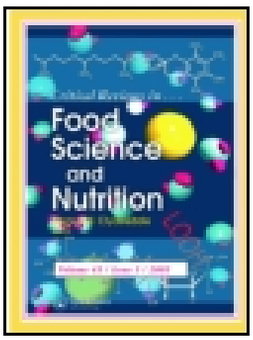

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The effect of brown rice compared to white rice on adiposity indices, lipid profile, and glycemic markers: a systematic review and meta-analysis of randomized controlled trials

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REVIEW

The effect of brown rice compared to white rice on adiposity indices, lipid profile, and glycemic markers: a systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

A few randomized controlled trials (RCTs) have assessed the effect of brown rice consumption on metabolic parameters compared to white rice, with inconsistent findings. Therefore, the present systematic review and meta-analysis was designed to evaluate the effect of brown rice on adiposity indices, lipid profile, and glycemic markers in adult subjects compared to white rice. In this study, PubMed/Medline, Scopus, Web of Sciences, and Embase databases were comprehensively searched until March 2021. Thirteen RCTs were selected and then included in the meta-analysis. As reported, brown rice significantly reduced weight by −1.63 kg (95% CI: −2.15 to −1.11, I^2=97%, n = 6), body mass index (BMI) by −0.58 kg/m^2 (95% CI: −0.78 to −0.37, I^2=96%, n = 6), and waist circumference by −2.56 cm (95% CI: −4.86 to −0.26, I^2=88%, n = 5) compared with white rice. Moreover, it had no significant effect on lipid profile and glycemic markers. Besides, pre-germinated brown rice significantly declined weight (-1.75 kg, 95% CI: −2.70 to −0.81, I^2=99%, n = 4), total cholesterol (-24.22 mg/dl, 95% CI: −33.03 to −15.41, I^2=78%, n = 5), triglyceride (TG) (-43.28 mg/dl, 95% CI: −74.05 to −12.50, I^2=90%, n = 5), low-density lipoprotein (LDL) (-20.05 mg/dl, 95% CI: −29.57 to −10.52, I^2=71%, n = 5), and fasting blood glucose (FBG) (-15.83 mg/dl, 95% CI: −25.20 to −6.46, I^2=91%, n = 5). In accordance with Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, the certainly of the included evidence was low and very low. The results of the present study indicate that, brown rice has anti-obesity effects in comparison with white rice; however, it has no beneficial effects on lipid profile and glycemic markers. Contrary to brown rice, it was shown that, pre-germinated brown rice significantly decreases body weight and improves lipid profile and FBG levels compared to white rice. Accordingly, our results indicate that, pre-germinated brown rice has better functional effects on promoting lipid profile and FBG compared to brown rice.

KEYWORDS

Brown rice; glycemia; lipid profile; meta-analysis; obesity; white rice

Introduction

Rice, and especially white rice, is a main part of diet in many countries, particularly Asian countries. White rice can be produced from milling and removing bran layer of whole rice. Thus, it contains less nutritive and non-nutritive compounds (Golozar et al. 2017). In this regard, several studies have reported that there is a relationship between white rice consumption and some cardiovascular risk factors such as obesity and diabetes (Azadbakht, Haghighatdoost, and Esmaillzadeh 2016, Bahadoran et al. 2014, Song et al. 2015, Zavitsanou et al. 2019, Mohan et al. 2014). In addition, two meta-analyses of observational studies indicated that, the highest category of white rice intake can increase the risk of type 2 diabetes by 27% (the lowest category ranged from 0 to 500 g/d and the highest category ranged from 56 to 750 g/d) (Hu et al. 2012) and metabolic syndrome by 30% (the lowest category ranged from 49 to 68 g/d and the highest category ranged from 142 to 280 g/d) (Krittanawong et al. 2017) in adults compared with its lowest category.

Contrary to white rice, brown rice is a whole grain that poses several functional properties. But due to its unpleasant taste and hard texture, it has less popularity among people (Uenobe et al. 2017). Thus, in some countries, it is soaked in water to improve its taste and texture and this product is called pre-germinated brown rice (Geng et al. 2016). Both brown rice and pre-germinated brown rice contain many bioactive compounds including fibers, phytochemicals, vitamins, minerals, and essential fatty acids, which have many beneficial effects on metabolic risk factors (Malik et al. 2019, Lee et al. 2019). In a randomized crossover trial conducted on 15 overweight subjects (Mohan et al. 2014), it was

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indicated that, consumption of brown rice can significantly reduce the daily changes in glucose concentration by 20%, fasting insulin by 54%, and glycemic response by 23% compared to white rice. Another trial (Araki et al. 2017) showed that, brown rice is more effective on decreasing triglyceride (TG) level of chylomicrons, very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and total cholesterol (TC) levels of chylomicrons in the patients with pre-diabetes compared to white rice. Hence replacing white rice with brown rice may have some protective effects against several chronic diseases such as diabetes and cardiovascular disease (CVD) (Uenobe et al. 2017, Sun et al. 2010). However, a few randomized controlled trials (RCTs) have assessed the effect of brown rice in comparison with white rice consumption on metabolic parameters, and their results are inconsistent. Correspondingly, some of the trials have stated that brown rice/pre-germinated brown rice is effective on improving obesity, glucose, and lipid metabolism (Araki et al. 2017, Shimabukuro et al. 2014), but the other studies have not supported these beneficial effects (Kuroda et al. 2019, Matsuzaki et al. 2019). Therefore, the present systematic review and meta-analysis was designed to evaluate the effect of brown rice on adiposity indices, lipid profile, and glycemic markers in adult subjects in comparison with white rice.

Methods

We performed the present systematic review and meta-analysis in terms of the PRISMA (the Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement guidelines (Moher et al. 2009). The protocol of the study is registered in PROSPERO (ID: CRD42020172017).

Data source and study selection

To conduct the present study, four electronic databases including PubMed/Medline, Scopus, Web of Sciences, and Embase were comprehensively searched until March 2021. Also, there was no restriction for language and date of publication. The search strategies used for the current study were as follows: "brown rice"[ti/ab] AND ((((((((((((("Triglycerides"[Mesh] OR ("Lipoproteins, LDL"[Mesh] OR "Cholesterol, HDL"[Mesh] OR "Lipoproteins, HDL"[Mesh])) OR ("Cholesterol"[Mesh] OR "Cholesterol, VLDL"[Mesh] OR "Cholesterol, LDL"[Mesh] OR "Cholesterol, HDL"[Mesh] OR "lipoprotein cholesterol"[Supplementary Concept])) OR "Hyperlipidemias"[Mesh]) OR "high density lipoprotein"[All Fields]) OR "low density lipoprotein"[All Fields]) OR "HDL"[All Fields]) OR "LDL"[All Fields]) OR "total cholesterol"[All Fields]) OR "lipid profile"[All Fields]) OR "blood lipid"[All Fields]) OR "blood lipids"[All Fields]) OR "dyslipidemia"[All Fields]) OR "triacylglycerol"[All Fields]) OR "triacylglycerols"[All Fields]) OR ((((((("Blood Glucose"[Mesh] OR ("Diabetes Mellitus"[Mesh] AND "Diabetes Mellitus, Type 2"[Mesh])) OR "Glycated Hemoglobin A"[Mesh]) OR "fasting blood sugar"[All Fields]) OR "glycemic index"[All Fields]) OR "glycemia"[All Fields]) OR "insulin"[All Fields]) OR "HOMA"[All Fields]) OR "HOMA-IR"[All Fields])) OR ((((((((((("Body Weight"[Mesh] OR "Weight Loss"[Mesh] OR "Weight Gain"[Mesh] OR "Body Weight Changes"[Mesh]) OR "Body Mass Index"[Mesh]) OR "Body Composition"[Mesh]) OR ("Obesity"[Mesh] OR "Obesity, Abdominal"[Mesh])) OR "Overweight"[Mesh]) OR "Adipose Tissue"[Mesh]) OR "fat mass"[All Fields]) OR "fat free mass"[All Fields]) OR "lean mass"[All Fields]) OR "weight reduction"[All Fields]) OR "waist circumference"[All Fields]) OR "waist circumferences"[All Fields]) OR "adiposity"[All Fields])). The reference list of the reviews and relevant papers were also checked for further studies.

Screening of the included articles was performed by two reviewers (M.G and K.T) to find the studies that assessed the effect of brown rice or pre-germinated brown rice on adiposity indices, lipid profile, and glycemic markers. The inclusion criteria were as follows: (a) parallel randomized controlled trials, (b) crossover trials reporting the results of the first and second phase separately, c) participants older than 18 years old, d) using brown rice or pre-germinated brown rice as intervention versus white rice as placebo, and e) measuring weight, body mass index (BMI), waist circumference (WC), percentage of body fat (PBF), TC, high-density lipoprotein (HDL), LDL, TG, fasting blood glucose (FBG), insulin, glycated hemoglobin (HbA1c), and homeostatic model assessment of insulin resistance (HOMA-IR) as outcomes. In addition, the exclusion criteria were as follows: (a) pregnant or lactating women, (b) using brown rice combined with other grains or foods as intervention, and (c) kin publication (i.e. the results for one RCT sample reported in two separate articles). Moreover, we excluded the trials that used one component of brown rice such as brown rice oil or brown rice glycoside as intervention; because the purpose of the present study was to assess the effect of whole brown rice on the above-mentioned outcomes. In addition, investigations on the other types of rice such as black rice, gold rice or rough rice were ignored due to lack of similarity in their composition with brown rice.

Data extraction

The following data were extracted: study design (parallel or crossover), sample size of each group, mean age and gender of the subjects, amount of brown rice, type of intervention (brown rice or pre-germinated brown rice), study duration, health status of the participants, mean and standard deviation (SD) of outcomes in both groups once at baseline and once at the end of follow-up (for parallel trials, end of study, and for crossover trials, end of the first phase), and mean and SD for changes from baseline in both groups if reported.

