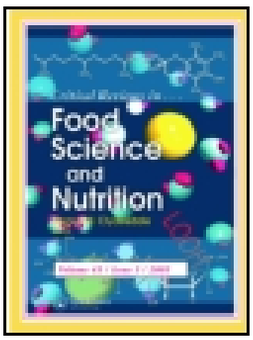

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REVIEW

The effects of magnesium supplementation on obesity measures in adults: a systematic review and dose-response meta-analysis of randomized controlled trials

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ABSTRACT

Previous studies reported inconsistent findings regarding the effects of magnesium supplementation on obesity measures. This study was done to quantify the effect of magnesium supplementation on body weight, Body Mass Index (BMI), Waist Circumference (WC), Body Fat (BF) percentage and Waist to Hip Ratio (WHR). Four online databases (Scopus, PubMed, Google Scholar and Cochrane library) were searched until March 2020 using relevant keywords. Random-effects model was used to pool effect sizes; Cochran's Q-test and I2 index assessed heterogeneity. Sensitivity analysis and Egger test were used to check the robustness of findings and the possibility of publication bias, respectively. Thirty-two RCTs including different dosage of magnesium (48–450 mg/d), and duration (6–24 weeks) were entered to this study. Magnesium supplementation resulted in a great reduction in BMI [Weighted Mean Difference (WMD): −0.21 kg/m^2, 95% CI: −0.41, −0.001, $P = 0.048$, $I^2 = 89.5\%$, $n = 22$], which was mainly driven by the effect among those with magnesium deficiency, insulin resistance related disorders, and obesity at baseline. No significant change was observed in bodyweight, WC, BF percentage and WHR as compared to controls. However, the change in body weight, and WC was significant in subgroups of participants with insulin resistance related disorders, hypertension, obesity, magnesium deficiency at baseline, and females. We found a significant reduction in BMI following magnesium supplementation. The change in body weight and WC were evident in certain subgroups.

KEYWORDS

Magnesium; weight; obesity; dose-response; meta-analysis

Introduction

A recent study has alarmed that the prevalence of obesity has been tripled since 1975 (Hassabou and Farag 2020). About 2 billion people (30% of total population) suffer from obesity worldwide, with each year 3 million die being attributed to obesity (Hassabou and Farag 2020). The huge economic and morbidity related burden of obesity cannot be neglected as well (Pi-Sunyer 2009; Ryan and Yockey 2017). Therefore, an immediate action is required to address this health issue. Currently, along with the usual weight loss practices, including calorie restriction, changes in makeup of dietary macronutrients, and physical activity a great attention has been laid on a variety of nutrients, particularly in the form of supplement (Dwyer, Allison, and Coates 2005; Fatahi et al. 2018).

Magnesium is one of the vital nutrients for the body which plays an important role in macronutrients metabolic pathways due to its ability to serve as a cofactor in many enzymatic reactions (Toprak et al. 2017). Magnesium is also responsible for maintaining integrity and stability of cell membrane (Cruz et al. 2014). Studies have shown that deficiency of magnesium can contribute to development of obesity (Huerta et al. 2005; Inoue 2005; Niranjan et al. 2014; Song et al. 2007) through targeting production of pro-inflammatory cytokines (Guerrero-Romero, Bermudez-Pena, and Rodriguez-Moran 2011). Therefore, given that about half of the Western populations has been reported not to meet the Estimated Average Requirement (EAR) for magnesium (Costello et al. 2016), it is probable that obesity may be arise from magnesium deficiency among this populations.

The existing evidence is indicative of an inverse relationship between magnesium intake from dietary sources (such as whole grains, nuts, and legumes, and dark green vegetables) with development (He et al. 2006a; Lu et al. 2020) and management (He et al. 2006b) of obesity-related measures. Consumption of nutritional elements in the context of supplement and in solitary may have even more appreciable effect than diet. However, the protective effect of magnesium against obesity is still controversial in the clinical experiments. To inform preventive actions, existing controversies should be reconciled.

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More recently, one meta-analysis showed that magnesium supplementation did not affect body weight, BMI, and waist circumference among type 2 diabetes patient (T2DM) (Asbaghi et al. 2020). Because only studies conducted on diabetic persons have been included in this meta-analysis, a considerable large number of studies that have examined the effect of magnesium supplementation on obesity measures in other health groups have not been included. Furthermore, this study has not assessed the dose-response association between magnesium supplementation and obesity measures. Therefore, this study was conducted to determine whether magnesium supplementation can positively affect obesity-related measures in adults.

Methods

Current systematic review and meta-analysis of randomized controlled trials (RCTs) were conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al. 2009).

Search and studies selection strategies

A systematic search of peer-reviewed literature was done using four bibliometric databases (Scopus, PubMed, Google Scholar and Cochrane library). The query syntax was set based on medical subject headings (MeSH) and thesaurus terms: ("magnesium*" OR ((magnesium) AND intake*) OR ((magnesium) AND supplement*) OR ((magnesium AND oral*) OR ((magnesium AND diet*)) AND (Obesity OR "Abdominal obesity" OR "Intra-abdominal fat" OR "Abdominal Fat" OR "body weight" OR "body mass index" OR "Waist Circumference" OR "Waist-Hip Ratio" OR "Waist-Height Ratio" "BMI" OR "WC" OR "WHR" OR "WHtR" OR anthropometry* OR "fatness" OR "visceral" OR "central obesity" OR viscera OR "body fat" OR "fat mass" OR "metabolic syndrome" OR "body composition"* OR "Obesity/complications" OR "percentage fat mass" OR FM OR %FMOR "visceral adipose tissue" OR overweight OR adiposity OR "Body Weight Changes" OR "Body Weight Maintenance"(. No filter was applied to limit the retrieval studies by journal categories, language, or publication date, and all studies published prior to March 2020 were imported to an EndNote library (version X9, for Windows, Thomson Reuters, Philadelphia, PA, USA) for duplicate removal and screening. To supplement the initial search in online databases, the reference list of retrieved studies and relevant review were checked.

Selection criteria

RCTs with either parallel or crossover design published in English and assessed the effect of oral magnesium supplementation on anthropometric measures (either weight, BMI, WC, BF percentage or WHR) compare to control group among adults (not pregnant women) were considered as eligible. Furthermore, studies which presented sufficient information on anthropometric indices at baseline and at the end of intervention or the net change values data in each group were included.

Exclusion criteria were defined as follow: (a) administration of magnesium with other supplements; (b) lack of control or placebo group; (c) exposure of interest lacking (e.g. diet education, nutritional counselling); (d) qualitive studies; (e) narrative reviews; f) behavior studies; (g) measurement validation studies; (h) book; (i) editorial; (j) position papers; (k) animal studies.

All titles and abstracts were screened for potential eligibility by two reviewers (MA, AJ) and unrelated publications were excluded. Whenever eligibility was not clear based on the title and abstract, the full text was read in full.

Data extraction

Data extraction from eligible studies was conducted by two reviewers (MA and AJ) using a standardized template with predefined headings: authorship, study location, sample size and sex, age range, study design, baseline level of serum magnesium, dosage and the content of magnesium supplement, duration of intervention, outcome types, mean and standard deviations (SD) for anthropometric measures, notes about participants, and outcome kind. Magnesium dosage were harmonized to a standardized unit across all studies to be pool able in the meta-analysis. In studies with multiple assessment of outcome during the follow up, the final assessment with the longest duration was extracted. Furthermore, in studies with the same dataset, study with a greater number of participants was selected for inclusion. In cases of ambiguous or missing information in the included studies, the corresponding authors were contacted by email (Hadjistavri et al. 2010; Pokan et al. 2006).

Quality of evidence

Using the Risk of Bias *2* (*RoB 2*) tool all studies were appraised for quality in terms of random allocation, adherence to intervention, objective measurement of the outcome, missing outcome data and selective report of results by two independent investigators (Sterne et al. 2019a). Each numbered item within the mentioned domains could be given 5 response categories (yes, probably yes, no, probably no, not indicated). Studies were classified as having low risk of bias, some concerns and high risk of bias based on affirmative responses (Sterne et al. 2019b) (Table 2).

Statistical method

Weighted mean differences (WMD) and SD were combined using random-effect models. In studies with only baseline and final values of obesity measures, the changes in means and SDs were estimated using the following equations:(Borenstein et al. 2011) [Mean change = mean after- mean before] and [SD change = square root ((SD baseline^2 +SD final^2) − (2 R × SD baseline × SD final))] (Borenstein et al. 2011). The best correlation coefficient (R) for each parameter was estimated from studies in which

mean (SD) changes were reported.(Borenstein et al. 2011) Standard errors (SEs) were converted to SDs using the following formula: SD = SEM × sqrt (n), where n is the number of participants. The I^2 statistic > 50% was used to assess statistically significant heterogeneity (Kerkhoffs et al. 2012) and potential sources were traced using subgroup analysis based on fixed model: baseline BMI (≥30 kg/m, <30 kg/m), baseline serum magnesium level (≥2 mg/dl, <2 mg/dl), duration of treatment (>12 weeks, ≤12 weeks), magnesium supplement dose (≥350 mg/d, <350 mg/d), sample size (≥50, <50), health status (healthy, insulin resistance related disease (diabetes, prediabetes, poly cystic ovary syndrome (PCOS) and nonalcoholic fatty liver disease (NAFLD), hypertension, coronary artery disease (CAD), depression), and sex (both, women, men). In addition, meta-regression was performed using the unrestricted maximum likelihood method to evaluate the association between differences in means of BMI, weight, WC with dosage, duration of magnesium supplementation and baseline values of BMI, weight, WC (Thompson and Sharp 1999). The symmetry of dots on the funnel plot and Egger's statistical test were used to investigate potential publication bias. If publication bias was detected, Duval & Tweedie's "trim and fill" method was used to adjust the analysis for its effects (Duval and Tweedie 2000). Sensitivity analysis was conducted to examine if any study contributed a high effect on the forest plot. To test dose-response relations, non-linear associations between pure magnesium dosage (mg/d) and duration of treatment (week) with the absolute mean change in each outcome using fractional polynomial (polynomials) was considered. All data analyses were carried out using Stata 14.0 software (Stata Corp LP, College Station, TX). $P < 0.05$ was considered as statistically significant.

