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# Nut consumption and risk of metabolic syndrome and overweight/obesity: a meta-analysis of prospective cohort studies and randomized trials

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## Abstract

**Background:** Nut consumption has been shown to reduce the risk of cardiovascular disease. However, its role in the prevention of metabolic disorders, such as metabolic syndrome (Mets) and overweight/obesity, remains controversial. We therefore conducted a meta-analysis to determine the association of nut consumption with Mets and overweight/obesity.

**Methods:** Eligible studies were identified by searching the PubMed and Embase databases and by reviewing the references of relevant literatures. We used random effect models to pool the studies-specific risk ratio (RR) and weighted mean difference (WMD).

**Results:** This meta-analysis included six prospective cohort studies with 420,890 subjects and 62 randomized feeding trials with 7184 participants. Among the cohort studies, the summary RR for every 1-serving/week increase in nut intake was 0.96 (95% confidence interval [CI]: 0.92 to 0.99;  $n = 3$ ) for Mets, 0.97 (95% CI: 0.95 to 0.98;  $n = 2$ ) for overweight/obesity, and 0.95 (95% CI: 0.89 to 1.02;  $n = 2$ ) for obesity. Pooling of randomized trials indicated that nut consumption was related to a significant reduction in body weight (WMD:  $-0.22$  Kg, 95% CI:  $-0.40$  to  $-0.04$ ), body mass index (WMD:  $-0.16$  Kg/m<sup>2</sup>, 95% CI:  $-0.31$  to  $-0.01$ ), and waist circumference (WMD:  $-0.51$  cm, 95% CI:  $-0.95$  to  $-0.07$ ). These findings remained stable in the sensitivity analysis, and no publication bias was detected.

**Conclusion:** Nut consumption may be beneficial in the prevention of Mets and overweight/obesity. Additional prospective studies are needed to enhance these findings and to explore the metabolic benefits for specific subclasses of nut.

**Keywords:** Nutrition, Metabolic syndrome, Overweight, Obesity

## Background

Metabolic syndrome (MetS) is recognized as a cluster of interrelated metabolic abnormalities, including central adiposity, hypertension, hyperglycemia, and dyslipidemia [1]. It has been estimated that nearly 20–30% of the global adult population are suffering from Mets [2]; and in the U.S., the overall prevalence is 33% [3]. Patients with

Mets have greater risks of developing cardiovascular disease, type 2 diabetes mellitus and common cancers [4, 5]. Overweight/obesity is also a widespread burdensome disease with severe health consequence. In the year 2016, the World Health Organization reported that more than 1.9 billion people aged 18 years or older worldwide were overweight, and over 650 million adults were obese [6]. Therefore, reducing the prevalence of these metabolic disorders is imperative to improve human health and to ameliorate the related social and economical burdens.

In recent decades, lifestyle modifications, in particular a healthy diet, have been increasingly considered to play

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critical roles in the prevention of metabolic diseases. Previous reports have suggested that dietary intake of fruits and vegetables, dairy products, and coffee may reduce the risk of Mets or overweight/obesity [7–10], while high consumption of red and processed meat increases this risk [11, 12]. Nuts are rich in bioactive nutrients such as healthy fats, dietary fiber, phytosterols, vitamins, and minerals, which are known to have salutary effects on cardiometabolic health [13]. For habitual nut intake, epidemiological studies have confirmed its preventive role against cardiovascular disease, type 2 diabetes mellitus, and cancers [14]. Although emerging evidence from clinical trials have also shown that nut supplementation could favorably affect metabolic features and body weight management [15, 16], whether nut consumption is associated with the overall risks of Mets and overweight/obesity remains in debate. This may be attributed to the fact that there are limited studies investigating these associations, and they yielded inconsistent results. Some of them showed that nut consumption was inversely correlated with risk of MetS or overweight/obesity [17–20], while others demonstrated null associations [21, 22]. Herein, we performed a meta-analysis of pertinent cohort studies to determine the role of nut intake in preventing Mets and overweight/obesity. To improve the reliability of the findings, the data of anthropometrical outcomes in randomized feeding trials were also pooled, including changes in body weight, body mass index (BMI), and waist circumference.