Assessment of the risk of bias and quality of the evidence

In each one of the included studies, the risk of bias was assessed by Cochrane risk-of-bias tool (Higgins et al. 2011).

Accordingly, this tool is comprised of several items including: random sequence generation and allocation concealment (selection bias), blinding of participants and personnel and blinding of outcome assessment (performance and detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and the other biases.

Quality of the evidence for each outcome was also evaluated in terms of the GRADE (Grading of Recommendations Assessment, Development and Evaluation) guideline using GRADEpro software. In this regard, we considered the risk of bias, inconsistency, indirectness, imprecision, and publication of bias to assess the certainly of evidence. Based on this tool, evidence was classified into high, moderate, low or very low quality. Our results are presented in summary of finding Table.

Statistical analysis

All the analyses were performed using STATA software version 12 (STATA corp, College Station, TX, USA). For each outcome, mean and SD (for changes from baseline) were used to calculate the weighted mean differences (WMD) and 95% confidence interval (95% CI). In addition, we estimated SD using the following equations when the studies have reported standard error (SE) (SD = SE$\times\sqrt{}$ n) or 95% CI (SD=((upper limit-lower limit)/3.92)$\times\sqrt{}$ n). In those studies that did not note the SD for changes, we calculated that using the correlation coefficient formula. The fixed-effect models were used to calculate pooled effect size if heterogeneity (I^2) was <50%, and the random-effect models were also used if heterogeneity was ≥50%. We run subgroup analysis to compare changes in outcomes between a subset of dose of brown rice (≤150 g/d vs. >150 g/d), and length of follow-up (≤6 weeks vs. >6 weeks). Meta-regression analysis was conducted to find the sources of heterogeneity. It was also performed to assess linear association between the clinical outcomes and explanatory variables (i.e. age, baseline BMI, amount of brown rice, and follow-up period). In this regard, the coefficient obtained from this analysis shows how the outcome variable alter per one unit increment in the explanatory variable (Egger, Davey-Smith, and Altman 2008). Afterward, sensitivity analysis was performed by excluding the study to assess the effect of each study on overall effect size. Egger's test was also used to investigate publication bias. The statistical significance level was defined as $P < 0.05$.

Results

The flow chart of the study is presented in Figure 1. Our basic search provided us with 1686 articles obtained from PubMed/Medline (n = 168), Scopus (n = 802), Embase (n = 317), and Web of Sciences (n = 399). Subsequently, 559 articles were removed due to duplication, and 1127 studies were screened according to the titles and abstracts. Of total, 1052 articles did not meet the inclusion criteria, so they were removed and 75 articles were assessed for more details. Finally, 13 relevant articles (Araki et al. 2017, Bui et al. 2014, Geng et al. 2016, Hsu et al. 2008, Kazemzadeh et al. 2014, Kondo et al. 2017, Kuroda et al. 2019, Nakayama et al. 2017, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011, Mai, Trang, and Hai 2020, Ren et al. 2020) conducted on 895 subjects (475 in brown rice group and 420 in white rice group) were selected and then included in the meta-analysis.

Characteristics of the included studies are presented in Table 1. Nine studies assessed the effect of brown rice (Araki et al. 2017, Kazemzadeh et al. 2014, Kondo et al. 2017, Kuroda et al. 2019, Nakayama et al. 2017, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011, Ren et al. 2020) and five studies investigated the effect of pre-germinated brown rice (Bui et al. 2014, Geng et al. 2016, Hsu et al. 2008, Mai, Trang, and Hai 2020, Ren et al. 2020) on the metabolic risk factors. Notably, nine studies were parallel randomized trials (Araki et al. 2017, Bui et al. 2014, Geng et al. 2016, Kondo et al. 2017, Kuroda et al. 2019, Wang et al. 2013, Zhang et al. 2011, Mai, Trang, and Hai 2020, Ren et al. 2020) and four studies were crossover trials (Hsu et al. 2008, Shimabukuro et al. 2014, Kazemzadeh et al. 2014, Nakayama et al. 2017). The mean age of the participants was 53.8 ± 10.8 years old and 54.8 ± 11.8 years old in brown rice groups and in white rice groups, respectively. Daily consumption amounts of cooked brown rice and pre-germinated brown rice were 50-400 g and 50-450 g, respectively. Duration of follow-up periods ranged from 4 to 104 weeks. The numbers of those studies reporting the effect of brown rice or pre-germinated brown rice on weight, BMI, WC, PBF, lipids profile, FBG, insulin, HbA1c, and HOMA-IR were 10, 10, 7, 4, 12, 12, 7, 8, and 6, respectively. Two studies did not report TC (Wang et al. 2013) and LDL (Hsu et al. 2008) and their value were calculated using the Friedewald equation.

The risk of bias for each study is presented in Figure 2. Most of studies did not provide any data on random sequence generation and allocation concealment. Three studies were outcome blind (Geng et al. 2016, Hsu et al. 2008, Zhang et al. 2011) and the remaining 10 studies did not explain blinding (Araki et al. 2017, Bui et al. 2014, Geng et al. 2016, Hsu et al. 2008, Kuroda et al. 2019, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011, Ren et al. 2020). High risk of attrition bias was detected in four studies (Kazemzadeh et al. 2014, Kuroda et al. 2019, Wang et al. 2013, Geng et al. 2016). There was no evidence of reporting bias or other biases among the included studies.

Quality of the evidence is presented in Supplementary Table 1. With respect to the GRADE approach, the certainly of the included evidence was low and very low quality. The risk of bias including lack of random sequence generation, allocation concealment, and blinding and incomplete data and inconsistency are known as responsible factors for these findings.

The effect of brown rice on adiposity indices, lipid profile and glycemic markers

Eight studies have examined the effect of brown rice on lipid profile (Araki et al. 2017, Kazemzadeh et al. 2014,

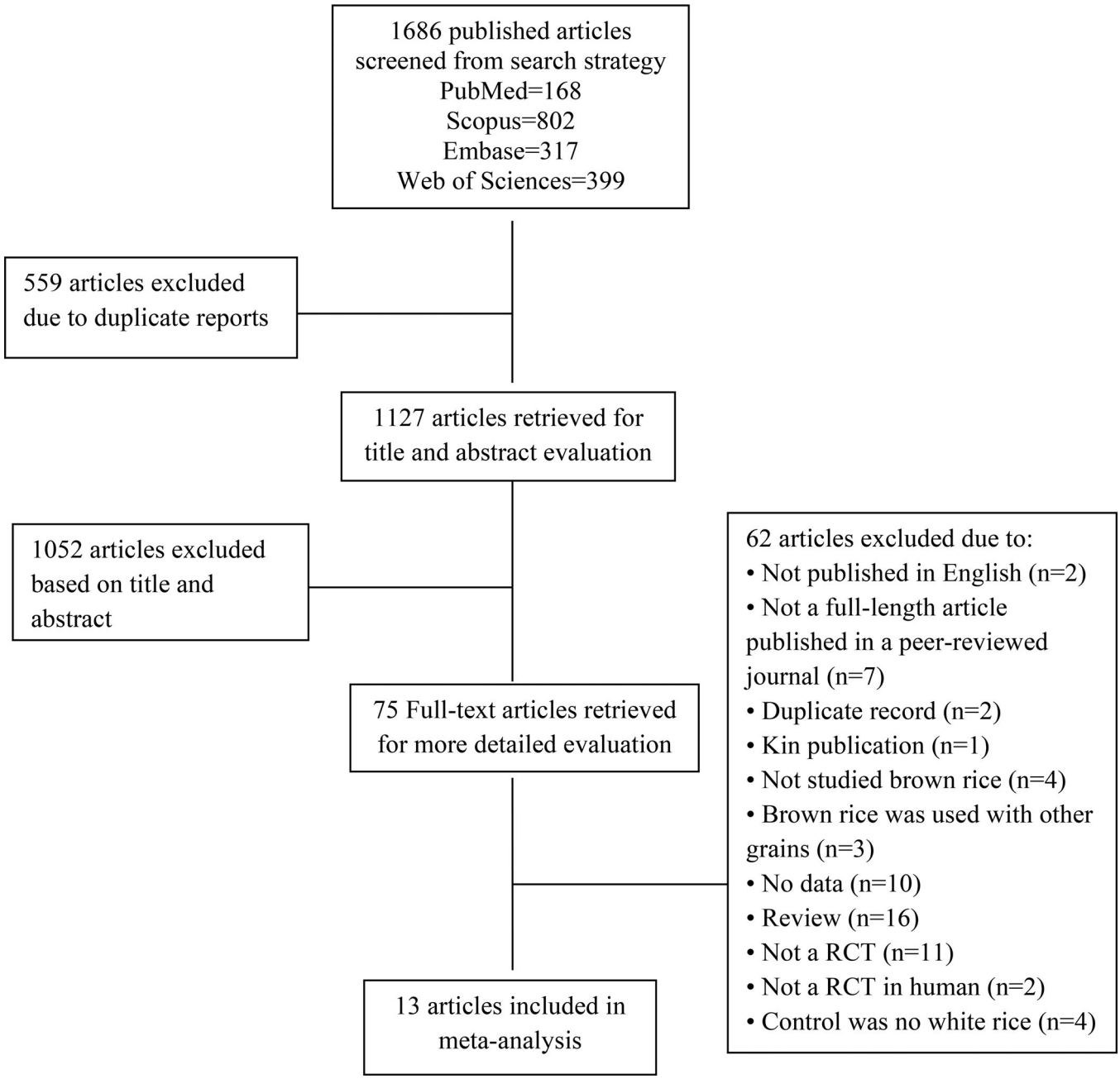


Figure 1. Flow chart of studies reviewed.