Results

Literature overview

Thirty-two randomized clinical trials were finalized for inclusion in this analysis (Figure 1). Initially, 2286 articles were found through electronic and manual searches. Removing duplicates, 1525 publications were screened. At first, 1236 irrelevant publications were excluded due to irrelevant titles and abstracts. Among 289 retrieved studies for full text evaluation, 257 were excluded: irrelevant outcomes ($n = 191$), trials lacking random allocation ($n = 14$), trials without a control or placebo group ($n = 8$), participants were children or the pregnant ($n = 4$), non-English publications ($n = 3$), the intervention was done in combination with other components ($n = 4$), review papers ($n = 10$), animal studies ($n = 13$), cell cultures ($n = 4$), and observational designs ($n = 3$), studies lacking baseline values and findings which prevent us to calculate change ($n = 3$).

Systematic review

General characteristics were extracted based on a standardized table of thirty-two included studies are described in Table 1. All included RCTs were in English language, and they were published between 1995 and 2019. In total, 2551 participants were included (1279 in the intervention and 1272 in the control group). Participants' age varied from 18 to 85 years. Participants were either healthy (Brilla et al. 2003; Day et al. 2010; Guerrero-Romero and Rodríguez-Morán 2011; Itoh, Kawasaka, and Nakamura 1997; Moslehi et al. 2012; Moslehi et al. 2013; Rodríguez-Moran and Guerrero-Romero 2014; Solati et al. 2019) or had medical conditions such as hypertension (Cappuccio et al. 1985; Guerrero-Romero and Rodriguez-Moran 2009; Hadjistavri et al. 2010; Rodríguez-Ramírez et al. 2017; Witteman et al. 1994; Yamamoto et al. 1995) diabetes (Guerrero-Romero et al. 2004; Mooren et al. 2011; Navarrete-Cortes et al. 2014; Rashvand, Mobasseri, and Tarighat-Esfanjani 2019; Razzaghi et al. 2018; Rodríguez-Morán and Guerrero-Romero 2003; Sadeghian et al. 2020; Solati et al. 2014; Talari et al. 2019), pre-diabetes (Guerrero-Romero et al. 2015; Simental-Mendía, Rodríguez-Morán, and Guerrero-Romero 2014; Simental-Mendía et al. 2012; Toprak et al. 2017), CAD (Pokan et al. 2006) NAFLD (Karandish et al. 2013), depression (Rajizadeh et al. 2017), metabolic syndrome (Rodríguez-Morán et al. 2018), PCOS (Farsinejad-Marj et al. 2020). One study had a crossover design (Navarrete-Cortes et al. 2014) while the other had a parallel design. Studies were conducted in the USA ($n = 3$) (Brilla et al. 2003; Pokan et al. 2006; Yamamoto et al. 1995), England ($n = 1$) (Cappuccio et al. 1985), Netherland ($n = 1$) (Witteman et al. 1994), Japan ($n = 1$) (Itoh, Kawasaka, and Nakamura 1997), Mexico ($n = 11$) (Guerrero-Romero and Rodriguez-Moran 2009; Guerrero-Romero et al. 2015; Guerrero-Romero et al. 2004; Guerrero-Romero and Rodríguez-Morán 2011; Navarrete-Cortes et al. 2014; Rodríguez-Moran and Guerrero-Romero 2014; Rodríguez-Morán and Guerrero-Romero 2003; Rodríguez-Morán et al. 2018; Rodríguez-Ramírez et al. 2017; Simental-Mendía, Rodríguez-Morán, and Guerrero-Romero 2014; Simental-Mendía et al. 2012), Australia ($n = 1$) (Day et al. 2010), Greece ($n = 1$) (Hadjistavri et al. 2010), Germany ($n = 1$) (Mooren et al. 2011), Iran (n = 11) (Farsinejad-Marj et al. 2020; Karandish et al. 2013; Moslehi et al. 2012; Moslehi et al. 2013; Rajizadeh et al. 2017; Rashvand, Mobasseri, and Tarighat-Esfanjani 2019; Razzaghi et al. 2018; Sadeghian et al. 2020; Solati et al. 2019; Solati et al. 2014; Talari et al. 2019), Turkey ($n = 1$) (Toprak et al. 2017). Fifteen studies were conducted on both genders (Cappuccio et al. 1985; Guerrero-Romero and Rodriguez-Moran 2009; Guerrero-Romero and Rodríguez-Morán 2011; Hadjistavri et al. 2010; Itoh, Kawasaka, and Nakamura 1997; Karandish et al. 2013; Navarrete-Cortes et al. 2014; Rajizadeh et al. 2017; Rashvand, Mobasseri, and Tarighat-Esfanjani 2019; Sadeghian et al. 2020; Simental-Mendía et al. 2012; Solati et al. 2019; Solati et al. 2014; Talari et al. 2019; Yamamoto et al. 1995) although seventeen studies provided gender-specific results (Brilla et al. 2003; Guerrero-Romero and Rodríguez-Morán 2011; Itoh, Kawasaka, and Nakamura 1997; Mooren et al. 2011; Moslehi et al. 2012; Rajizadeh et al. 2017; Razzaghi et al. 2018; Rodríguez-Morán and Guerrero-Romero 2003; Rodríguez-Morán et al. 2018; Rodríguez-Ramírez et al. 2017; Sadeghian et al. 2020; Simental-Mendía et al. 2012; Solati et al. 2019;

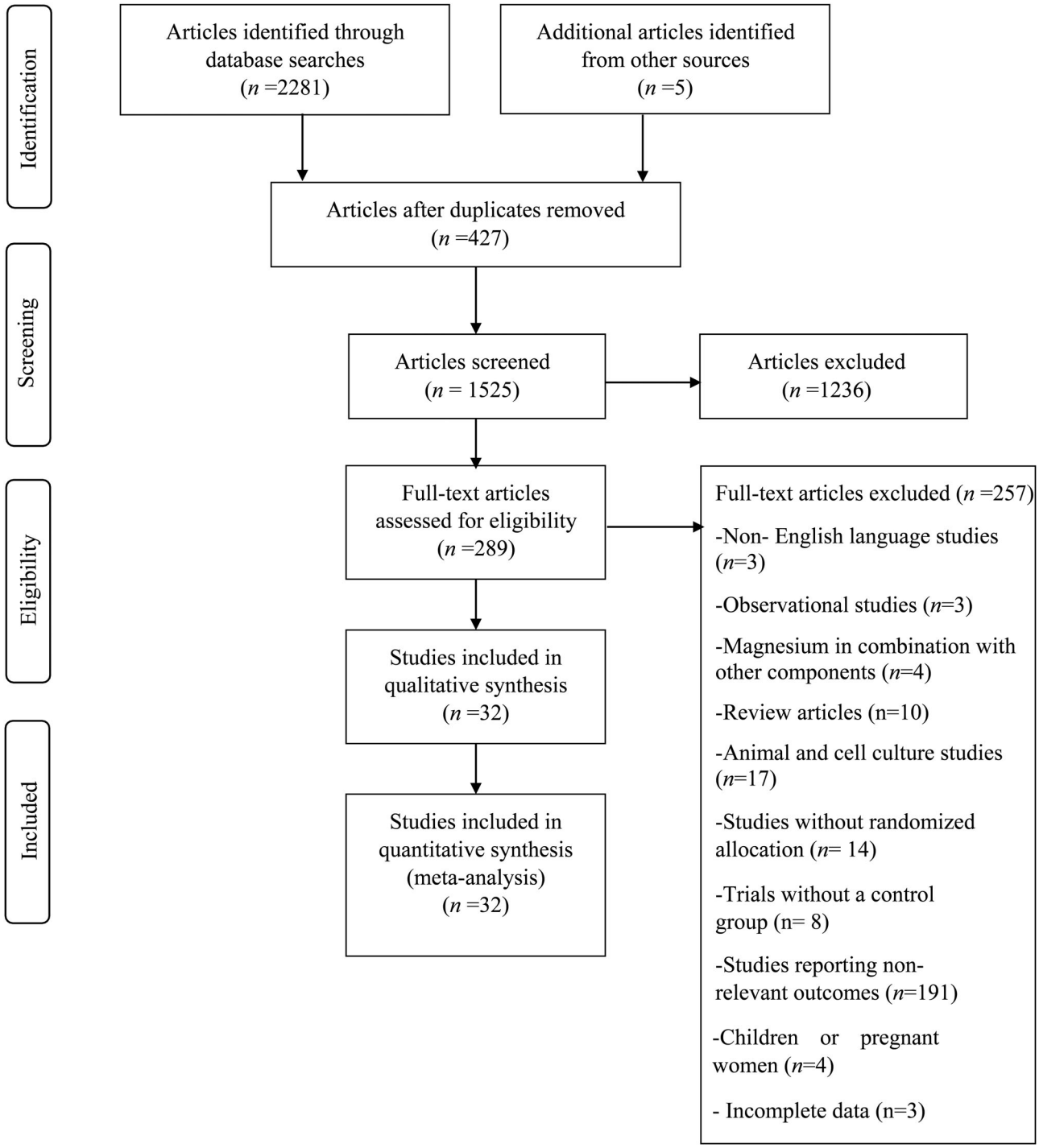

Figure 1. Flow diagram of study selection.