## Methods

### Search strategy

This work was implemented in accordance with the Meta-analysis Of Observational Studies in Epidemiology guidelines [23]. We identified eligible studies by systematically searching the PubMed and Embase databases from inception to December 2017, utilizing the free-text word and Medical Subject Headings terms as follows: (“nut” OR “walnut” OR “peanut” OR “hazelnut” OR “almond” OR “pistachio” OR “cashew” OR “macadamia” OR “pecan” OR “pine nut” OR “brazil nut”) AND (“metabolic syndrome” OR “Mets” OR “overweight” OR “weight gain” OR “obesity” OR “obese” OR “adiposity” OR “adipose” OR “body weight” OR “body mass index” OR “BMI” OR “waist circumference” OR “hypertension” OR “blood pressure” OR “hypercholesterolemia” OR “dyslipidemia” OR “cholesterol” OR “triglycerides” OR “diabetes mellitus” OR “glucose” OR “glycemia”). Detailed search strategies were listed in Additional file 1: Table S1. Moreover, the references of relevant literature were manually scrutinized to find potential complements. Only full-text studies published in English were considered.

### Inclusion criteria

To be included in this meta-analysis, the cohort studies should meet the following conditions: 1) the exposure of interest was nut consumption; 2) the outcomes of interest included incidence of Mets or overweight/obesity; 3) the adjusted risk estimates, such as relative risks (RRs), were provided for at least three quantitative categories of nut consumption. Alternatively, studies that reported the risk estimates for every 1-serving/week increment in nut consumption were also eligible; 5) the median or mean consumption (or cut-off values) and number of cases were available for each category of nut intake. We also included randomized feeding trials that examined the effects of a nut-enriched diet on anthropometrical outcomes, including body weight, BMI, and waist circumference. Animal studies, reviews, editorials, and studies of children or adolescents were excluded. When studies pertained to overlapping populations, only the report with the longest follow-up was retained.

### Data collection and quality evaluation

Two reviewers (H.L. and X.L.) independently abstracted the study details, including study author, publication year, study design, country, baseline age, and sample size. For cohort studies, the number of cases, measurement of nut intake, outcomes evaluated, confounders adjusted in multivariable models, and the maximally-adjusted risk estimates of Mets or overweight/obesity for each category of nut intake were additionally recorded. For clinical trials, we also extracted the type and amount of nuts consumed, details of comparative diet, and intervention duration. If necessary, the corresponding author of the original study was contacted for missing data. The methodological quality was appraised by using the Newcastle-Ottawa Scale [24] for cohort studies and the CONSolidated Standards Of Reporting Trials statement [25] for clinical randomized trials. Any divergence between the two reviewers was resolved by discussion with a third reviewer (Y.J.).

### Statistical analyses

In the meta-analysis of cohort studies, RRs and its 95% confidence intervals (CIs) were used to report the summary risk estimates for Mets or overweight/obesity. Because the cut-off points for intake categories were varied among the studies, we calculated an RR for an increase of one serving (equals to 30 g of nuts) per week in nut consumption for each report. The median or mean intake level of nut in each category was defined as the corresponding dose. If the mean or median intake level was not reported, the midpoint of the upper and lower boundaries of each category was used instead. If the highest category was open-ended, we assumed the median level as 1.5-times the lower boundary; and, when the lower

boundary of the lowest category was unavailable, we set it to be zero. The method described by Greenland and Longnecker [26] and Orsini et al. [27] was used to compute the trend from the correlated estimates for log RR across categories of nut consumption.

In the meta-analysis of randomized feeding trials, the summarized estimates of changes in body weight, BMI, or waist circumference were presented as weighted mean differences (WMDs). To enable the pooling of data, standard errors or CIs were converted to standard deviations. All anthropometrical data were evaluated at the longest follow-up time according to the intention-to-treat analysis.