Kondo et al. 2017, Kuroda et al. 2019, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011, Ren et al. 2020), and FBG (Araki et al. 2017, Kazemzadeh et al. 2014, Kondo et al. 2017, Kuroda et al. 2019, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011, Ren et al. 2020), seven studied on HbA1c (Araki et al. 2017, Kondo et al. 2017, Kuroda et al. 2019, Nakayama et al. 2017, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011); six studies on weight (Araki et al. 2017, Kazemzadeh et al. 2014, Kondo et al. 2017, Kuroda et al. 2019, Shimabukuro et al. 2014, Wang et al. 2013) and BMI (Kazemzadeh et al. 2014, Kondo et al. 2017, Kuroda et al. 2019, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011); five studies on WC (Kazemzadeh et al. 2014, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011, Araki et al. 2017), insulin (Araki et al. 2017, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011, Kondo et al. 2017), and HOMA-IR (Araki et al. 2017, Kondo et al. 2017, Shimabukuro et al. 2014, Wang et al. 2013, Zhang et al. 2011); and two studies only on PBF (Kondo et al. 2017, Kuroda et al. 2019). Forest plot for the effect of brown rice on adiposity indices is shown in Figures 3a-5a. It was indicated that, brown rice significantly reduces weight (-1.63 kg, 95% CI: −2.15 to −1.11), BMI (-0.58 kg/m^2, 95% CI: −0.78 to −0.37), and WC (-2.56 cm, 95% CI: −4.86 to −0.26) compared with white rice. Due to a few number of studies that reported PBF, its forest plot is not shown, but brown rice consumption had no significant effect on PBF (-2.13%, 95% CI: −7.42 to 3.15). Also, there was a sever heterogeneity among the studies performed on weight (I^2=97%), BMI (I^2=96%), WC (I^2=88%), and PBF (I^2=89%). Moreover, the results of dose-response analysis revealed no evidence of nonlinear

Table 1. Characteristics of included RCTs.

Author, year, Country	Design	Study population (intervention/control)	Intervention group	Control group	Amount of cooked rice	Follow-up (wk)	Outcome measured	Compliance	Conflict of interest
Ren et al. 2020, China	Parallel RCT in the real world	Health status: Patients with MetS initial sample = 28/28 female/male = 62/52 age = 18.0-70.0 yr BMI = Not reported final sample = 28/28 included in analysis = 28/28	Brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	50 g/d	4	FBG, TC, TG, HDL, LDL	Not monitored	None
		Health status: Patients with MetS initial sample = 56/28 female/male = 62/52 age = 18.0-70.0 yr BMI = Not reported final sample = 56/28 included in analysis = 56/28	Pre-germinated brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	50 g/d	4	FBG, TC, TG, HDL, LDL	Not monitored	None
Mai, Trang, and Hai 2020, Vietnam	Parallel RCT in the real world	Health status: Patients with MetS initial sample = 43/43 female/male = 64/16 age = 65.2/65.0 yr BMI = 25.9/25.5 kg/m^2 final sample = 40/40 included in analysis = 40/40	Pre-germinated brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	450 g/d	12	weight, BMI, WC, FBG, insulin, HOMA, TC, TG, HDL, LDL	Not monitored	None
Kuroda et al. 2019, Japan	Parallel RCT in the real world	Health status: Healthy elderly initial sample size = 25/27 female/male = 19/15 age = 70.5/75.4 yr BMI = 24.8/22.5 kg/m^2 final sample size = 17/17 included in analysis = 17/17	Brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	225 g/d	104	weight, BMI, PBF, FBG, HbA1c, TC, TG, HDL, LDL	Not monitored	None
Araki et al. 2017, Japan	Parallel RCT in the real world	Health status: Overweight subjects with pre-diabetes initial sample size = 21/21 female/male = 22/19 age = 54.8/52.9 yr BMI = 27.5/27.2 kg/m^2 final sample size = 20/21 included in analysis = 21/21	Brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	400 g/d	12	weight, WC, FBG, insulin, HbA1c, HOMA, TC, TG, HDL, LDL	Not monitored	None
Kondo et al. 2017, Japan	Parallel RCT in the real world	Health status: DM II initial sample size = 14/15 female/male = 10/18 age = 65.2/68.1 yr BMI = 24.2/25.0 kg/m^2 final sample size = 14/14 included in analysis = 14/15	Brown rice Isocaloric diet, planned: 28-30 kcal/IBW; 15% PRO, 25% FAT and 60% CHO Rice provided to the participants	White rice Isocaloric diet, planned: 28-30 kcal/IBW; 15% PRO, 25% FAT and 60% CHO	150 g/d	8	weight, BMI, PBF, FBG, insulin, HbA1c, HOMA, TC, TG, HDL, LDL	Not monitored	Yes
Nakayama et al. 2017, Japan	Crossover RCT in the real world	Health status: DM II initial sample size = 9/9 female/male = 4/12 age = 64 yr BMI = 25.7 kg/m^2 final sample size = 8/8 included in analysis = 8/8	Brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	300 g/d	8	HbA1c	Not monitored	None
Geng et al. 2016, China	Parallel RCT in the real world	Health status: Patients with hypercholesterolemia initial sample size = 123/115	Pre-germinated brown rice No isocaloric diet	White rice No isocaloric diet	150 g/d	12	weight, BMI, WC, FBG, TC, TG, HDL, LDL	Monitored by phone or face-	None

(*continued*)

Table 1. Continued.

Author, year, Country	Design	Study population (intervention/control)	Intervention group	Control group	Amount of cooked rice	Follow-up (wk)	Outcome measured	Compliance	Conflict of interest
		female/male = 109/73 age = 56.7/56.7 yr BMI = 25.6/25.9 kg/m^2 final sample size = 94/97 included in analysis = 94/97	Rice provided not reported					to-face interview every 4 weeks	
Shimabukuro et al. 2014, Japan	Crossover RCT in the real world	Health status: Men with MetS initial sample size = 14/13 female/male = 0/27 age = 41 yr BMI = 26.7/26.7 kg/m^2 final sample size = 14/13 included in analysis = 14/13	Brown rice No isocaloric diet Rice provided not reported	White rice No isocaloric diet	150 g/d	8	weight, BMI, WC, FBG, insulin, HbA1c, HOMA, TC, TG, HDL, LDL	Monitored by participants records after each ingestion	None
Kazemzadeh et al. 2014, Iran	Crossover RCT in the real world	Health status: Overweight & obese non-menopausal women initial sample size = 20/20 female/male = 35/0 age = 32.6 yr BMI = 30.7/28.2 kg/m^2 final sample size = 20/15 included in analysis = 20/15	Brown rice Isocaloric diet, planned: deficit 200-500 kcal/d; 15-20% PRO, <30% FAT and 50-60% CHO Rice provided to the participants	White rice Isocaloric diet, planned: deficit 200-500 kcal/d; 15-20% PRO, <30% FAT and 50-60% CHO	150 g/d	6	weight, BMI, WC, FBG, TC, TG, HDL, LDL	Monitored by 3-day food record at baseline and end of intervention	None
Bui et al. 2014, Vietnam	Parallel RCT in the real world	Health status: Women with IGT initial sample size = 30/30 female/male = 60/0 age = 56.9/56.6 yr BMI = 23.9/23.5 kg/m^2 final sample size = 30/30 included in analysis = 30/30	Pre-germinated brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	540 g/d	16	weight, BMI, WC, PBF, FBG, HbA1c, TC, TG, HDL, LDL	Not monitored	None
Wang et al. 2013, USA	Parallel RCT in the real world	Health status: Pre-diabetics patients initial sample size = 49/51 female/male = 28/19 age = 50/55 yr BMI = 26.5/25.0 kg/m^2 final sample size = 28/29 included in analysis = 28/29	Brown rice Isocaloric diet, planned: weight maintenance diet Rice provided to the participants	White rice Isocaloric diet, planned: weight maintenance diet	Free	12	weight, BMI, WC, FBG, insulin, HbA1c, HOMA, TC, TG, HDL, LDL	Not monitored	None
Zhang et al. 2011, China	Parallel RCT in the real world	Health status: Patients with MetS initial sample size = 101/101 female/male = 94/108 age = 49.8/49.6 yr BMI = 25.9/25.4 kg/m^2 final sample size = 101/101 included in analysis = 101/101	Brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	225 g/d	16	BMI, WC, FBG, insulin, HbA1c, HOMA, TC, TG, HDL, LDL	Monitored by researchers by weighing leftovers	None
Hsu et al. 2008, Japan	Crossover RCT in the real world	Health status: DM II initial sample size = 5/6 female/male = 5/6 age = 51.5 yr BMI = 25.6/24.6 kg/m^2 final sample size = 5/6 included in analysis = 5/6	Pre-germinated brown rice No isocaloric diet Rice provided to the participants	White rice No isocaloric diet	540 g/d	6	weight, BMI, PBF, FBG, insulin, TC, TG, HDL, LDL	Not monitored	None

body mass index; BMI, carbohydrate; CHO, type 2 diabetes; DM II, fat; FAT, fasting blood glucose; FBG, glycated hemoglobin; HbA1c, high-density lipoprotein-cholesterol; HDL, homeostatic model assessment of insulin resistance; HOMA-IR, ideal body weight; IBW, Impaired glucose tolerance; IGT, intervention; In, low-density lipoprotein-cholesterol; LDL, metabolic syndrome; MetS, percentage of body fat; PBF, protein; PRO, total cholesterol; TC, triglyceride; TG, waist circumference; WC

dose-response trend among amount of brown rice consumption, duration of follow-up, and changes in weight, BMI, and WC from baseline.