Solati et al. 2014; Talari et al. 2019; Witteman et al. 1994; Yamamoto et al. 1995). The elemental dosage of mg prescribed in these trials varied from 48 to 450 mg/days and the duration of mg supplementation ranged from 6 to 24 weeks.

Study quality

Generally, most studies were of good quality (Table 2). Sixteen studies were scored as of low risk of bias, 12 as of medium; only 4 were considered as of high risk of bias. Major concerns for quality were mainly due to unclear or unjustified random allocation ($n = 8$), missing outcome data ($n = 6$), deviation from intended intervention ($n = 3$), and bias associated with reporting results ($n = 3$).

Meta-analysis results

Body mass index

Twenty-two studies with twenty-four arms including a total of 2126 participants (case = 1103, and control = 1023) reported BMI as an outcome measure. Four studies reported a great reduction in BMI following magnesium

Table 1. Demographic characteristic of included studies.

						Intervention type				outcome				
Code/author(year)	Study location	Subjects and gender	Age, y1	Design	Serum	Intervention (name and composition)	Control (name and composition)	Duration (wk)	Outcomes	Intervention mean ± SD	Control mean ± SD	Notes about subjects	Outcome (yes/no)	Outcome kind
1.Yamamoto et al. (1995)	USA	M:301 F:143 M + F: MG:227 CON:234	30-45 MG:42.7 CON:43.2	Parallel	1.9 (mg/dl)	Magnesium diglycine(360mg) pill	Placebo	24	BMI	BMI (kg/m): Before:27.6 ± 9.1 After:27.7 ± 9.6	BMI (kg/m): Before:28.6 ± 4.2 After:28.9 ± 4.7	461 hypertension patients	BMI (no)	Secondary
2. Cappuccio et al. (1985)	England	M:9 F:8 M + F: MG:9 CON:8	33-66 MG: CON:	Parallel	0.89(mg/dl)	Magnesium aspartate hydrochloride(15mmol) tablet	Placebo	4	Weight	Weight (kg): Before:79 ± 12.3 After:78.4 ± 12.3	Weight (kg): Before:79 ± 11.6 After:78.3 ± 11.31	17 hypertensions	Weight (no)	Secondary
3.Witteman et al. (1994)	Netherland	F:91 MG:47 CON:44	35-77 MG:57.4 CON:57.1	Parallel	0.85(mg/dl)	Magnesium aspartate(485mg) tablet	Placebo	24	Weight	Weight (kg): Before:69.2 ± 10.97 After:69.1 ± 10.28	Weight (kg): Before:70.9 ± 10.6 After:70 ± 10.6	91 hypertensions	Weight (no)	Secondary
4.Itoh, Kawasaka, and Nakamura (1997)	Japan	M:11 F:22 M + F: MG:64 CON:66	48-84 MG:64 CON:66	Parallel	0.86(mg/dl)	Magnesium hydroxide tablet	Placebo	4	Weight	Weight (kg): Before:57.4 ± 7.7 After:57.3 ± 7.8	Weight (kg): Before:56 ± 7.8 After:57.3 ± 8.5	33 healthy	Weight (no)	Secondary
5.Brilla et al. (2003)	USA		19-24 MG:22 CON:	Parallel		Magnesium oxide plus creatine capsule	Placebo (malto dextrin)	2	Weight	Weight (kg): Before:67.28 ± 11.33 After:68.03 ± 10.96 Weight (kg): Before:71.48 ± 16.86 After:71.88 ± 17.15	Weight (kg): Before:71.84 ± 11.32 After:71.88 ± 10.62	35 healthy	Weight (yes)	Secondary
6.Rodríguez-Morán and Guerrero-Romero (2003)	Mexico	MG:32 CON:31	44-68 MG:59.7 CON:54.1	Parallel	0.65(mg/dl)	Magnesium chloride(2500ml) solution	Placebo	16	BMI, Weight, WHR	BMI (kg/m): Before:27.6 ± 9.1 After:27.7 ± 9.6 Weight (kg): Before:72.9 ± 10.7 After:73.1 ± 10.4 WHR Before:0.98 ± 0.06 After:0.98 ± 0.07	BMI (kg/m): Before:28.6 ± 4.2 After:28.9 ± 4.7 Weight (kg): Before:69.3 ± 10.1 After:69.6 ± 9.9 WHR Before:0.96 ± 0.04 After:0.96 ± 0.06	63 T2DM	BMI (no), Weight (no), WHR (no)	Secondary
7.Guerrero-Romero et al. (2004)	Mexico	MG:30 CON:30	35-51 MG:43 CON:42.2	Parallel	0.61(mg/dl)	Magnesium chloride(2500ml) solution	Placebo	12	BMI, WHR	BMI (kg/m): Before29.3 ± 6.3 After:29.1 ± 6.1 WHR: Before:0.93 ± 0.14 After:0.93 ± 0.17	BMI (kg/m): Before:29.1 ± 3.1 After:29.2 ± 3 WHR: Before:0.91 ± 0.9 After:0.91 ± 0.1	60 insulin resistance	BMI (no), WHR (no)	Secondary
8.Pokan et al. (2006)	USA	M:53 MG:28 CON:25	48-70 MG:61 CON:58	Parallel		magnesium citrate(30mmol) solution	Placebo	24	Weight	Weight (kg): Before:79 ± 10 After:80 ± 10	Weight (kg): Before:79 ± 10 After:79 ± 10	53 coronary artery disease	Weight	Secondary
9.Guerrero-romero et al. (2009)	Mexico	M:38 F:41 M + F: MG:40 CON:39	40-75 MG:58.9 CON:60.5	Parallel	0.62(mg/dl)	Magnesium chloride(50mmol) solution	Placebo	16	BMI	BMI (kg/m): Before:29.9 ± 5.2 After:29.4 ± 4.7	BMI (kg/m): Before:29 ± 5.1 After:28.6 ± 4.9	79 diabetic hypertensions	BMI (no)	Secondary
10.Day et al. (2010)	Australia	F:37 MG:34 CON:33	50-70 MG:59 CON:57	Parallel		Magnesium bicarbonate (1500-1800ml) solution	Placebo (spring water)	12	BMI, Weight	BMI (kg/m): Before:24.16 ± 3.14 After:24.16 ± 3.14 Weight (kg): Before:64.22 ± 8.15 After:64.07 ± 8.61	BMI (kg/m): Before:25.05 ± 3.64 After:25.02 ± 3.59 Weight (kg): Before:67.99 ± 11.58 After:67.86 ± 11.54	67 menopauses	BMI (no), Weight (no)	Secondary
11.Hadjistavri et al. (2010)	Greece	M:30 F:18 M + F: MG:24 CON:24	35-56 MG:45.3 CON:46.9	Parallel	2.3(mg/dl)	Magnesium pidolate (600mg) solution	Recommendation	12	BMI, WHR	BMI (kg/m): Before:28.3 ± 2.8 After:28.2 ± 2.8 WHR: Before:0.98 ± 0.1 After:0.98 ± 0.1	BMI (kg/m): Before:27.4 ± 4.1 After:27.3 ± 3.7 WHR: Before:0.97 ± 0.6 After:0.96 ± 0.7	48 hypertensions	BMI (no), WHR (no)	Secondary
12.Guerrero-Romero, Bermudez-Pena, and Rodriguez-Moran (2011)	Mexico	M:53 F:40 M + F: MG:49 CON:48	40-65 MG:39.8 CON:41.4	Parallel	0.66(mg/dl)	Magnesium chloride(50mmol) solution	Placebo(water)	12	BMI, WC	BMI (kg/m): Before:29.8 ± 4.9 After:29.5 ± 4.7 WC (cm) Before:92.6 ± 11.7 After:92.5 ± 11.6	BMI (kg/m): Before:28.4 ± 6.8 After:28.1 ± 6.5 WC (cm) Before:89.8 ± 14.5 After:89.6 ± 13.9	77 healthy	BMI (no), WC (no)	Secondary
13.Mooren et al. (2011)	Germany	MG:25 CON:22	30-70	Parallel	0.89(mg/dl)	Magnesium aspartate hydrochloride(365mg) solution	Placebo	24	BMI	BMI (kg/m): Before:30.9 ± 3.23 After:30.82 ± 3.63	BMI (kg/m): Before:29.98 ± 2.3 After:29.86 ± 2.54	47 insulin resistance	BMI (no)	Secondary
14.Moslehi et al. (2012)	Iran	F:74 MG:35 CON:34		Parallel	2.2(mg/dl)	Magnesium oxide(250mg) pill	Placebo	8	BMI, Weight	BMI (kg/m): Before:28 ± 3.2 After:27 ± 3.2	BMI (kg/m): Before:28.1 ± 2.9 After:27.9 ± 3	74 overweight	BMI (no), Weight (no)	Secondary

(*continued*)

Table 1. Continued.