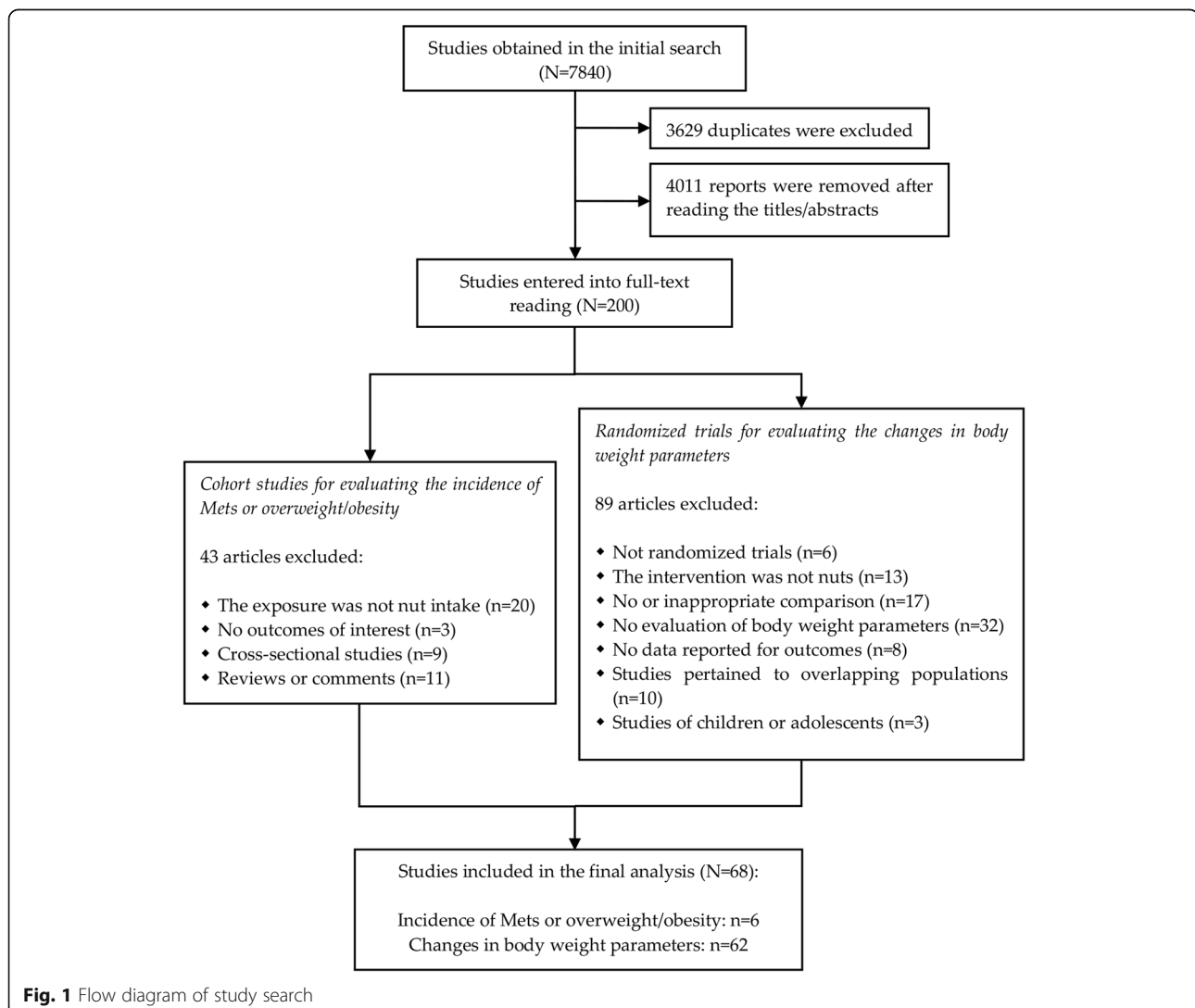
The heterogeneity between studies were explored by using the Cochran Q test (significant level:  $p < 0.1$ ). We also quantified the heterogeneity by the  $I^2$  statistic, with adoption of the following cut-off values: little or no heterogeneity ( $< 25\%$ ), moderate heterogeneity ( $25\text{--}75\%$ ), and substantial heterogeneity ( $> 75\%$ ). The

study-specific estimates were aggregated using a random effect model. Subgroup analyses were conducted according to diagnostic criteria of outcomes (for Mets only), with between-subsets difference confirmed by the Altman and Bland test [28]. To assess the robustness of results from clinical trials, we also performed a sensitivity analysis by omitting study one at a time. Potential publication bias was appraised by Egger's test. All data analyses were realized using R 3.4.2 (The R Foundation for Statistical Computing, Vienna, Austria) and STATA 13.0 (StataCorp, College Station, TX) software, and  $p$  values  $< 0.05$  were considered as significant.