Forest plot for the effect of brown rice on lipid profile is shown in Figures 6a-9a. It was also reported that, brown rice has no significant effect on TC (1.95 mg/dl, 95% CI: −6.48 to 2.57), TG (-1.66 mg/dl, 95% CI: −12.97 to 9.64), HDL (0.39 mg/dl, 95% CI: −1.96 to 2.75), and LDL (-0.51 mg/dl, 95% CI: −4.39 to 3.38). In addition, a mild heterogeneity was observed among the trials of TC (I^2=34%) and LDL (I^2=32%) as well as a moderate heterogeneity among the trials of TG (I^2=60%) and HDL (I^2=75%).

Forest plot for the effect of brown rice on glycemic markers is shown in Figures 10a-13a. Following the brown rice consumption, FBG significantly increased (2.39 mg/dl, 95% CI: 0.44 to 4.34); however, its elevation was not clinically important. No significant changes in insulin (-0.59 μU/ml, 95% CI: −1.36 to 0.18), HbA1c (0.03%, 95% CI: −0.33 to 0.39), and HOMA-IR (-0.14, 95% CI: −0.36 to 0.08) were found. Furthermore, heterogeneity among the included studies was 34% for FBG, 14% for insulin, 96% for HbA1c, and 0% for HOMA-IR.

According to subgroup analyses, brown rice decreased weight, BMI, and WC from baseline in studies that used ≤150 g/d for ≤6 weeks. In trials with brown rice >150 g/d and a period >6 weeks, however, there was a substantial increase in FBG (Supplementary Table 2).

Meta-regression analysis for the changes in weight, BMI, WC, lipid profile, FBG and HbA1c is presented in Supplementary Figures 1–9, respectively. The results of the meta-regression analysis show that, there is no significant linear relationship between the changes in weight, BMI, WC, lipid profile, FBG and HbA1c and age, baseline BMI, amount of brown rice consumption, and duration of follow-up periods. In addition, it was shown that, these explanatory variables are not sources of heterogeneity.

Sensitivity analysis revealed that the removal of one study had no significant effect on overall effect size of anthropometric indices, lipid profile, and glycemic markers. Egger's regression symmetry test indicated that, no publication bias was detected among the studies conducted on weight (P = 0.83), BMI (P = 0.21), WC (P = 0.15), TC (P = 0.72), TG (P = 0.78), HDL (P = 0.07), LDL (P = 0.54), FBG (P = 0.22), Insulin (P = 0.41), HbA1c (P = 0.08), and HOMA (P = 0.75).

The effect of pre-germinated brown rice on adiposity indices, lipid profile, and glycemic markers

The effect of pre-germinated brown rice on adiposity indices, lipid profile, and glycemic markers is presented in Figures 3b-10b. In this regard, five studies assessed the effect of pre-germinated brown rice on FBG (Bui et al. 2014, Geng et al. 2016, Hsu et al. 2008, Mai, Trang, and Hai 2020, Ren et al. 2020), and lipid profile (Bui et al. 2014, Geng et al. 2016, Hsu et al. 2008, Mai, Trang, and Hai 2020, Ren et al. 2020); four trials were conducted on weight (Bui et al. 2014, Geng et al. 2016, Hsu et al. 2008, Mai, Trang, and Hai 2020), and BMI (Bui et al. 2014, Geng et al. 2016, Hsu et al. 2008, Mai, Trang, and Hai 2020); two studies on WC (Bui et al. 2014, Geng et al. 2016, Mai, Trang, and Hai 2020), PBF (Bui et al. 2014, Hsu et al. 2008), and insulin (Hsu et al. 2008, Mai, Trang, and Hai 2020); and one study was performed on HbA1c (Bui et al. 2014) and HOMA-IR (Mai, Trang, and Hai 2020). Weight significantly reduced (-1.75 kg, 95% CI: −2.69 to −0.81) after the consumption of pre-germinated brown rice, but BMI (-0.05 kg/m^2, 95% CI: −0.65 to 0.55), WC (-2.40 cm, 95% CI: −5.93 to 1.13), and PBF (-1.82%, 95% CI: −3.81 to 0.16) remained unchanged (Frost plot for WC and PBF was not shown). Notably, there was high heterogeneity among the studies on weight (I^2=99%), BMI (I^2=99%), and WC (I^2=93%), and moderate heterogenity on PBF (I^2=64%).

Pre-germinated brown rice significantly declined TC (-24.22 mg/dl, 95% CI: −33.03 to −15.41), TG (-43.28 mg/dl, 95% CI: −74.05 to −12.50), LDL (-20.05 mg/dl, 95% CI: −29.57 to −10.52), and FBG (-15.83 mg/dl, 95% CI: −25.20 to −6.46), with no significant effect on HDL (5.28 mg/dl, 95% CI: −5.53 to 16.08). Heterogeneity among the included studies was 78% for TC, 90% for TG, 99% for HDL, 71% for LDL, and 91% for FBG. Due to lack of studies reporting the insulin level, HbA1c, and HOMA-IR following the consumption of pre-germinated brown rice; we did not include these factors in meta-analysis.

In studies that used >150 g/d, pre-germinated brown rice significantly reduced weight, TC, TG, LDL, and FBG, and increased HDL from baseline, as compared to white rice, based on subgroup analyses. On the other hand, the daily amount of pre-germinated brown rice ≤ 150 g did not affect on HDL, TG, or FBG, but it did have a greater effect on TC and especially LDL than rice at >150 g/d (Supplementary Table 3).

Meta-regression analysis for the changes in weight, BMI, lipid profile and FBG is presented in Supplementary Table 4. The results of the meta-regression analysis show that, age, baseline BMI, amount of brown rice, and follow-up periods are not sources of heterogeneity.

Sensitivity analysis indicated that the removal of one study had no significant effect on overall effect size of anthropometric indices, lipid profile, and FBS. But after remove Ren et al. (2020)HDL increased significantly in pre-germinated brown rice compared with white rice (9.16 mg/dl, 95% CI: 5.15 to 13.88). According to Egger's regression symmetry test, no publication bias was detected among the studies conducted on weight (P = 0.93), BMI (P = 0.86), TC (P = 0.63), TG (P = 0.87), HDL (P = 0.06), LDL (P = 0.41), and FBG (P = 0.01).

Discussion

In the present systematic review and meta-analysis, nine trials conducted on brown rice and five studies on pre-germinated brown rice were included. Our findings indicated that, the consumption of brown rice significantly reduced weight, BMI, and WC but not PBF in comparison to white rice. However, due to a high heterogeneity among these studies,

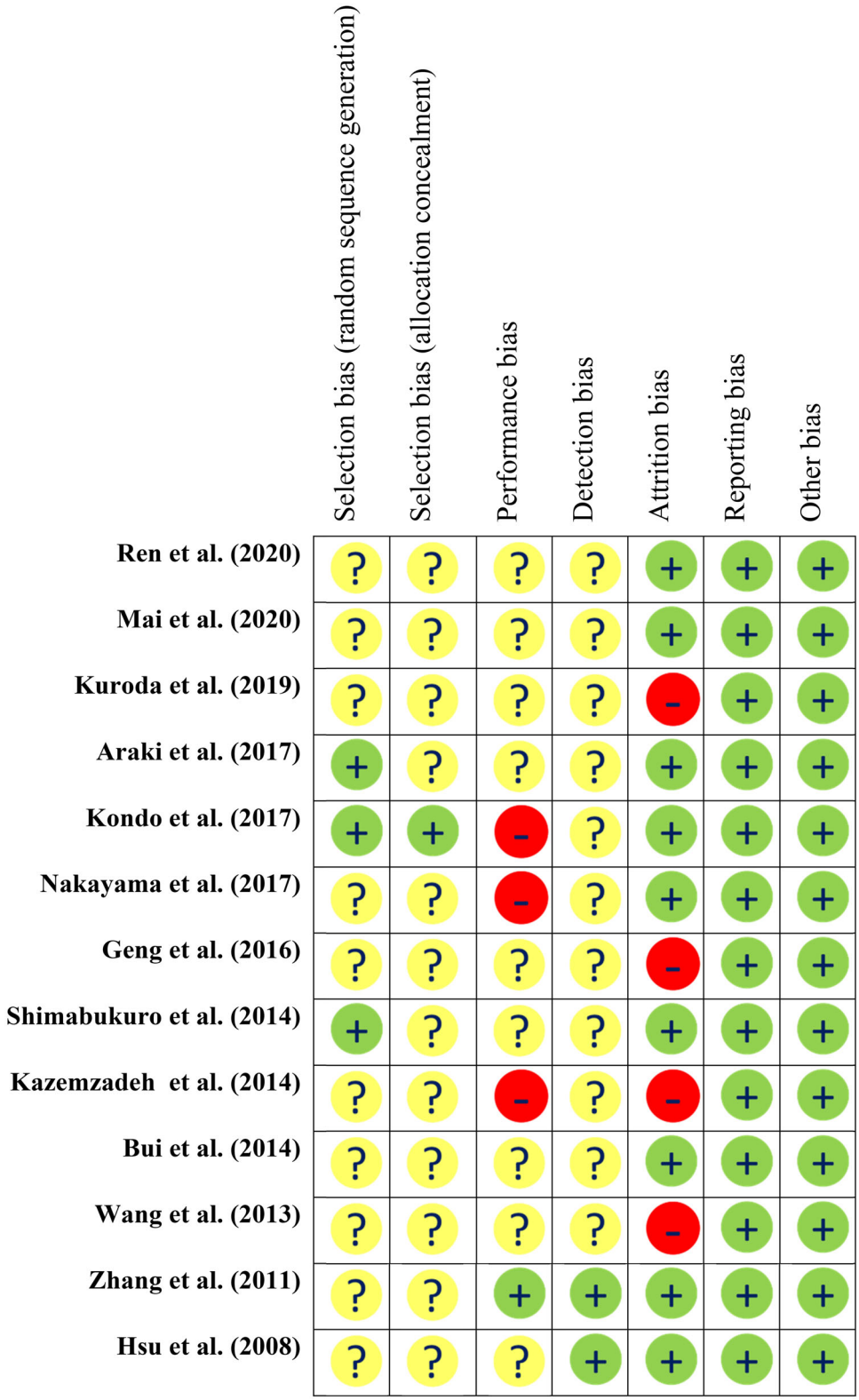


Figure 2. Quality assessment of included articles according to Cochrane tool.

the results should be interpreted with cautious. The results of meta-regression analysis showed that the variables of age, baseline BMI, amount of brown rice and follow-up periods were not sources of heterogeneity. When assessing the dose-responses, we found no evidence of nonlinear dose-response association among amount of brown rice; duration of intervention; and changes in weight, BMI, and WC. Moreover, brown rice had no significant effect on lipid profile and glycemic markers compared to white rice. In addition, pre-germinated brown rice significantly decreased body weight and also improved lipid profile and FBG levels compared to white rice; however, it did not change adiposity indices. In the present study, the certainly of evidence was low, and very low.