Code/author(year)	Study location	Subjects and gender	Age, y1	Design	Serum	Intervention type: Intervention (name and composition)	Intervention type: Control (name and composition)	Duration (wk)	Outcomes	outcome: Intervention mean ± SD	outcome: Control mean ± SD	Notes about subjects	Outcome (yes/no)	Outcome kind
										Weight (kg): Before:69.6 ± 8.9 After69.5 ± 8.8	Weight (kg): Before:68.2 ± 8.4 After:68 ± 8.6			
15.Simental-Mendia et al. (2012)	Mexico	M:14 F:8 M + F: MG:11 CON:11	20-65 MG:44.2 CON:43.2	Parallel	0.82(mg/dl)	Magnesium oxide(250mg) solution	Placebo	12	BMI, WC, BF	BMI (kg/m): Before:30.5 ± 4.4 After:39.8 ± 3.8 WC (cm): Before:97.2 ± 11.1 After:94.8 ± 9.8 BF: Before:36.6 ± 9.4 After:35.5 ± 9.8	BMI (kg/m): Before:35.1 ± 3.7 After:34.4 ± 3.7 WC (cm): Before:101.7 ± 9.4 After:103.3 ± 9.4 BF: Before:40 ± 7.7 After:38.2 ± 8.9	22 prediabetes	BMI (no), WC (no), BF (no)	Secondary
16.Moslehi et al. (2013)	Iran	F:74 MG:35 CON:34	40-55 MG:46.5 CON:46.1	Parallel	2.2(mg/dl)	Magnesium chloride tablet	Placebo (corn starch, lactose, and stearic acid)	8	BF	BF: Before:37.6 ± 3.8 After:36.4 ± 4.8	BF: Before:38.1 ± 3.8 After:37.9 ± 3.8	74 overweight	BF (yes)	Primary
17.Karandish et al. (2013)	Iran	M:64 F:4 M + F: MG:34 CON:34	18-59 MG:36 CON:36	Parallel	2.03(mg/dl)	Magnesium oxide(250mg) capsule + diet + physical activity	Placebo(lactose)+ diet + physical activity	12	BMI, Weight, BF	BMI (kg/m): Before:30.69 ± 4.36 After:29.54 ± 4.65 Weight (kg): Before:91.05 ± 13.77 After:87.6 ± 14.37 BF: Before:31.2 ± 5.54 After:29.31 ± 5.87	BMI (kg/m): Before:31.74 ± 5.65 After:30.68 ± 4.59 Weight (kg): Before:94.59 ± 16.85 After91.45 ± 16.39 BF: Before:31.87 ± 6.85 After:29.4 ± 6.54	68 NAFLD	BMI (yes), Weight (yes), BF (yes)	Secondary
18.Solati et al. (2014)	Iran	M:13 F:34 M + F:47 MG:25 CON:22	20-60 MG:46.7 CON:50.1	Parallel	2.1(mg/dl)	Magnesium sulfate capsule	Placebo	12	BMI	BMI (kg/m): Before:26.19 ± 2.86 After:26.41 ± 3.29	BMI (kg/m): Before:26.89 ± 5.23 After:27.28 ± 5.13	47 T2DM	BMI (no)	Secondary
19.Navarrete-Cortes et al. (2014)	Mexico	M:36 F:64 M + F: MG:35 CON:34	30-65 52.84	Cross over	0.92(mg/dl)	magnesium lactate(1500mg) tablet	Placebo	12	BMI, WC	BMI (kg/m): Before:30.56 ± 5.65 After:30.4 ± 5.61 WC (cm) Before:97.05 ± 12.04 After:95.45 ± 12.16	BMI (kg/m): Before:30.62 ± 5.8 After:30.52 ± 5.71 WC (cm) Before:97.63 ± 13.08 After:97.63 ± 13.08	63 T2DM	BMI (no), WC (no)	Secondary
20.Simental-mendia, Rodríguez-Morán, and Guerrero-Romero (2014)	Mexico	MG:37 CON:37	18-65	Parallel	0.65(mg/dl)	Magnesium chloride(30mmol) solution	Placebo (sodium bicarbonate)	12	BMI, Weight, WC	BMI (kg/m): Before:30.5 ± 4.4 After:29.8 ± 3.8 Weight (kg): Before:80.4 ± 14 After:79.2 ± 15.3 WC (cm) Before:106.6 ± 12.5 After:102.2 ± 14.7	BMI (kg/m): Before:35.1 ± 7 After:34.4 ± 6.7 Weight (kg): Before:82.2 ± 11.6 After:74.2 ± 15.8 WC (cm) Before:107.5 ± 12.7 After:102.3 ± 12.4	57 pre diabetic	BMI (no), Weight (no), WC (no)	Secondary
21.Rodriguez-moran and Guerrero-Romero (2014)	Mexico	M:16 F:31 MG:24 CON:23	MG:31.9 CON:39.5	Parallel	1.34(mg/dl)	Magnesium chloride(30ml) solution + diet + physical activity	Placebo + diet + physical activity	16	BMI, WC	BMI (kg/m): Before:22.4 ± 1.6 After:22.3 ± 1.6 WC (cm) Before:101.9 ± 12.4 After:82.9 ± 9.6	BMI (kg/m): Before:22.7 ± 1.9 After:22.6±.8 WC (cm) Before:87 ± 8.5 After:86.9 ± 8.3	47 hypo magnetic	BMI (no), WC (no)	Secondary
22.Guerrero-Romero et al. (2015)	Mexico	MG:59 CON:57	30-65 MG:42.4 CON:42.3	Parallel	1.53(mg/dl)	Magnesium chloride(30mmol) solution	Placebo	16	BMI, WC	BMI (kg/m): Before:30.6 ± 6.4 After:30.3 ± 5.8 WC (cm) Before:101.9 ± 12.4 After:99.4 ± 15.2	BMI (kg/m): Before:31.7 ± 4.7 After:30.6 ± 4.6 WC (cm) Before:100.3 ± 15.4 After:96.5 ± 15.3	116 IGF	BMI (no), WC (yes)	Secondary
23.Rajizadeh et al.(2017)	Iran	M:14 F:39 M + F: MG:26 CON:27	20-60 MG:32.2 CON:32	Parallel	1.8(mg/dl)	Magnesium oxide(500mg) tablet	Placebo (starch)	8	BMI	BMI (kg/m): Before:28.58 ± 4.5 After:25.89 ± 5.64	BMI (kg/m): Before:25.67 ± 4.09 After:25.94 ± 4.31	53 depressed	BMI (no)	Secondary
24.Razzaghi et al. (2018)	Iran	MG:26 CON:27	40-85 MG:60.1 CON:59	Parallel	2(mg/dl)	Magnesium oxide(250mg) + protocol	Placebo + protocol	12	BMI, Weight	BMI (kg/m): Before:28.2 ± 5.2 After:28.2 ± 5.2 Weight (kg): Before:79.4 ± 12.3 After:79.5 ± 12.2	BMI (kg/m): Before:26.2 ± 4.1 After:26.3 ± 4.2 Weight (kg): Before:74.9 ± 13.9 After:75 ± 14.1	70 diabetics	BMI (no), Weight (no)	Secondary
25.Toprak et al. (2017)	Turkey	MG:57 CON:61	20-70 MG:55.5 CON:57	Parallel	1.7(mg/dl)	Magnesium oxide solution + diet + physical activity	Placebo (sodium-free carbonated water) + diet	12	BMI, WC	BMI (kg/m): Before:33.86 ± 2.81 After:32.9 ± 3.21 WC (cm)	BMI (kg/m): Before:33.99 ± 2.63 After:33.88 ± 2.83 WC (cm)	128 pre diabetic	BMI (no), WC (yes)	Secondary

(*continued*)

Table 1. Continued.

