the grain was WG. There was also an indication of possible publication bias suggesting that smaller studies with results that did not confirm the main study hypothesis were not as likely to be published. Finally, there were no studies in participants with type 2 diabetes that met the inclusion criteria and provided data for the meta-analysis. Furthermore, only 1 study in the meta-analysis was completed in participants with metabolic syndrome (38). Thus, more investigation is needed in these populations to determine whether effects of WG consumption on appetite differs between groups with and without metabolic dysregulation.

In summary, the results from this systematic review and meta-analysis show that consumption of WG foods, compared with RG foods, modestly but significantly reduced hunger and desire to eat and increased fullness and satiety, but showed only a small, nonsignificant reduction in energy intake at the next meal or across the day. Thus, although it is plausible that effects of WG consumption on appetite and subsequent energy intake contribute to the associations of greater WG intake with lower risks for weight gain and overweight or obesity reported in observational studies, additional research, especially with longer feeding periods, will be needed before firm conclusions can be drawn in this regard. More studies are warranted to further clarify the effects of different WG types and of consumption in amounts consistent with current recommendations. Particular attention should be paid to the research design to ensure calories and volume are matched because these factors can greatly influence appetite and subsequent energy intake.

Acknowledgments

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