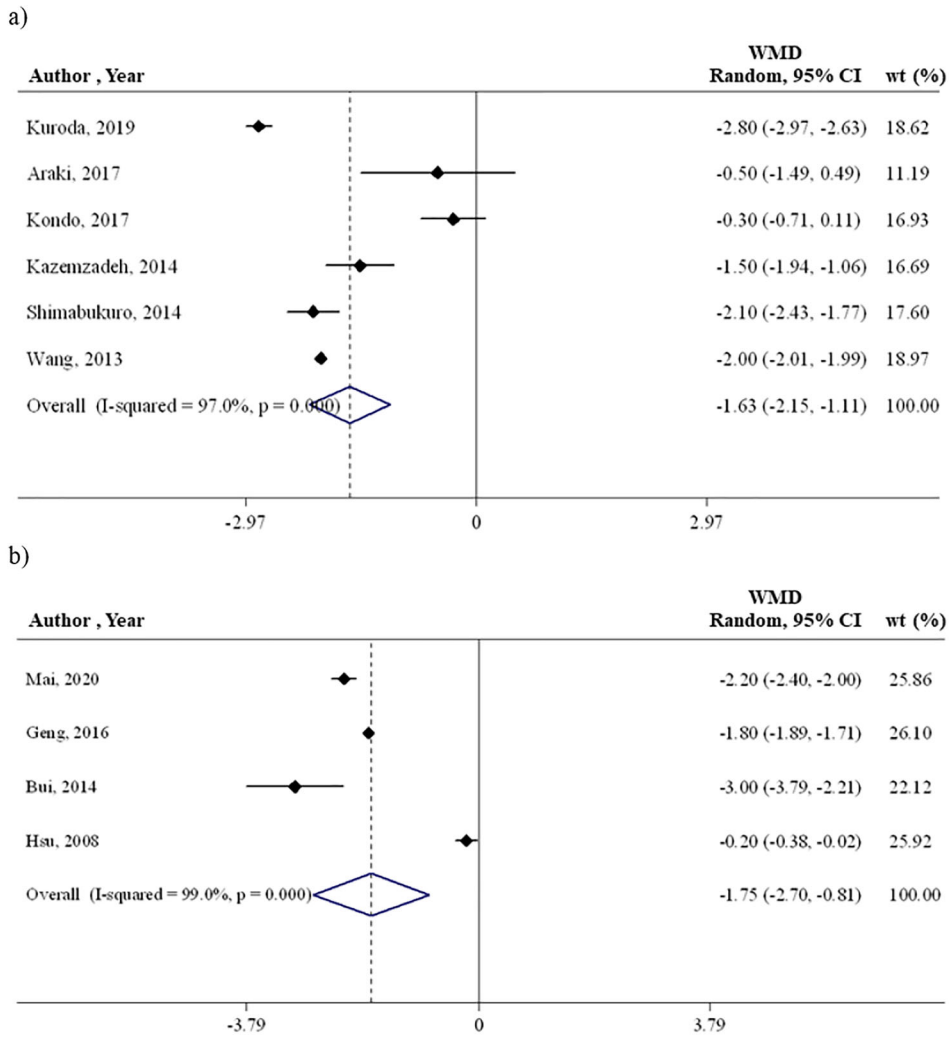


Figure 3. Forest plot for effect of (a) brown rice and (b) pre-germinated brown rice on weight.

Previous meta-analyses revealed an inverse association among whole grains consumption and the risk of mortality, obesity, diabetes, CVD (McRae 2017, Schlesinger et al. 2019), inflammation (Hajihashemi and Haghighatdoost 2019) and metabolic risk factors (Kelly et al. 2017, Musa-Veloso et al. 2018, Schwingshackl et al. 2018). The results of a meta-analysis of 10 cohort studies conducted on 782751 subjects, reported that, daily consuming a single serving of whole grains (30 grams) decreased the risk of mortality from all-cause, CVD, and coronary heart disease (CHD) (Li et al. 2016). Notably, brown rice is a subclass of whole grains, which contains some nutraceutical compounds such as fiber and phytochemicals. Therefore, it has been supposed that brown rice has anti-obesity, anti-diabetic, and anti-lipemic effects (Masuzaki et al. 2019).

Several RCTs assessed the effect of brown rice on weight and body composition. In this regard, some of them showed a significant effect of brown rice on adiposity indices, (Araki et al. 2017, Shimabukuro et al. 2014, Wang et al. 2013, Kazemzadeh et al. 2014) while the other RCTs have reported that, brown rice has no effect on adiposity indices (Kondo et al. 2017, Kuroda et al. 2019, Zhang et al. 2011). Moreover, brown rice has some functional compounds that can affect body weight. Accordingly, among these functional compounds, fiber plays the most important role. Fiber content of brown rice is four-fold higher than white rice. Also, an inverse association between dietary fiber and obesity was reported in some studies (Du et al. 2010, Lairon 2007). A cohort study on 89432 European adults indicated that, each 10 g/d increment of fiber intake from grains can reduce weight by 77 g/year (-127 to −26 g/year) and WC by 0.10 cm/year (-0.18 to −0.02 cm/year) over 6.5 years follow-up (Du et al. 2010). It has been stated that, dietary fiber contributes to the treatment of obesity by performing several mechanisms. Correspondingly, fiber increases the time of gastric emptying and also manages body weight via affecting the postprandial responses (Pletsch and Hamaker 2018). It also decreases hunger as well as increasing satiety that consequently results in food intake suppression. Recently, it has been suggested that, dietary fiber through modification gut microbiota and subsequently modulation of energy balance involves in the process of weight reduction (Chen et al. 2017). Moreover, some phytochemical compounds in brown rice may play a role in weight reduction. The anti-obesity mechanisms of phytochemicals attribute to adipogenesis suppression and fat accumulation, apoptosis of pre-

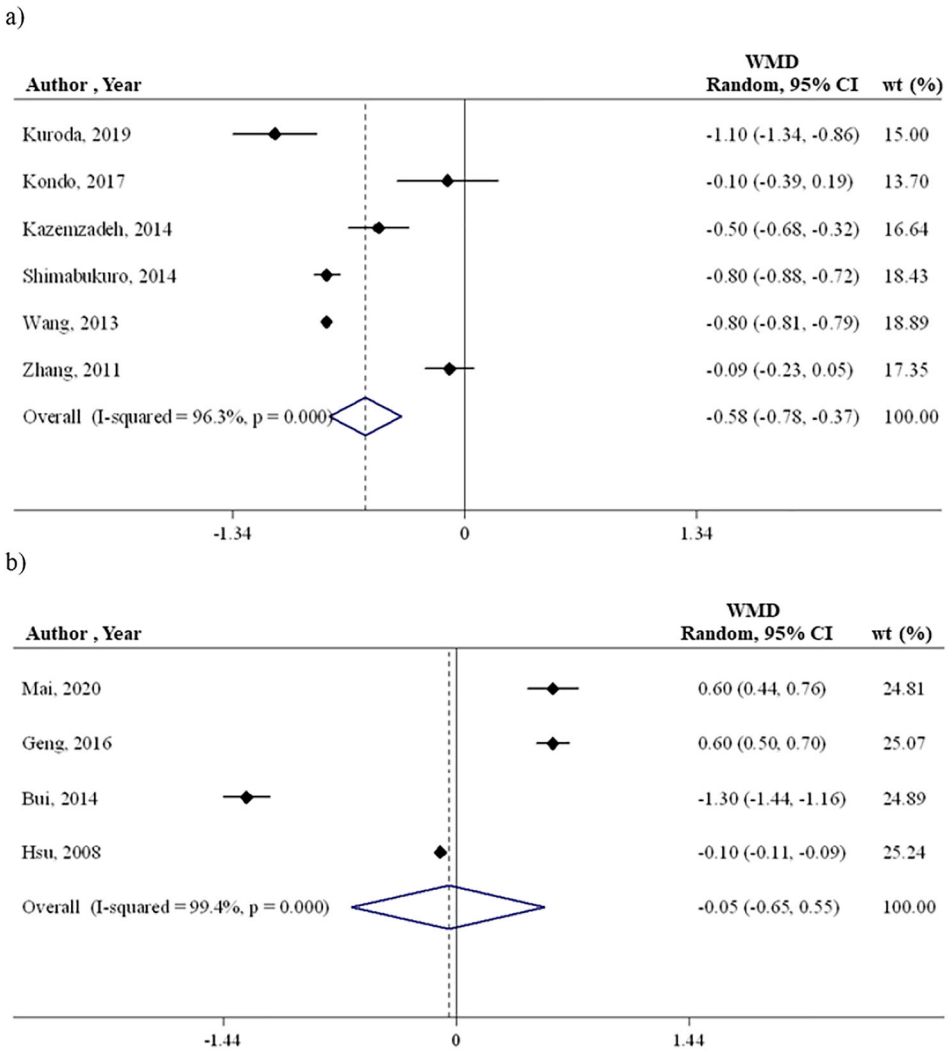


Figure 4. Forest plot for effect of (a) brown rice and (b) pre-germinated brown rice on BMI.

adiopocytes, lipolysis increment, and fat oxidation (Gonzalez-Castejon and Rodriguez-Casado 2011).