						Intervention type				outcome				
Code/author(year)	Study location	Subjects and gender	Age, y1	Design	Serum	Intervention (name and composition)	Control (name and composition)	Duration (wk)	Outcomes	Intervention mean ± SD	Control mean ± SD	Notes about subjects	Outcome (yes/no)	Outcome kind
							+ physical activity			Before:104.54 ± 11.3 After:99.5 ± 11.07	Before:103.17 ± 10.98 After:103.72 ± 11.01			
26.Ramirez et al. (2017)	Mexico	MG:18 CON:18	35-65	Parallel	0.71(mg/dl)	magnesium lactate(750mg) tablet	Placebo	16	BMI, WC	BMI (kg/m): Before:27.3 ± 3.1 After:28.1 ± 6.6 WC (cm) Before:97.1 ± 8.3 After:97.2 ± 8.4	BMI (kg/m): Before:29.4 ± 6.9 After:27.9 ± 3.1 WC (cm) Before:96.4 ± 16 After:91.6 ± 7.4		BMI (yes), WC (yes)	Secondary
27.Rodriguez-moran et al. (2018)	Mexico	MG:98 CON:98	30-60 MG:39.4 CON:40.4	Parallel	1.5(mg/dl)	Magnesium chloride(30mmol) solution	Placebo	16	BMI, WC	BMI (kg/m): Before:29.7 ± 6.5 After:28.8 ± 6.1 WC (cm) Before:100.8 ± 13.3 After:99.3 ± 14.4	BMI (kg/m): Before:30.5 ± 5.9 After:30 ± 5.5 WC (cm) Before:101.1 ± 13.8 After:100.8 ± 12.2	196 metabolic syndromes	BMI (no), WC (no)	Primary
28.Farsinejad-marj et al. (2020)	Iran	F:60 MG:30 CON:30	20-45 MG:26.3 CON:26	Parallel	2.4(mg/dl)	Magnesium oxide(250mg) tablet	Placebo (lactose, starch, calcium stearate, and calcium phosphate)	8	BMI, Weight, WC	BMI (kg/m): Before:27.8 ± 4.98 After:27.48 ± 5.03 Weight (kg): Before:72.09 ± 2.3 After:71.54 ± 2.25 WC (cm) Before:94.58 ± 2.36 After:94.85 ± 2.41	BMI (kg/m): Before:27.72 ± 5.53 After:27.79 ± 5.64 Weight (kg): Before:72.24 ± 2.47 After:72.3 ± 2.5 WC (cm) Before:94.24 ± 2.51 After:95.39 ± 2.52	60 PCOS	BMI (yes), Weight(no), WC (no)	Primary
29.Sadeghian et al. (2020)	Iran	M:37 F:53 M + F: MG:40 CON:40	32-51 MG:41.2 CON:42.8	Parallel	2.3(mg/dl)	Magnesium oxide(250mg) tablet	Placebo (lactose, starch, calcium stearate, and calcium phosphate)	12	BMI, Weight	BMI (kg/m): Before:31.2 ± 5.5 After:30.4 ± 5.4 Weight (kg): Before:82.1 ± 12.1 After:80.7 ± 12.5	BMI (kg/m): Before:30.9 ± 4.4 After:30.6 ± 4.6 Weight (kg): Before:77.7 ± 13.2 After:77.1 ± 13.6	80 T2DM	BMI (yes), Weight (yes)	Secondary
30.Solati et al. (2019)	Iran	M:31 F:39 M + F:70 MG:35 CON:35	19-69 MG:40.7 CON:40.6	Parallel	1.9(mg/dl)	Magnesium sulfate (300mg) capsule	Placebo (wheat bran)	24	BMI	BMI (kg/m): Before:28.81 ± 5.2 After:28.81 ± 5.2	BMI (kg/m): Before:28.92 ± 4.14 After:28.92 ± 4.14	70 overweight	BMI (no)	Secondary
31.Talari et al. (2019)	Iran	M:25 F:29 M + F:54 MG:27 CON:27	18-80 MG:58.8 CON:61.8	Parallel	2.1(mg/dl)	Magnesium oxide(250mg) capsule	Placebo	24	BMI, Weight	BMI (kg/m): Before:27.2 ± 5.6 After:27.2 ± 5.7 Weight (kg): Before73.5 ± 14 After:73.6 ± 14.4	BMI (kg/m): Before:26.1 ± 4.5 After:26.2 ± 4.4 Weight (kg): Before:71.9 ± 11.8 After:72.1 ± 11.7	54 diabetics	BMI (no), Weight (no)	Secondary
32.Rashvand, Mobasseri, and Tarighat-Esfanjani (2019)	Iran	M:19 F:18 M + F:37 MG:18 CON:19	30-60 MG:49.8 CON:48.2	Parallel	2.05(mg/dl)	Magnesium oxide(500mg) capsule	Placebo (starch)	8	BMI, Weight, WHR, WC, BF	BMI (kg/m): Before:26.69 ± 3.24 After:29.54 ± 3.5 Weight (kg): Before:81.18 ± 11.44 After:80.8 ± 11.57 WHR: Before:0.92 ± 0.07 After:0.92 ± 0.07 WC (cm) Before:100.56 ± 10.15 After:100.22 ± 10.07 BF: Before:29.83 ± 6.27 After:28.71 ± 7.12	BMI (kg/m): Before:29.34 ± 3.71 After:29.26 ± 3.78 Weight (kg): Before78.43 ± 8.75 After:78.18 ± 8.97 WHR: Before:0.92 ± 0.06 After:0.92 ± 0.06 WC (cm) Before:100.05 ± 8 After:99.78 ± 8.12 BF: Before:32.4 ± 8.86 After:31.83 ± 8.36	37 diabetics	BMI (no), Weight(no), WHR (no), WC (no), BF (no)	Secondary

Abbreviation: F: female; M: male; MG: magnesium; CON: control; BMI: body mass index; WHR wait to hip ratio' WC: waist circumference; BF: body fat; T2DM: type 2 diabetes mellitus; PCOS: polycystic ovary syndrome; NAFLD: nonalcoholic fatty liver disease.

1Values are overall ranges and means ± SDs in each group.

Table 2. Risk of bias for randomized controlled trials on the effect of magnesium supplementation assessed according to the Revised Cochrane risk-of-bias tool for randomized trials (RoB 2).*

Publications	Randomization process	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall Bias
1. Yamamoto et al. (1995)	L	L	L	L	L	L
2. Cappuccio et al. (1985)	L	L	L	L	L	L
3. Witteman et al. (1994)	S	L	L	L	L	S
4. Itoh, Kawasaka, and Nakamura (1997)	L	L	S	L	L	S
5. Brilla et al. (2003)	L	S	L	L	H	H
6. Rodríguez-Morán and Guerrero-Romero (2003)	L	S	L	L	L	S
7. Guerrero-Romero et al. (2004)	L	L	L	L	L	L
8. Pokan et al. (2006)	S	L	L	L	S	H
9. Guerrero-romero et al. (2009)	L	L	L	L	L	L
10. Day et al. (2010)	S	L	S	L	L	H
11. Hadjistavri et al. (2010)	S	L	L	L	L	S
12. Guerrero-Romero, Bermudez-Pena, and Rodriguez-Moran (2011)	L	S	L	L	L	S
13. Mooren et al. (2011)	L	L	S	L	L	S
14. Moslehi et al. (2012)	L	L	S	L	S	H
15. Simental-Mendia et al. (2012)	L	L	L	L	L	L
16. Moslehi et al. (2013)	L	L	L	L	L	L
17. Karandish et al. (2013)	S	L	L	L	L	S
18. Solati et al. (2014)	L	L	S	L	L	S
19. Navarrete-Cortes et al. (2014)	S	L	L	L	L	S
20. Simental-mendia, Rodríguez-Morán, and Guerrero-Romero (2014)	L	L	L	L	L	L
21. Rodriguez-moran and Guerrero-Romero (2014)	S	L	L	L	L	S
22. Guerrero-Romero et al. (2015)	L	L	L	L	L	L
23. Rajizadeh et al. (2017)	L	L	L	L	L	L
24. Razzaghi et al. (2018)	L	L	L	L	L	L
25. Toprak et al. (2017)	L	L	S	L	L	S
26. Ramirez et al. (2017)	L	L	L	L	L	L
27. Rodriguez-moran et al. (2018)	L	L	L	L	L	L
28. Farsinejad-marj et al. (2020)	L	L	L	L	L	L
29. Sadeghian et al. (2020)	S	L	L	L	L	S
30. Solati et al. (2019)	L	L	L	L	L	L
31. Talari et al. (2019)	L	L	L	L	L	L
32. Rashvand, Mobasseri, and Tarighat-Esfanjani (2019)	L	L	L	L	L	L

*L, Low risk of bias; H, High risk of bias; S, Some concerns.

supplementation (Farsinejad-Marj et al. 2020; Guerrero-Romero and Rodríguez-Morán 2011; Karandish et al. 2013; Toprak et al. 2017), while other did not provide any beneficial (Day et al. 2010; Guerrero-Romero and Rodriguez-Moran 2009; Guerrero-Romero et al. 2015; Guerrero-Romero et al. 2004; Hadjistavri et al. 2010; Mooren et al. 2011; Navarrete-Cortes et al. 2014; Rajizadeh et al. 2017; Razzaghi et al. 2018; Rodríguez-Moran and Guerrero-Romero 2014; Rodríguez-Morán et al. 2018; Rodríguez-Ramírez et al. 2017; Sadeghian et al. 2020; Simental-Mendía, Rodríguez-Morán, and Guerrero-Romero 2014; Solati et al. 2019; Solati et al. 2014; Talari et al. 2019; Yamamoto et al. 1995). Combining effect sizes showed that magnesium supplementation could result in lower BMI (MD: −0.21 kg/m^2, 95% CI: −0.41, −0.001, $p = 0.048$) (I^2 = 89.5%, $p < 0.001$) compared to control group (Figure 2).

Subgroup analysis. Health status, sample size, baseline serum magnesium were potential sources of heterogeneity. The effect of magnesium on BMI was significant in studies that had duration ≤12 week ($P < 0.001$), higher sample size (≥50) ($P < 0.001$), and conducted on participants suffering from insulin resistance related disorders ($P < 0.001$) (Table 3).A greater reduction in BMI was observed in studies that used magnesium in dosage ≥350 mg/d ($P < 0.001$), included participants with low level of baseline magnesium (<2 mg/dl) ($P < 0.001$) and obesity (BMI ≥ 30) ($P < 0.001$) (Table 3).

Furthermore, the sensitivity analysis showed that no individual study made an excessive contribution to the overall effect size (Supplementary material, Figure 1). The possibility of publication bias was refuted by both symmetric funnel plot (Supplementary material, Figure 2) and result of Egger's regression test ($P = 0.836$). Meta-regression analysis suggested no influence of supplementation dosage ($P = 0.46$) (Supplementary material, Figure 3A), study duration ($P = 0.30$) (Supplementary material, Figure 3B) or baseline values of BMI ($P = 0.12$) (Supplementary material, Figure 3C) on the effects of magnesium supplementation on BMI.