## Results

### Search process and characteristics of studies

We obtained 7840 reports in the preliminary search, of which 3629 duplicates and 4011 irrelevant articles were removed. After full-text screening of the retained studies, 132 records were excluded because they failed to meet the



**Fig. 1** Flow diagram of study search

eligibility criteria (see the detailed reasons for exclusion in Additional file 1: Table S2). As a result, 68 publications including six prospective cohort studies [17–22] and 62 clinical feeding trials [15, 16, 29–88] were included in this meta-analysis (Fig. 1).

Among the cohort studies, there were 420,890 participants with 4625 Mets cases and 47,235 overweight/obesity cases (Table 1). All studies assessed the nut intake using food-frequency questionnaires. Mets was ascertained by the harmonized definition [1] in one study and by the AHA/NHLBI diagnostic criteria [89] in the other two studies, and overweight/obesity was consistently confirmed by BMI. The most commonly adjusted factors were age, sex, smoking, alcohol intake, physical activity, and total calories intake. In the clinical trials, a total of 7184 subjects were documented, with follow-up duration ranging from 3 to 336 weeks. Other characteristics were shown in Additional file 1: Table S3.

#### Nut consumption and risk of Mets

Three studies [18, 20, 22] reported the correlation relating nut consumption and risk of Mets, with no statistical heterogeneity across them ( $I^2 = 0\%$ ,  $p = 0.65$ ). The summary RR of Mets for an increase of 1-serving/week in nut intake was 0.96 (95% CI: 0.92 to 0.99; Fig. 2). The benefits of nut consumption in prevention of Mets may be also existed among studies using the harmonized definition (RR: 0.95, 95% CI: 0.91 to 1.00) or the AHA/NHLBI diagnostic criteria (RR: 0.96, 95% CI: 0.91 to

1.02;  $p$  for interaction = 0.78). There was no indication of publication bias from Egger's test ( $p = 0.72$ ).

#### Nut consumption and risk of overweight/obesity

Three studies [17, 19, 21] reported the risk of overweight and/or obesity associated with nut intake. The pooled RR (95% CI) of overweight/obesity for each 1-serving/week increment in nut consumption was 0.97 (0.95 to 0.98), with no heterogeneity across the studies ( $I^2 = 0\%$ ,  $p = 0.45$ ; Fig. 2). Likewise, nut intake may be also related to a reduced risk of becoming obesity (RR: 0.95, 95% CI: 0.89 to 1.02;  $I^2 = 74\%$ ,  $p = 0.05$ ; Fig. 2). Evaluation of publication bias was infeasible due to the quite limited number of studies.