The effects of brown rice on lipidemia and glycemia statuses were assessed by several RCTs; however, no systematic review or meta-analysis has investigated these effects, so far. In this regard, in a randomized crossover study on the patients with metabolic syndrome, indicated that the consumption of brown rice (150 g/d) significantly declined the levels of LDL, HDL, and HOMA-IR after an 8-week follow-up period (Shimabukuro et al. 2014). In two other studies performed by Zhang et al. (2011) and Nakayama et al. (2017), beneficial effects of brown rice on LDL and HbA1c were reported, respectively. Nevertheless, Kondo et al. (2017) in a trial on type 2 diabetic patients exhibited that, an eight-week consumption of brown rice (150 g/d) had no significant effects on blood lipids and glycemic status. In another trial on the pre-diabetic patients, lipid profile and diabetes markers did not change at the end of a twelve-week follow-up period (Araki et al. 2017). Moreover, the other RCTs also identified no significant effects of brown rice on lipidemia and glycemia statuses (Kazemzadeh et al. 2014, Kuroda et al. 2019, Wang et al. 2013). The present meta-analysis in agreement with the above-mentioned studies (Araki et al. 2017, Kazemzadeh et al. 2014, Kondo et al. 2017, Kuroda et al. 2019, Wang et al. 2013) revealed the lack of profitable effects of brown rice on lipid profile and glycemic markers in adults.

In contrast to brown rice, pre-germinated brown rice significantly ameliorated lipid profile and FBG. In this regard, some previous animal studies also demonstrated the lipid-lowering (Ho et al. 2013, Lim et al. 2016, Roohinejad et al. 2010, Sarkar et al. 2019) and anti-diabetics (Torimitsu et al. 2010, Hagiwara, Seki, and Ariga 2004, Shallan et al. 2010) effects of germinated brown rice. In the present study, we could not assess the changes of other glycemic markers due to lack of relevant studies. In addition, a high heterogeneity among the studies made the results interpretation more difficult. Although we could not find source of heterogeneity by meta-regression analysis, it was may related to methodological or clinical factors. However, it seems that the effects of pre-germinated brown rice on improving lipid profile and FBG are stronger than brown rice.

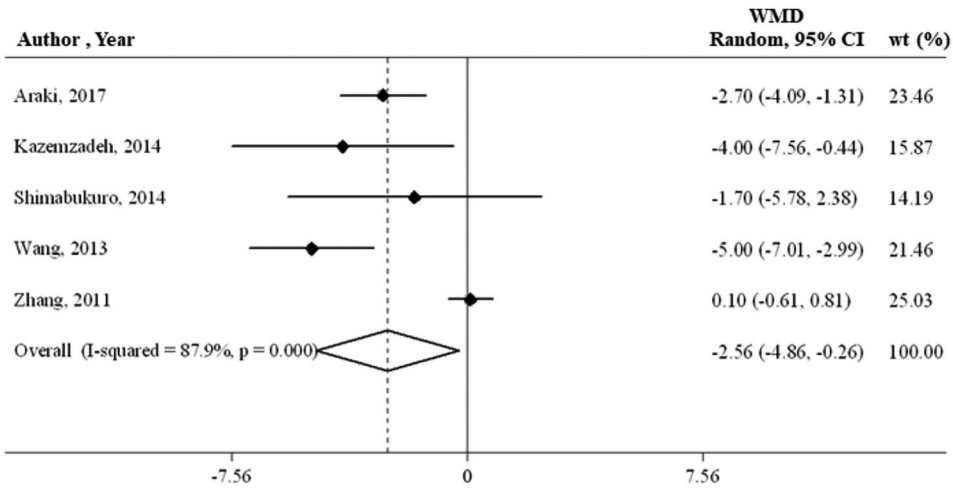
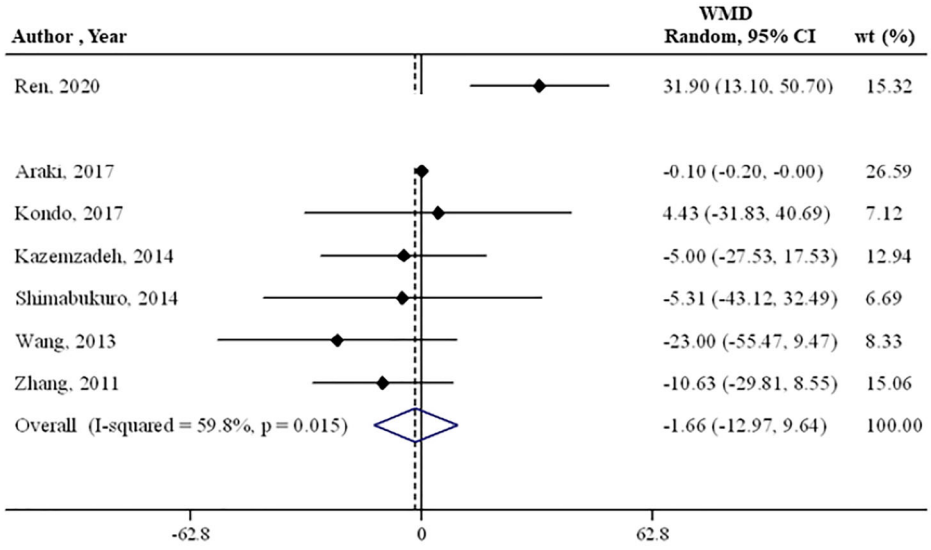


Figure 5. Forest plot for effect of brown rice on WC.

a)



b)

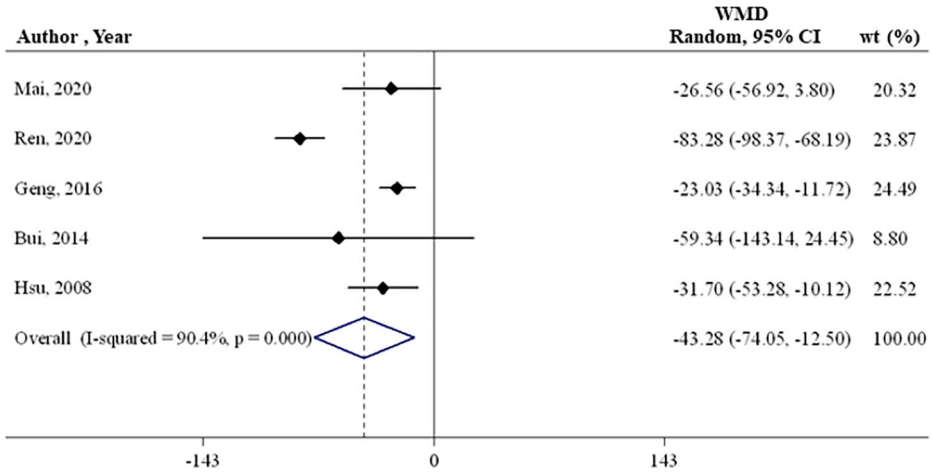


Figure 6. Forest plot for effect of (a) brown rice and (b) pre-germinated brown rice on TG.