Body weight

Fourteen studies with sixteen arms, including a total of 976 participants (case = 510, and control = 466) reported body weight as an outcome measure. Magnesium supplementation reduced body weight in some studies (Brilla et al. 2003; Karandish et al. 2013), whereas others did not report any effect (Cappuccio et al. 1985; Day et al. 2010; Farsinejad-Marj et al. 2020; Itoh, Kawasaka, and Nakamura 1997;

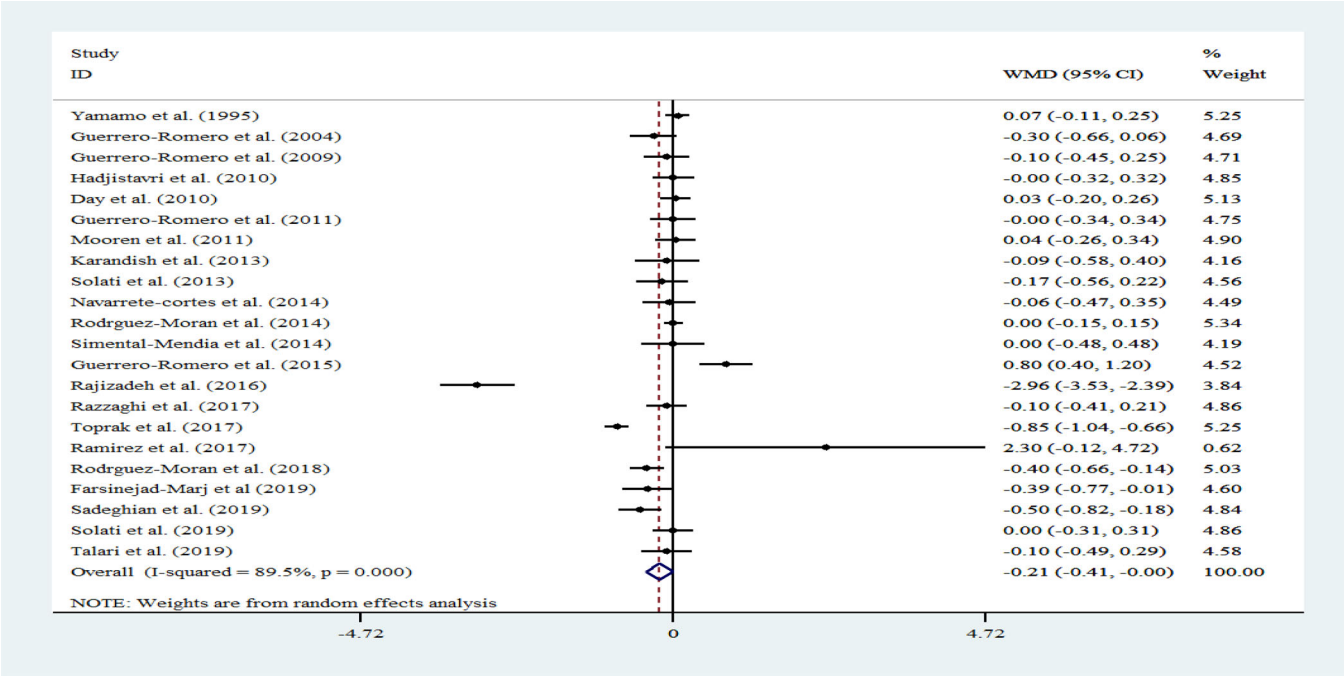

Figure 2. Forest plot showing the effects of magnesium supplementation on BMI (WMDs and 95% CIs) in adults using the random effects model.CI, confidence interval; BMI, body mass index; WMD, weighted mean difference.

Pokan et al. 2006; Rashvand, Mobasseri, and Tarighat-Esfanjani 2019; Razzaghi et al. 2018; Rodríguez-Morán and Guerrero-Romero 2003; Sadeghian et al. 2020; Simental-Mendía, Rodríguez-Morán, and Guerrero-Romero 2014; Talari et al. 2019; Witteman et al. 1994). Combining results showed that magnesium supplementation had no effect on body weight compared to control group (MD: 0.20 kg, 95% CI: −0.28, 0.67, $p = 0.418$) (I^2 = 84.9%, $P < 0.001$) (Figure 3).

Subgroup analysis. Duration, health status, sample size were potential sources of heterogeneity. The effect of interest was significant in studies that included lower dosage of magnesium (<350 mg/d.; $P < 0.001$), female ($P < 0.001$), patients with insulin resistance related disorders ($P < 0.001$), hypertension ($P = 0.022$) and coronary artery disease ($P = 0.010$), higher sample size ($N > 50$) ($P < 0.001$) (Table 3). Magnesium supplementation had more beneficial effects in studies with lower duration (≤12 wk) ($P < 0.001$) (Table 3). We could not perform subgroup analysis based on baseline serum BMI and serum magnesium due to insufficient data in some studies.

Sensitivity analysis (Supplementary material, Figure 4) showed that the study by Mendia et al. (Simental-Mendía et al. 2012) was outside the average confidence interval of meta-analysis as the reduction of body weight was more noticeable in the placebo group than that of intervention group. Although removing that study and repeating the analysis did not change the results significantly (MD: −0.06 kg, 95% CI: −0.41, 0.29, $p = 0.739$) (I^2 = 70%, $P < 0.001$). The findings of subgroup analysis remained unchanged after removing this study. Both visual inspection of the funnel plot (Supplementary material, Figure 5) and results of Egger's test ($P = 0.018$) were evident of publication bias. Therefore, we conducted the trim and fill test to correct for this issue; the nonsignificant effect of magnesium on weight turned out to be marginal (MD: −0.47 kg, 95% CI: −0.96, 0.014, $p = 0.057$) and seven additional studies were recommended to add.

Meta-regression analysis suggested no influence of supplementation dosage ($P = 0.48$) (Supplementary material, Figure 6A), study duration ($P = 0.61$) (Supplementary material, Figure 6B) or baseline values of weight ($P = 0.37$) (Supplementary material, Figure 6C) on the effects of magnesium supplementation on weight.

Waist circumference (WC)

Eleven studies including a total of 870 participants (case = 434, and control =436) reported the effect of magnesium consumption on WC. Three studies suggested the protective effect of magnesium supplementation against high WC (Guerrero-Romero et al. 2015; Rodríguez-Ramírez et al. 2017; Toprak et al. 2017), while others failed to detect any association (Farsinejad-Marj et al. 2020; Guerrero-Romero and Rodríguez-Morán 2011; Navarrete-Cortes et al. 2014; Rashvand, Mobasseri, and Tarighat-Esfanjani 2019; Rodríguez-Moran and Guerrero-Romero 2014; Rodríguez-Morán et al. 2018; Simental-Mendía, Rodríguez-Morán, and Guerrero-Romero 2014; Simental-Mendía et al. 2012). Magnesium supplementation did not show any influence on WC (MD: −0.52 cm, 95% CI: −1.69, 0.65, $p = 0.382$) (I^2 = 86.5%, $p < 0.001$) (Figure 4).

Subgroup analysis. Magnesium dosage, baseline serum magnesium and health status were potential sources of heterogeneity. The effect of magnesium supplementation on WC was significant in studies with lower duration (≤12 wk),

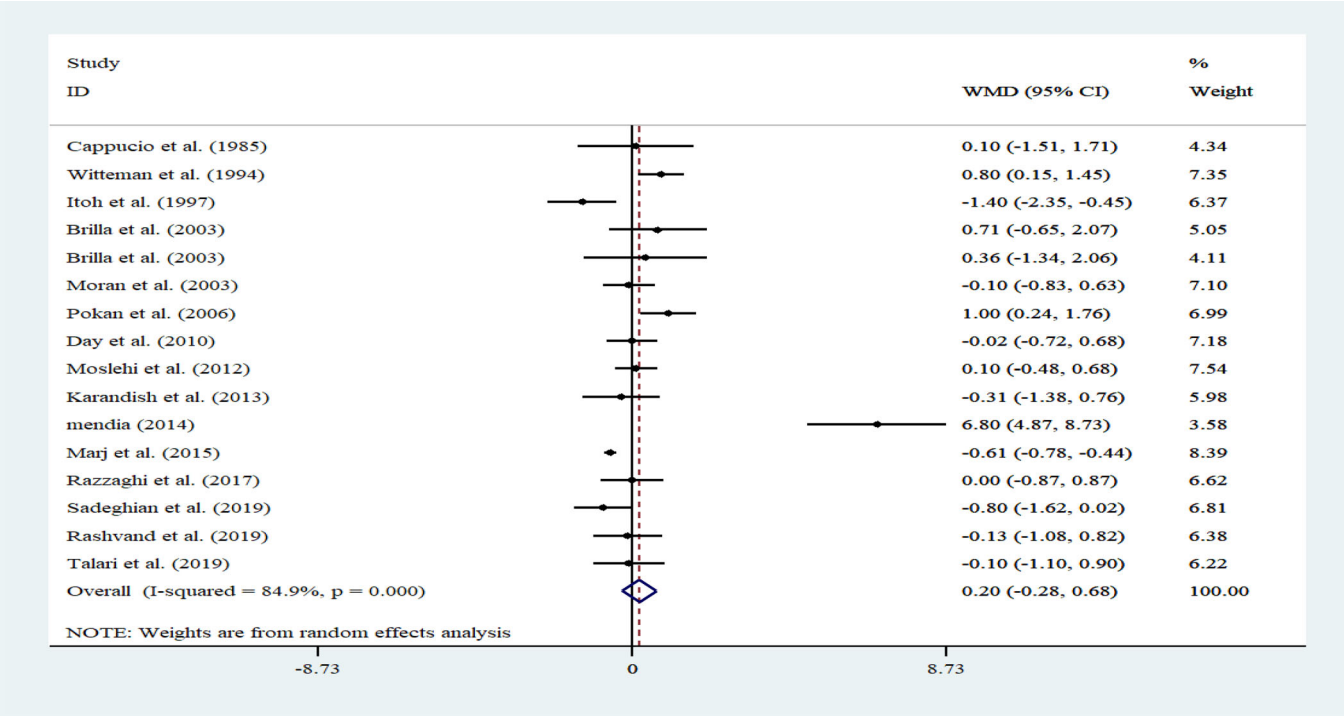

Figure 3. Forest plot showing the effects of magnesium supplementation on body weight (WMDs and 95% CIs) in adults using the random effects model.CI, confidence interval; WMD, weighted mean difference.

higher sample size and those conducted on patients with insulin resistance related disorders (P < 0.001) and hypertension (P = 0.03) (Table 3). Magnesium supplementation had more beneficial effects in studies conducted on individuals with magnesium deficiency (<2mg/dl), and obesity (BMI ≥ 25 kg/m2) and those who were on high dosage of magnesium (≥350 mg/dl) ($P < 0.001$) (Table 3).

In addition, sensitivity analysis showed that none of the studies contributed a high effect on the forest plot for WC (Supplementary material, Figure 7). No evidence for publication bias was detected due to symmetric funnel plot (Supplementary material, Figure 8) and non-significant Egger's test ($P = 0.569$). Meta-regression analysis suggested no influence of supplementation dosage ($P = 0.29$) (Supplementary material, Figure 9A), study duration ($P = 0.43$) (Supplementary material, Figure 9B) or baseline values of WC ($P = 0.33$) (Supplementary material, Figure 9C) on the effects of magnesium supplementation on WC.