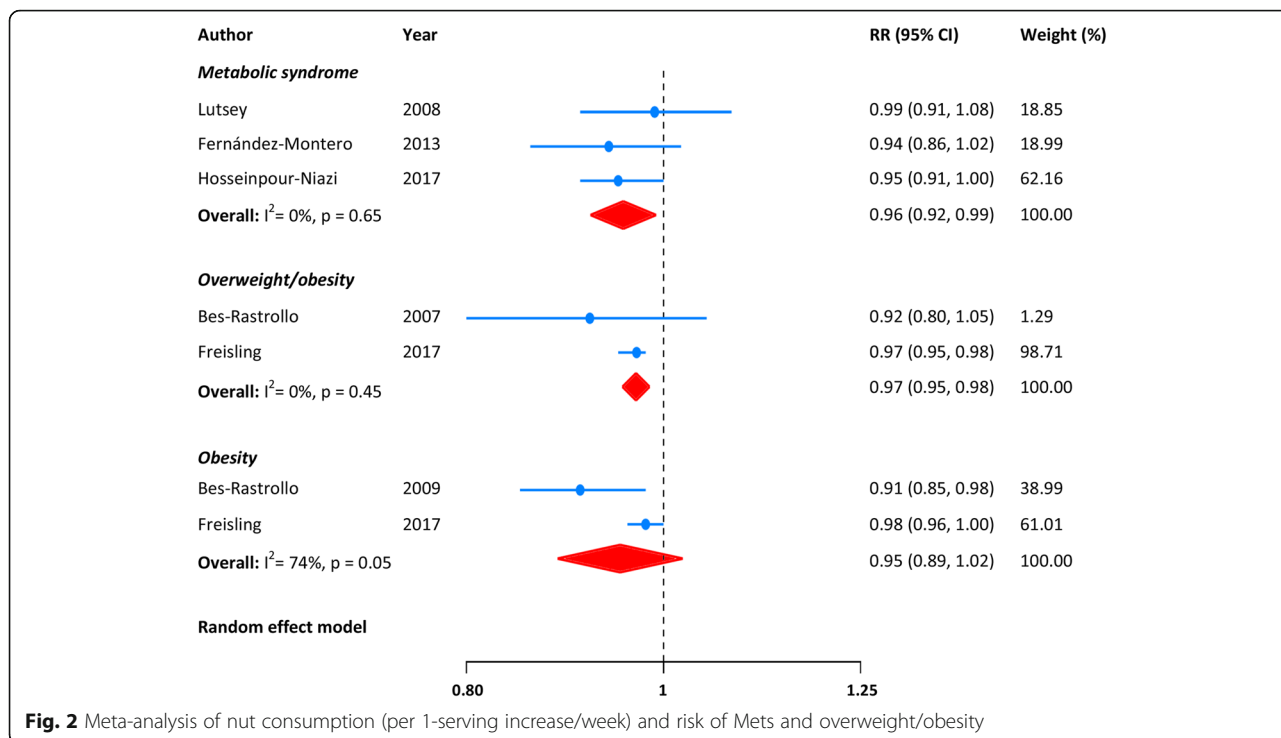
#### Nut consumption and changes in body weight parameters

The data of body weight, BMI, and waist circumference were provided in 56, 39, and 23 randomized feeding trials, respectively, with substantial heterogeneity across them. Compared with control diet, a nut-enriched diet was associated with a significant decrease in body weight (WMD:  $-0.22$  Kg, 95% CI:  $-0.44$  to  $-0.04$ ; Fig. 3), BMI (WMD:  $-0.16$  Kg/m<sup>2</sup>, 95% CI:  $-0.31$  to  $-0.01$ ; Fig. 4), and waist circumference (WMD:  $-0.51$  cm, 95% CI:  $-0.95$  to  $-0.07$ ; Fig. 4). Exclusion of each study in sequence had no significant influence on the pooled results. Egger's test indicated no potential of publication bias (body weight:  $p = 0.52$ ; BMI:  $p = 0.37$ ; waist circumference:  $p = 18$ ). The detailed results from the individual studies were displayed in Additional file 1: Figures S1–S3.

**Table 1** Characteristics of the included studies

Study	Country	Age (yrs)	Sample size	Cases	Outcomes	Measurement of nuts	Adjustments	NOS score
Bes-Rastrollo 2007 [21]	Spain	38 (mean)	6300	434	Overweight/obesity	FFQ	Age, sex, baseline BMI, leisure time PA, smoking, snacking and television watching	8
Bes-Rastrollo 2009 [17]	US	20–45	51,188	5924	Obesity	FFQ	Age, alcohol intake, PA, smoking, postmenopausal hormone use, oral contraceptive use, baseline BMI, glycemic load, changes in the adherence of prudent and Western dietary patterns and food groups	8
Fernández-Montero 2013 [18]	Spain	38 (mean)	9887	567	Mets	FFQ	Age, BMI, smoking, PA, alcohol intake and total energy intake	8
Freisling 2017 [19]	10 European countries	25–70	197,291 127,445	28,244 12,633	Overweight/obesity Obesity	FFQ	Age, sex, country, baseline BMI, follow-up time in years, total energy intake, educational level, PA, smoking, plausibility of dietary energy reporting and modified relative Mediterranean diet score	8
Hosseinpour-Niazi 2017 [20]	Iran	19–74	1265	276	Mets	FFQ	Age, sex, BMI, smoking, family history of diabetes, PA, fasting glucose, HDL-C, total energy intake, total fiber, percent of protein, percent of carbohydrates, percent of total fat, cholesterol intake, fruit, vegetables and dairy products	7
Lutsey 2008 [22]	US	45–64	9514	3782	Mets	FFQ	Age, sex, race, education, center, total calories, smoking, pack-years, PA and intakes of meat, dairy, fruits, vegetables, whole grains and refined grains	9