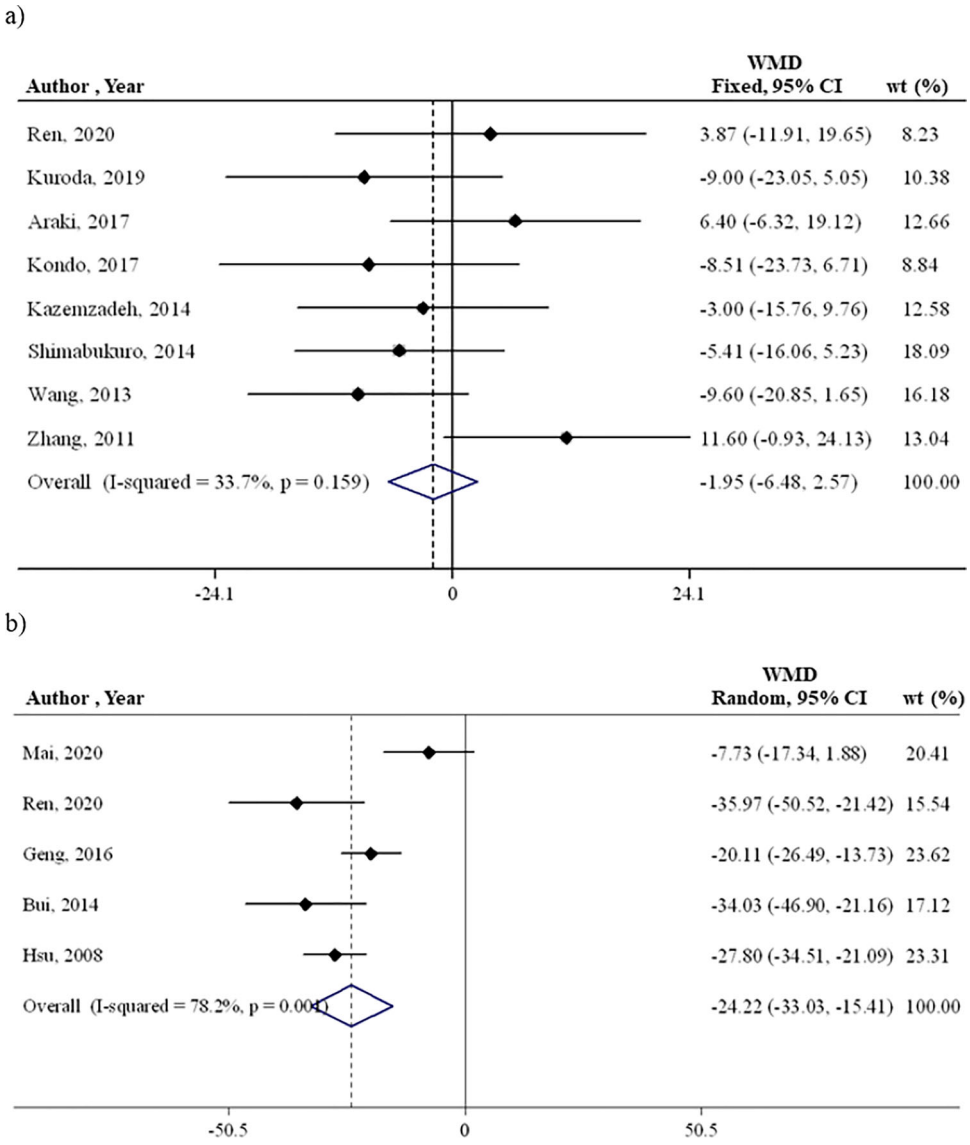


Figure 7. Forest plot for effect of (a) brown rice and (b) pre-germinated brown rice on TC.

Pre-germinated brown rice is produced by soaking brown rice in water to germinate slightly, which is performed due to less palatability and digestibility of brown rice compared to white rice. This process by inducing some enzymes that exist in brown rice increases the concentrations of phenolic compounds, antioxidants, fibers, γ-aminobutyric acid (GABA), γ-oryzanol, and vitamins as well as decreasing amylase and sugars. Hence it results in the reinforcement of the functional effects of pre-germinated brown rice compared to brown rice. In addition, germination process elevates the bioavailability of theses bioactive compounds by softening the texture and increasing the digestibility of brown rice (Imam et al. 2012, Cho and Lim 2016). Accordingly, in the present study, this phenomenon may better explain the functional effects of pre-germinated brown rice on promoting lipid profile and FBG, compared to brown rice.

Anti-diabetic and anti lipidemic effects of pre-germinated brown rice are attributed to several mechanisms. Fiber, γ-oryzanol, and GABA are the main factors involved in the amelioration of lipid profile and glycemia status. So, these bioactive compounds manage anti-lipidemic effects of brown rice by reducing intestinal absorption of cholesterol, increasing bile acid excretion, and up-regulating LDL receptors (LDL-R) (Chen et al. 2017, Veronese et al. 2018, Ravichanthiran et al. 2018, Sarkar et al. 2019). In addition, pre-germinated brown rice has a low glycemic index (GI) due to the large amount of fiber, which results in the decreased glucose absorption from gut tract and postprandial response (Chen et al. 2017). Furthermore, the large amount of fiber of pre-germinated brown rice modulates gut microbiota composition by increasing *Bifidobacterium* and *lactobacillus* levels and regulating glycemic status (Ravichanthiran et al. 2018). Accordingly, these bacteria are known as the main producers of propionate in gut, which lead to glucagon-like peptide 1 (GLP-1) secretion and also to the improvement of glycemic markers (Nakayama et al. 2017). Moreover, γ-oryzanol, a phytosterol, in rice bran oil induces glucose-stimulated insulin secretion (GSIS) and controls glycemic responses through a direct effect on pancreas (Kozuka et al. 2013).

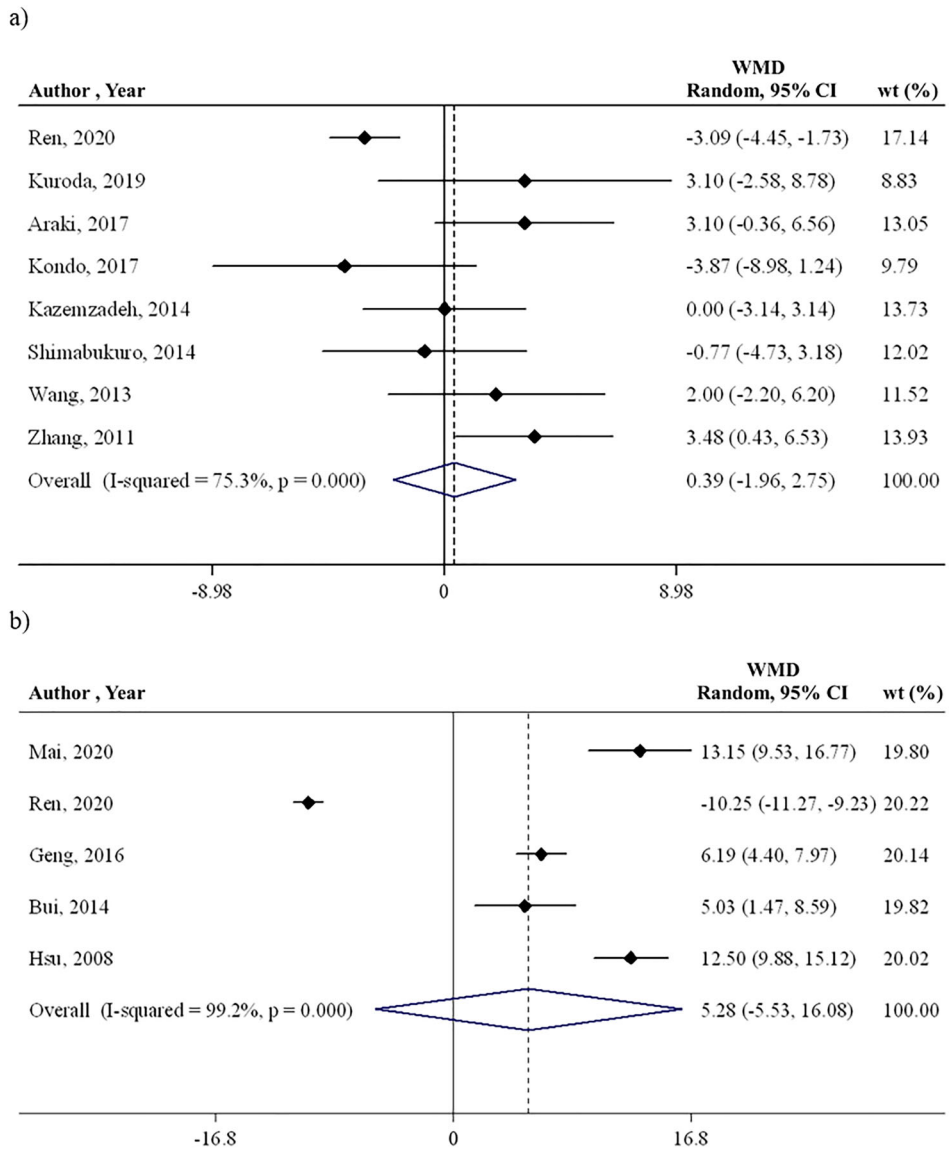


Figure 8. Forest plot for effect of (a) brown rice and (b) pre-germinated brown rice on HDL.

In the present study, there were several positive points and limitations. This study was the first meta-analysis that assessed the effect of brown rice on adiposity indices, lipid profile, and glycemic markers in adult subjects. No publication bias was observed among the included studies. Moreover, in the present study, we excluded those trials that used brown rice in combination with various forms of rice or grains as intervention to calculate the effect of brown rice on the quantitative variables accurately in comparison with white rice. Also, the main limitation of the present study was the insufficient number of studies that met the inclusion criteria. Moreover, some of these studies had small sample size, which affected overall effect size. Furthermore, the other limitation of our study was lack of quality of the included studies due to the performance bias.

In conclusion, the results of the present study indicate that, brown rice has anti-obesity effects in comparison with white rice. However, it has no beneficial effects on lipid profile and glycemic markers. Contrary to brown rice, it was shown that, pre-germinated brown rice significantly decreases body weight and improves lipid profile and FBG levels compared to white rice. Moreover, our results demonstrate that pre-germinated brown rice has better functional effects on promoting lipid profile and FBG compared to brown rice. But due to a high heterogeneity among the studies, the results should be interpreted with cautious. With respect to the GRADE approach, the certainly of the included evidence was low and very low, so further RCTs with better design are required in this area. Investigators should be focused on randomization and blinding to reduce risk of selection, performance and detection bias. They also should be conducted intention-to-treat (ITT) analysis to avoid attrition bias. Compliance monitoring is needed to make sure participants proceed according to schedule. In addition administration of isocaloric diet is essential to control calorie intake of intervention and control groups during follow-up periods.