Body fat and waist to hip ratio (WHR)

Two studies reported a significant increase in body fat following magnesium supplementation (Karandish et al. 2013; Moslehi et al. 2013), whereas two others did not find any effect (Rashvand, Mobasseri, and Tarighat-Esfanjani 2019; Simental-Mendía et al. 2012). Upon pooling effect sizes no significant changes in body fat were found (WMD: −0.21%, 95% CI: −1.20, 0.77, $P = 0.67$) (I^2=62.5%, P = 0.046). In addition, four available studies investigating the effect of magnesium supplementation on WHR did not find significant effects, compared to a placebo (Guerrero-Romero et al. 2004; Hadjistavri et al. 2010; Rashvand, Mobasseri, and Tarighat-Esfanjani 2019; Rodríguez-Morán and Guerrero-Romero 2003). Our meta-analysis also did not show a significant reduction in WHTR after intake of magnesium supplements compared to a placebo (WMD: 0.001, 95% CI: −0.009, 0.009, $P = 0.984$) (I^2=0.0%, P = 0.998).

Non-linear dose-responses findings

We failed to show nonlinear dose-response effect of magnesium on BMI (P-nonlinearity = 0.36) (Figure 5A), body weight (P-nonlinearity = 0.35) (Figure 5B) as well as WC (P-nonlinearity = 0.30) (Figure 5C). Duration of magnesium consumption was shown to have not a significant non-linear relationship with body weight (P-nonlinearity = 0.07) (Figure 6B), and WC (P-nonlinearity = 0.53) (Figure 6C). A significant association between duration of treatment and BMI (P-nonlinearity = 0.02) (Figure 6A) was observed.

Discussion

The present study was conducted to quantify the extent to which magnesium supplementation could affect BW-related indices in adults. A significant reduction in BMI was observed following magnesium supplementation. However, we could not find any beneficial effect of magnesium supplementation on body weight, WC, WHR and FM.

The present study showed that magnesium supplementation decreased BMI. In line with our finding, a cross-sectional study involving 11,686 middle-aged and older American women found an inverse association between dietary magnesium intake and BMI (Song et al. 2005). Obesity can lead to development of several chronic diseases such as metabolic syndrome, type 2 diabetes, hypertension, and

Table 3. Pooled estimates of effects of magnesium on anthropometric indices in adults in different subgroups.

	Number of trials			WMD (95% CI)			*P* value			P-heterogeneity			I^2 (%)		
	weight	BMI	WC	weight	BMI	WC	weight	BMI	WC	weight	BMI	WC	weight	BMI	WC
Total	16	22	11	0.20 (−0.28, 0.68)	−0.20 (−0.40, −0.001)	−0.52 (−1.69, 0.65)	0.544	0.048	0.382	0.002	<0.001	<0.001	58.6	71.3	86.5
Mg dose															
< 350 mg/d	9	12	3	−0.43 (−0.58, −0.28)	−0.14 (−0.23, −0.05)	−0.89 (−1.27, −0.52)	<0.001	0.001	<0.001	0.001	<0.001	0.357	72	90.2	2.9
≥ 350 mg/d	7	10	8	0.29 (−0.08, 0.66)	−0.20 (−0.29, −0.11)	−1.18 (−1.78, −0.58)	0.121	<0.001	<0.001	<0.001	<0.001	<0.001	88	89.6	90.2
Baseline BMI															
Normal (<30 kg/m^2)	–	14	6	–	−0.14 (−0.22, −0.06)	−0.77 (−1.12, −0.42)	–	<0.001	<0.001	–	<0.001	0.112	–	88.4	43.9
Obese (≥30 kg/m^2)	–	7	5	–	−0.35 (−0.47, −0.23)	−1.98 (−2.75, −1.21)	–	<0.001	<0.001	–	<0.001	<0.001	–	91.6	93
Health status															
Insulin resistance − related disorders	8	13	7	−0.44 (−0.78, −0.09)	−0.28 (−0.37, −0.19)	−1.07 (−1.41, −0.72)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	88	94.6	90.7
Healthy	5	5	2	−0.11 (−0.49, 0.26)	0.01 (−0.09, 0.12)	−0.09 (−1.26, 1.06)	0.55	0.839	0.867	0.057	<0.001	0.736	57	84.3	0
High blood pressure	2	2	1	0.70 (−0.59, 2.00)	0.05 (−0.10, 0.21)	4.9 (0.45, 9.35)	0.022	0.515	0.031	0.429	0.48	–	0	0	–
Depression	–	1	–	–	−2.96 (−3.52, −2.39)	–	–	<0.001	–	–	0.707	–	–	0	–
Metabolic syndrome	–	1	1	–	−0.40 (−0.66, −0.13)	−1.2 (−2.44, 0.04)	–	0.003	0.06	–	–	–	–	–	–
Coronary artery disease	1	–	–	1.00 (−0.70, 2.70)		–	0.01		–	–	–	–	–	–	–
Duration of treatment															
≤12 wk	12	13	6	−0.45 (−0.60, −0.31)	−0.36 (−0.45, −0.27)	−1.16 (−1.51, −0.81)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	84.9	91.2	91.1
>12 wk	4	9	5	0.47 (0.09, 0.85)	0.004 (−0.08, 0.09)	−0.003 (−0.79,0.78)	0.013	0.92	0.994	0.091	<0.001	0.024	53.6	72.2	64.3
Sample size															
<50	5	5	3	−0.33 (−0.86, 0.20)	−0.004(−0.11, 0.11)	0.16 (−1.02 ,1.35)	0.227	0.949	0.784	0.084	0.373	0.095	51	5.9	57.6
≥50	11	17	8	−0.33 (−0.47, −0.19)	−0.24 (−0.31, −0.17)	−1.06 (−1.39, −0.73)	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	89	91.3	89.3
Baseline serum magnesium															
Normal (≥ 2 mg/dl)	–	7	3	–	−0.19 (−0.33, −0.06)	−0.89 (−1.27, −0.52)	–	0.004	<0.001	–	0.34	0.357	–	11.7	2.9
Deficiency (<2 mg/dl)	–	14	8	–	−0.18 (−0.26, −0.11)	−1.18 (−1.78, −0.58)	–	<0.001	<0.001	–	<0.001	<0.001	–	93.1	90.2
gender															
men	2	–	–	0.56 (−0.007, 1.14)	–	–	0.057	–	–	0.091	–	–	64	–	–
women	4	–	–	−0.44 (−0.60, −0.29)	–	–	<0.001	–	–	<0.001	–	–	86	–	–
both	10	–	–	−0.12 (−0.45, 0.21)	–	–	0.47	–	–	<0.001	–	–	85	–	–

Abbreviation: BMI, body mass index; WC, waist circumference; WMD, weighted mean difference; CI, confidence interval.
Insulin resistance related disorders: diabetes, pre-diabetes, insulin resistance, impaired fasting glucose, poly cystic ovary syndrome, nonalcoholic fatty liver disease.

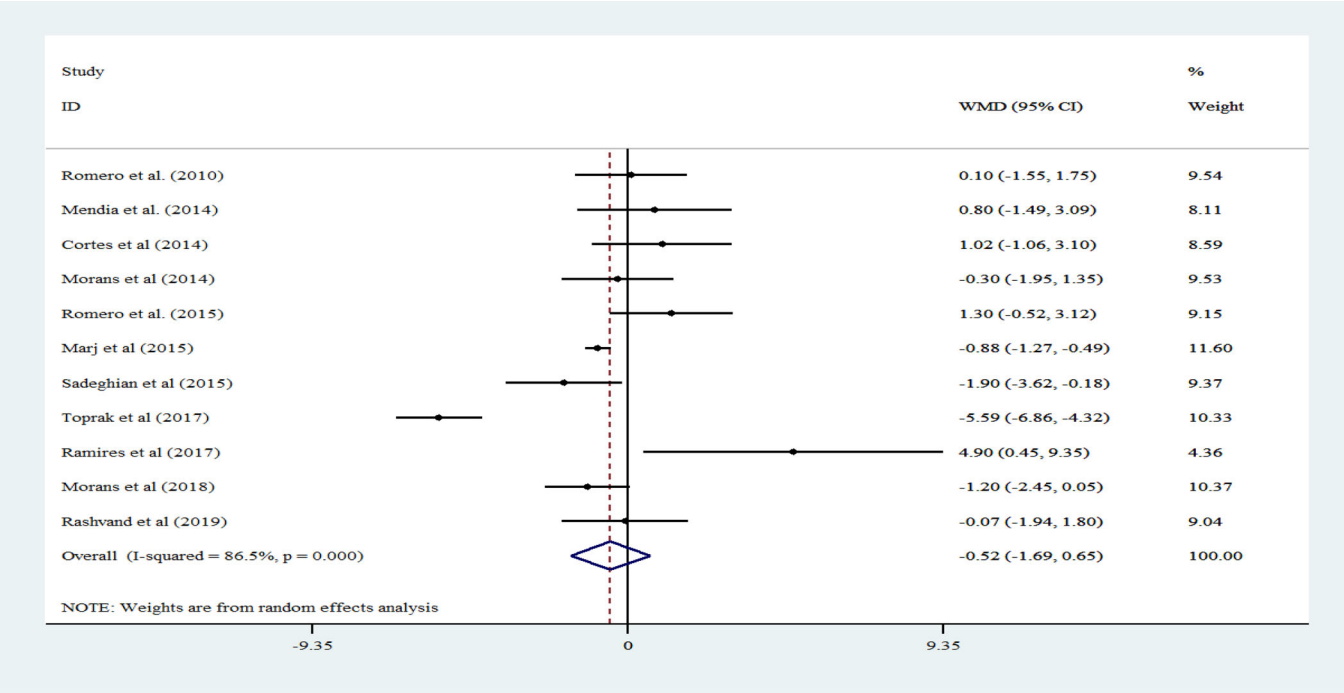

Figure 4. Forest plot showing the effects of magnesium supplementation on WC (WMDs and 95% CIs) in adults using the random effects model. CI, confidence interval; WC, waist circumference; WMD, weighted mean difference.