BMI, body mass index; FFQ, food-frequency questionnaire; HDL-C, high density lipoprotein cholesterol; Mets, metabolic syndrome; NOS, Newcastle-Ottawa Scale; PA, physical activity

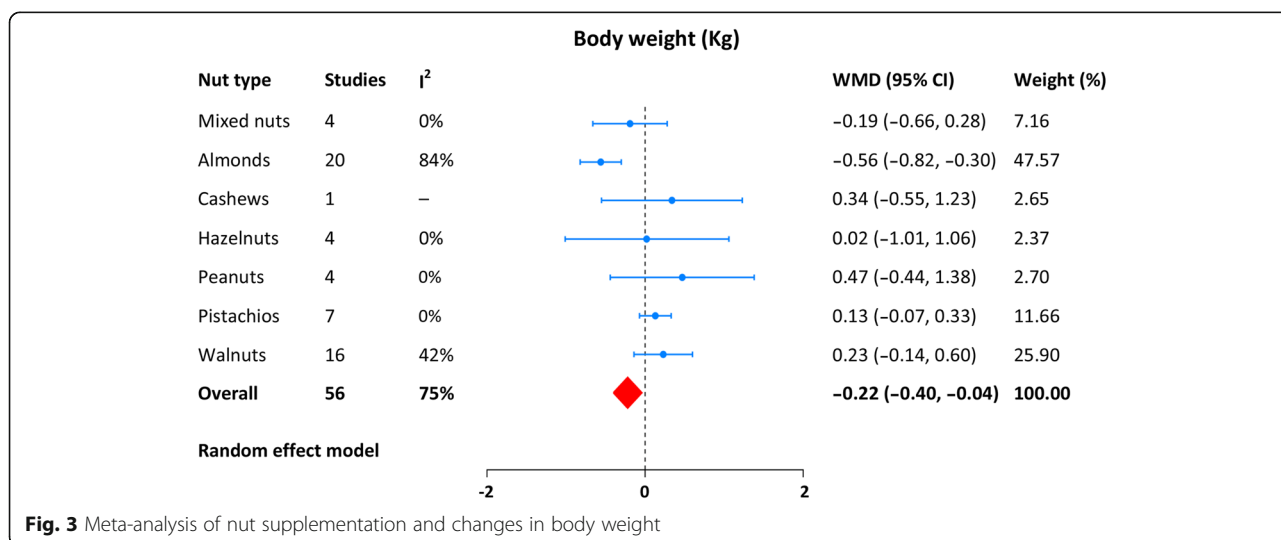


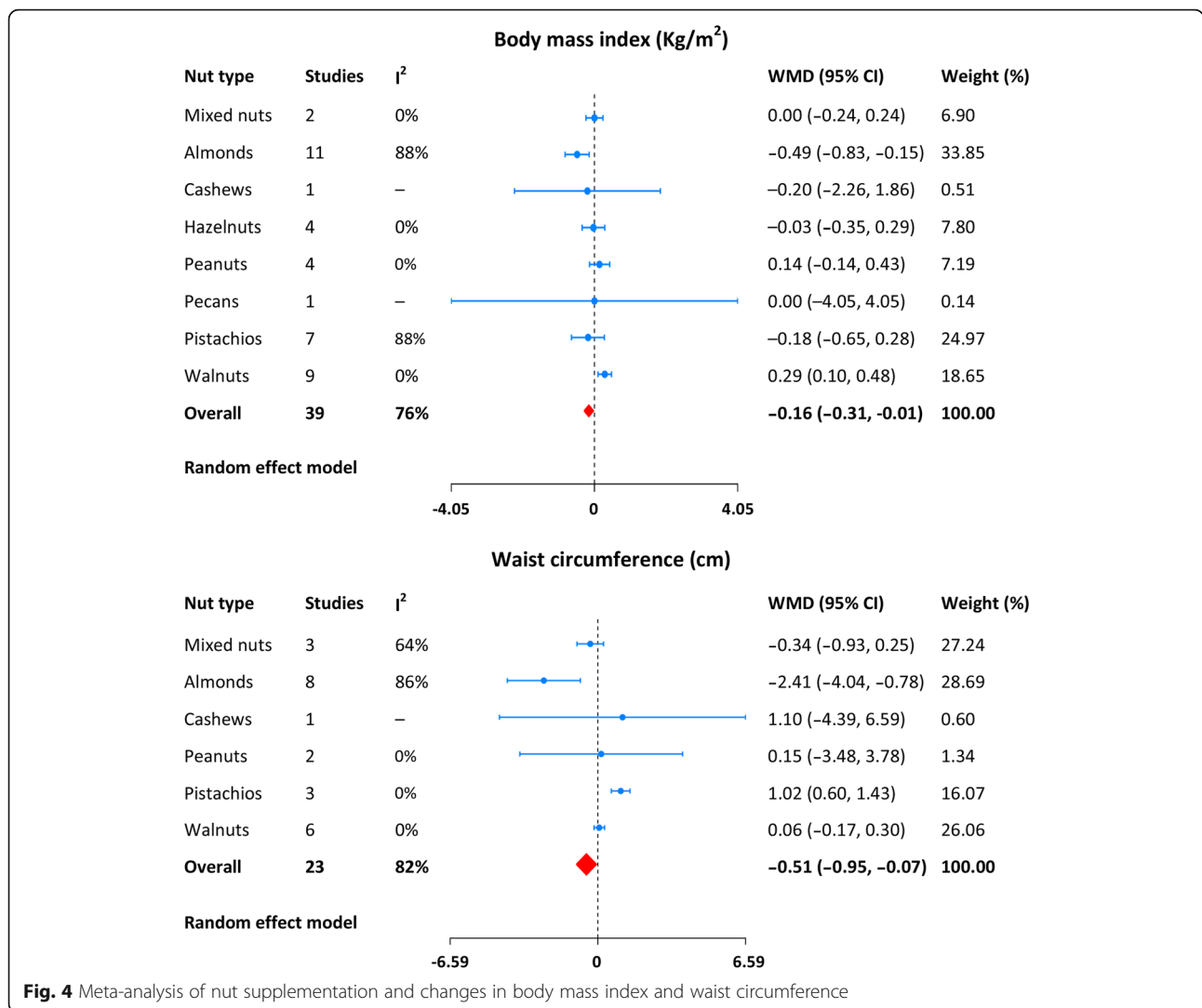
**Discussion**

Nut consumption has been recommended as an important component of healthy diet by the American Heart Association since 2000 [90], but most of the relevant epidemiological studies are to date focused on its protective role against cardiovascular diseases. The present meta-analysis of prospective cohort studies showed that for every 1-serving/week increase in nut consumption, the risk was reduced by 4% for Mets, by 3% for overweight/obesity, and by 5% for obesity only. In addition, the pooled data of randomized feeding trials suggested that nut supplementation could lower body weight, BMI,

and waist circumference, further supporting the metabolic benefits of nuts.

Previous reports have suggested a protective role of nut-rich diet against the development of Mets or overweight/obesity. In a meta-analysis of 50 studies totaling 534,906 individuals, Kastorini et al. demonstrated that adherence to the Mediterranean diet enriched with nuts conferred a lower risk of Mets (log hazard ratio: -0.69, 95% CI: -1.24 to -1.16) and improved waist circumference (-0.42 cm, 95% CI: -0.82 to -0.02) [91]. Similarly, a recent nationwide survey of Chilean adults found an inverse correlation between Mediterranean diet score and the





**Fig. 4** Meta-analysis of nut supplementation and changes in body mass index and waist circumference

prevalence of Mets and overweight or obesity [92]. For dietary intake of nut, accumulating evidence from feeding trials shows that it can reduce blood pressure, improve lipid profiles, and regulate glycemia metabolism and insulin sensitivity [15, 93]. In prospective cohort studies, nut consumption has also been identified to be correlated with decreased weight gain [17, 21]. All of these findings pointed towards the potentially preventive effects of nuts on Mets and overweight/obesity.