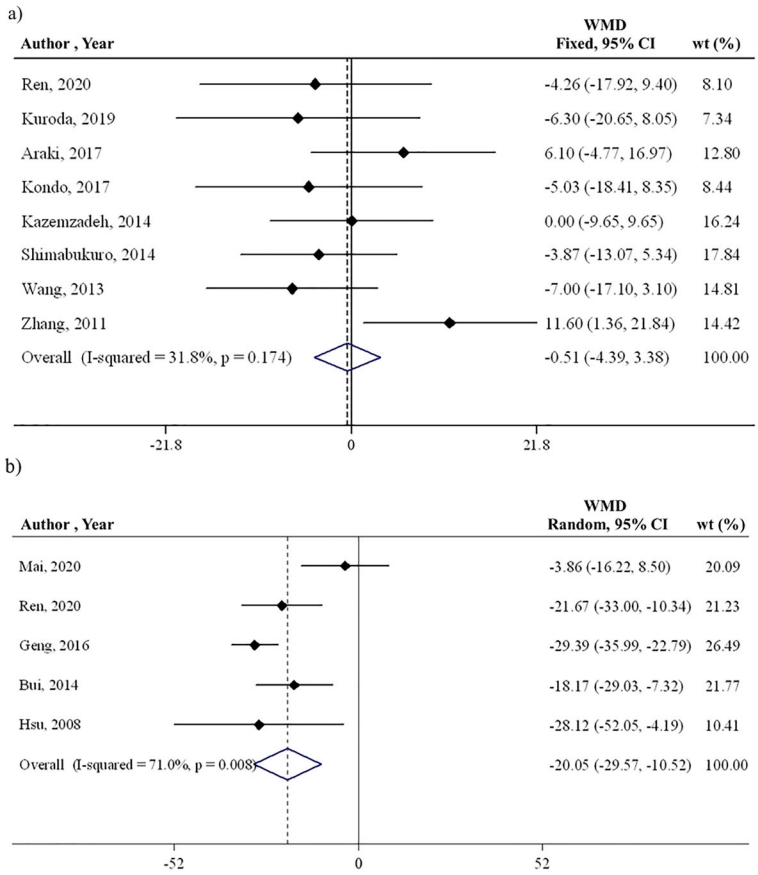


Figure 9. Forest plot for effect of (a) brown rice and (b) pre-germinated brown rice on LDL.

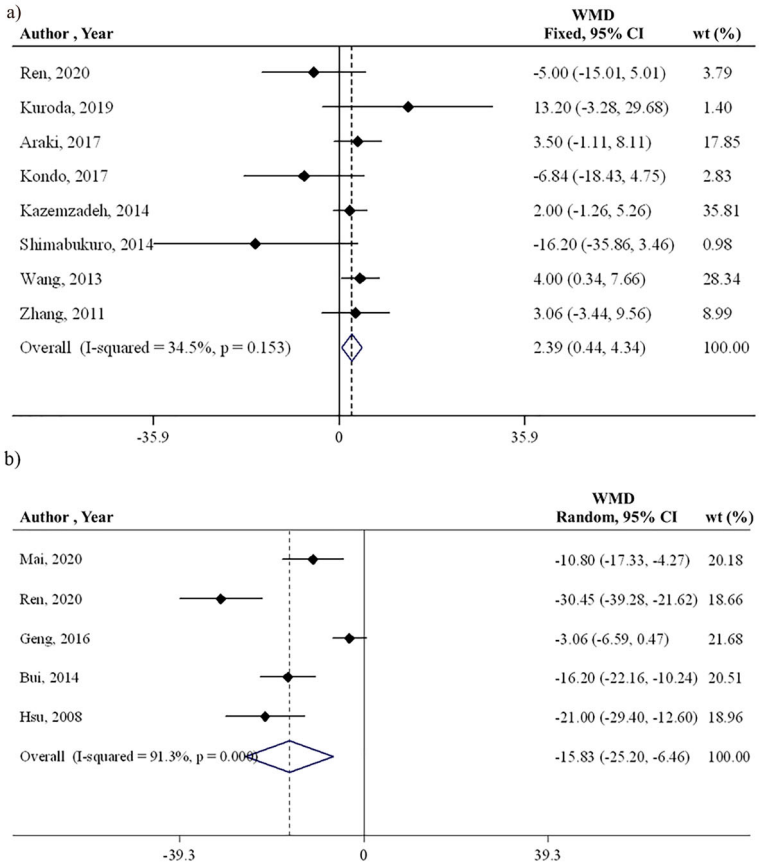


Figure 10. Forest plot for effect of (a) brown rice and (b) pre-germinated brown rice on FBG.

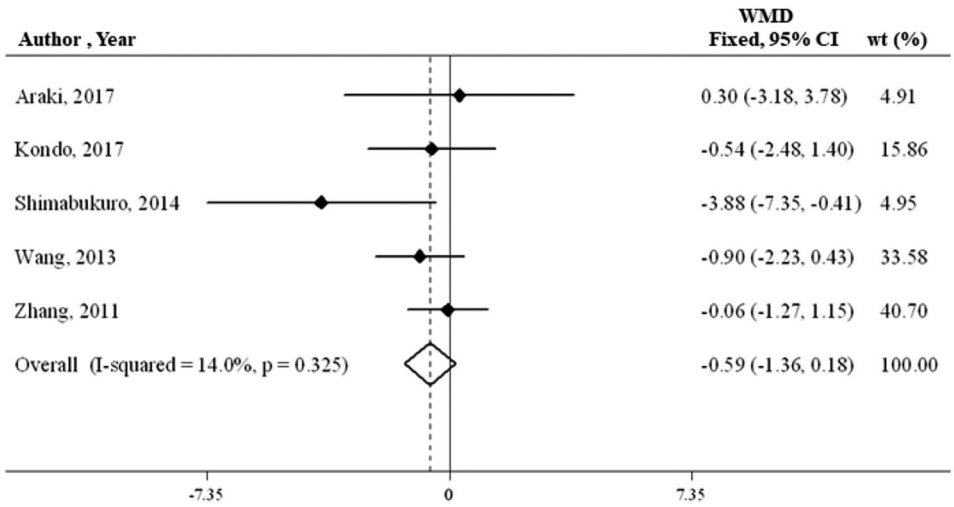


Figure 11. Forest plot for effect of brown rice on insulin.

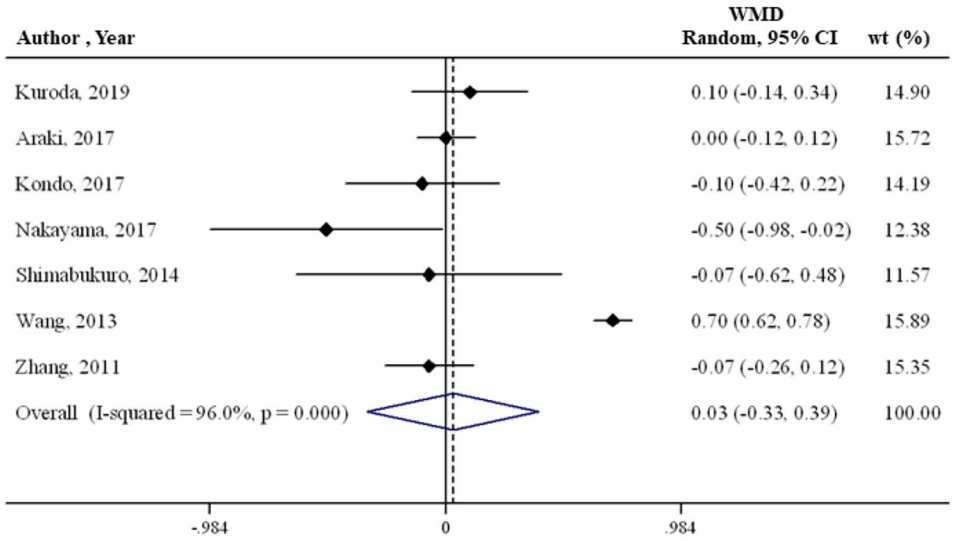


Figure 12. Forest plot for effect of brown rice on HbA1c.

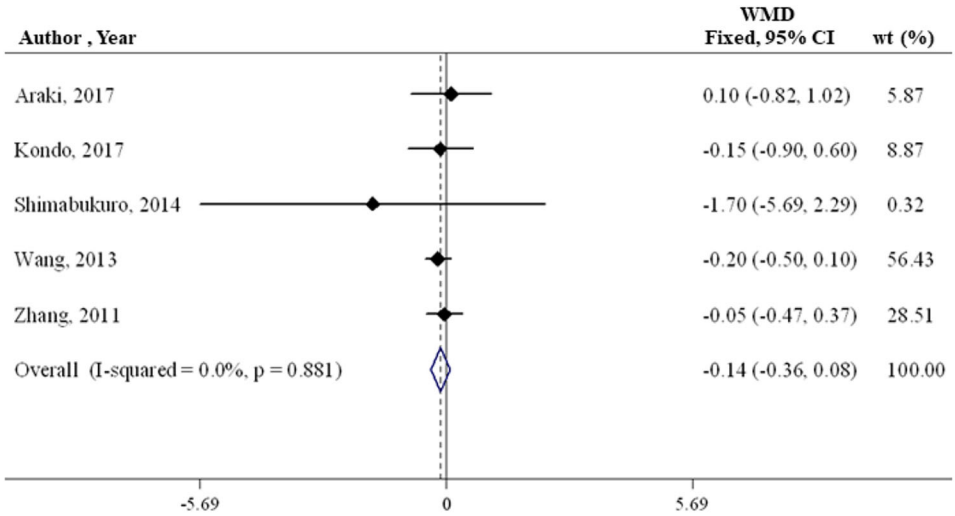


Figure 13. Forest plot for effect of brown rice on HOMA-IR.

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All authors have read and approved the final manuscript.

Disclosure statement

The authors declare there is no conflict of interest.

Abbreviation

CVD	cardiovascular disease
CHD	coronary heart disease
FBG	fasting blood glucose
GABA	γ-aminobutyric acid
GLP-1	glucagon-like peptide 1
GSIS	glucose-stimulated insulin secretion
HbA1c	glycated hemoglobin
GRADE	grading of recommendation sassessment, development and evaluation
HDL	high-density lipoprotein
HOMA-IR	homeostatic model assessment of insulin resistance
I^2	I-squared
LDL	low-density lipoprotein
LDL-R	LDL receptors
MD	mean differences
PBF	percentage of body fat
PRISMA	the preferred reporting items for systematic reviews and meta-analyses
RCTs	randomized controlled trials
TC	total cholesterol
TG	triglyceride
VLDL	very low-density lipoprotein

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