There are some possible explanations for the observed benefits of nuts. As a nutritious food, high intake of nuts provides abundant bioactive compounds including unsaturated fatty acids, dietary fiber, plant protein, antioxidants, vitamin E, arginine, phytosterols, and minerals like potassium, calcium, and magnesium. These healthy nutrients alone or in combination may improve inflammatory response, oxidative stress, and endothelial function, thus contributing to the improvements in individual Mets component [94]. Recent viewpoints have also highlighted

the importance of gut microbiota in the pathophysiological process of metabolic disease and obesity [95]. There is a notion that the non-bioaccessible substances from nuts (polymerized polyphenols, polysaccharides, and fiber) have prebiotics properties, which serve as substrates for human gut microbiome and cause favorable alterations in microbiome structure [96]. Hence, the health benefits of nut may be, as least in part, explained by its prebiotic effects on gut microbiome. The weight-loss effects of nuts were also likely to be related to the enhanced satiety, increased resting energy expenditure and diet-induced thermogenesis, and incomplete mastication and fat malabsorption [97, 98]. In addition, it deserves to be noted that subjects consuming higher amounts of nut tend to eat less red and processed meat [98]. Such a substitution appears to be helpful for the prevention of Mets and overweight/obesity because intakes of red and processed meat have been suggested to increase the risk of these metabolic abnormalities, as already mentioned above [11, 12].

In this meta-analysis, the inverse association of nut consumption with overweight and/or obesity seems to be counterintuitive, since nuts are a group of foods with high fats and dense calories. However, a previous pooled analysis of controlled feeding trials has shown borderline significant benefits of nut supplementation in the management of body weight, body mass index, and waist circumference [99]. Also, in a recent clinical trial with 6-month interventions, a walnut-enriched reduced-energy diet was found to promote weight loss, which is comparable to a standard reduced-energy-density diet in the context of a behavioral weight loss intervention [87]. These evidences, together with our findings, allay the fear that nut intake may promote overweight or obesity.

To the best of knowledge, this is the first meta-analysis examining the effects of nut intake in risk reduction of Mets and overweight/obesity. Nevertheless, the limitations of our study should not be ignored. First of all, the recall and selection bias cannot be avoided in the analyses of Mets and overweight/obesity due to the observational nature of the original studies. Second, heterogeneity was present among the randomized feeding trials, which may influence the pooled estimates of body weight parameters. Third, owing to the lack of data, we cannot conduct stratified analyses for the risk estimates by some important factors (e.g., nut subtype, age and sex). Fourth, due to the quite limited number of cohort studies, the potential of a non-linear association between nut consumption and risk of Mets or overweight/obesity cannot be evaluated. Last but not the least, this meta-analysis has geographical restrictions, as the majority of the included studies were from North America or Europe. Thus, generalization of our finding needs to be considered with caution.

## Conclusion

In summary, the results from this meta-analysis suggest that nut intake may be associated with decreased risks of Mets and overweight/obesity and lower body weight measures. The result supports the current recommendation of nut intake for the prevention of chronic diseases. Future prospective studies are still warranted to enhance our findings and to determine the health benefits of specific nuts.

## Additional files

**Additional file 1:** Table S1. Detailed search strategies. **Table S2.** Excluded articles with reasons at the stage of eligibility. **Table S3.** Baseline characteristics of feeding trials. **Figure S1.** Body weight changes from the individual studies in this meta-analysis. **Figure S2.** Body mass index changes from the individual studies in this meta-analysis. **Figure S3.** Waist circumference changes from the individual studies in this meta-analysis. (DOCX 1311 kb)

## Abbreviations

BMI: Body mass index; CIs: Confidence intervals; Mets: Metabolic syndrome; RRs: Relative risks; WMDs: Weighted mean differences

## Availability of data and materials

The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

## Authors' contributions

JL conceived and designed the experiments; HL and XL performed the experiments and analyzed the data; SY and YJ contributed reagents/materials/analysis tools; HL wrote the paper, with key intellectual contents revised by JL. All authors read and approved the final manuscript.

## Ethics approval and consent to participate

Not applicable.

## Consent for publication

Each author meets the criteria for authorship and assumes the corresponding responsibility.

## Competing interests

The authors declare that they have no competing interest.

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