some types of cancer (Matsuda and Shimomura 2013). A dose-response meta-analysis of 10 observational studies indicates that each additional 150 mg/day dietary magnesium intake is associated with 12% reduction in the risk of metabolic syndrome which is one of BW-related metabolic disorders (Ju et al. 2014). An updated meta-analysis of 13 prospective cohort studies involving 536,318 participants and 24,516 cases determined a significant inverse association between dietary magnesium intake and risk of type 2 diabetes in a dose-response manner. This study showed 14% reduction in risk of diabetes per 100 mg/day increment in magnesium intake (Dong et al. 2011). High magnesium intake may have greater effects on improving insulin sensitivity in overweight individuals who are prone to insulin resistance (Song et al. 2004). The underlying assumption in these studies is that magnesium supplementation may protect against chronic conditions through reducing body weight which may have a mediator role. By contrast, Cosaro et al. (2014), Showed that 2 months Mg supplementation (368 mg/d) had no significant effect on BP, vascular function and glycolipid profile in healthy young men with family history of metabolic syndrome. These inconsistent findings may partly be due to different target population, serum magnesium status, obesity status and dose and duration of magnesium supplementation.

Subgroup analysis showed that the beneficial effect of magnesium supplementation on BMI was more pronounced among those suffered from insulin resistance-related disorders, obesity and magnesium deficiency. Previous studies have shown that type 2 diabetes, hypertension, metabolic syndrome and aging are conditions frequently associated with magnesium deficiency (Barbagallo and Dominguez 2007; Barbagallo et al. 2003; Barbagallo et al. 2000). In addition, some studies showed higher prevalence of magnesium deficiency among the obese which may be due to lower dietary intake of magnesium (Agarwal et al. 2015), decreased absorption or increased excretion of magnesium (Jose et al. 2012).

Magnesium supplementation did not affect body weight, WC, FM, WHR in the current study. More recently, one meta-analysis showed that magnesium supplementation did not affect body weight, BMI, and waist circumference among T2DM (Asbaghi et al. 2020). Because only studies conducted on diabetic persons have been included in this meta-analysis, a considerable large number of studies that have examined the effect of magnesium supplementation on obesity measures in other health groups have not been included. Furthermore, this study has not assessed the dose-response association between magnesium supplementation and obesity measures.

However, subgroup analysis showed that the effect of magnesium supplementation on body weight and WC was significant in studies conducted on patients with insulin resistance related disorders and hypertension. The fact that mentioned disorders are associated with magnesium deficiency (Barbagallo, Dominguez, and Resnick 2007; Rude 1992) may partly explain and justify this observation. Findings from some meta-analyses also showed that supplementation with magnesium significantly improved body weight-related chronic conditions such as hypertension, high fasting glucose and insulin in humans (Veronese et al. 2016; Zhang et al. 2016). The underlying hypothesis in these studies is that magnesium supplementation may influence body weight and WC, thereby improving obesity-related metabolic disturbances.

Subgroup analysis also showed that magnesium supplementation could reduce body weight in women. There is evidence that women tend to have lower blood magnesium

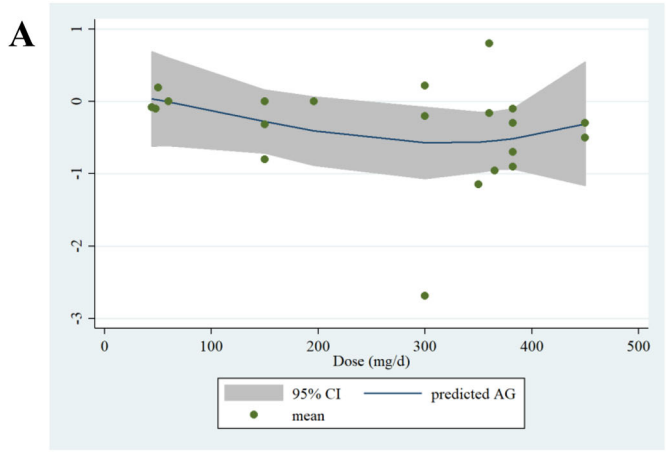

Figure 5. Non-linear dose-responses between dose of magnesium supplementation and unstandardized mean differences on BMI (A), body weight (B), WC (C) in adults. CI, confidence interval; BMI, body mass index; WC, waist circumference.

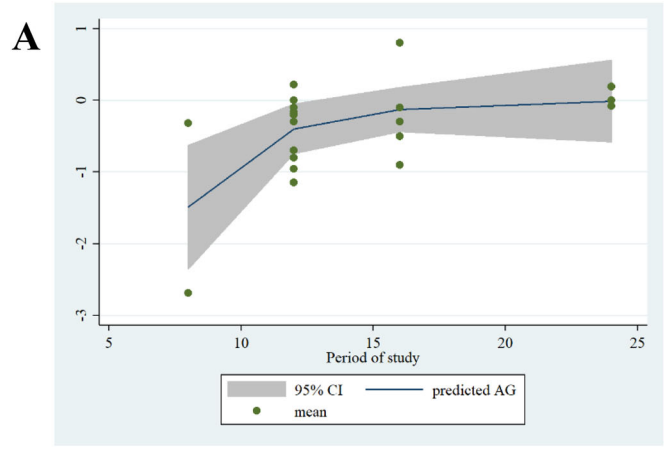

Figure 6. Non-linear dose-responses between duration of magnesium supplementation and unstandardized mean differences on BMI (A), body weight (B), WC (C) in adults. CI, confidence interval; BMI, body mass index; WC, waist circumference.

concentrations than men due to differences in body composition, such as muscle mass which has high magnesium content in body (Ryschon et al. 1996).

Although subgroup analysis showed significant effect of magnesium supplementation on WC in those with low serum magnesium and baseline obesity (as also shown for BMI). However, due to insufficient number of studies, we could not conduct subgroup analysis based on these factors for body weight. In agreement with this finding, the study by Castellanos-Gutiérrez et al. showed an inverse association between dietary magnesium intake and high WC only in those Mexican who had high weight (Castellanos-Gutiérrez et al. 2018).

Only 4 studies were focused on BF percentage which provided null effect after being combined and averaged. However, we are aware of animal experiments that shows magnesium supplementation can prevent accumulation of

fat in the adipose tissue (Devaux et al. 2016). It seems we still need more study to be able to draw a frim conclusion regarding BF percentage.

Magnesium is involved in energy metabolism since intracellular adenosine triphosphate (ATP) is in the form of ATP-Mg (Morais et al. 2017) and may influence insulin secretion by interacting with cellular calcium homeostasis. Thus, magnesium is involved in the physiological pathways that regulate macronutrients metabolism (Mooren 2015). Magnesium may have an anti-obesity effect because of its capability of forming soaps with fatty acids in the intestine and thus reducing absorption of fat from the diet (Shamnani et al. 2018).

This is the first systematic review and meta-analysis to investigate the effect of magnesium supplementation on obesity measures on all health conditions. All entered studies were placebo-controlled RCTs. Low evidence for the presence of publication bias was found for WC and BMI. Most of the included studies were of high quality according to ROB2 (Sterne et al. 2019a). Although participants in the included studies had a diverse set of health conditions or baseline levels of magnesium, we were able to address this issue by performing subgroups analysis based on health status and baseline serum magnesium level.

However, limitations cannot be neglected. First, one potential limitation is the lack of data on dietary intake of magnesium. In this regard, in the western world daily magnesium intake is often below the recommended daily allowances (Walti et al. 2002). Second, some of the pooled effect sizes were of high between-study heterogeneity, increasing concern with validity of findings.

The evidence we reviewed showed that less attention has been laid on accurate measure of obesity such as BF percentage. Moreover, the effects of different forms of magnesium supplements was not adequately examined and further investigations are warranted to address questions specific to efficacy, bioavailability, and complete metabolite profiles.

Conclusion

In conclusion, magnesium supplementation may have a favorable effect on BMI, but not on body weight, WC, BF percentage, and WHR as compared to controls. Subgroup analyses indicated that baseline BMI and serum magnesium level, prevalent insulin resistance-related disorders, dose and duration could be contributing factors for favorable effects. Because subgroup analysis revealed greater efficacy of magnesium supplementation in studies that included participants with several risk factors of metabolic disorders, prospective studies are warranted in participants with specific condition to ascertain these findings.

Disclosure statement

The authors declare that they have no conflict of interest.

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Authors contribution

MDM, MA, HM designed the study. MA and AJ independently carried out the literature search and screening of articles; MDM analyzed the data and MDM and HM contributed to interpration the data. MDM, MGH, HM and MA wrote the manuscript and HM helped edit the writing MDM supervised the study. All authors read and approved the final manuscript.

References

Agarwal, S., C. Reider, J. R. Brooks, and V. L. Fulgoni. III, 2015. Comparison of prevalence of inadequate nutrient intake based on body weight status of adults in the United States: An analysis of NHANES 2001–2008. *Journal of the American College of Nutrition* 34 (2):126–34. doi: 10.1080/07315724.2014.901196.

Asbaghi, O., R. Hosseini, B. Boozari, E. Ghaedi, S. Kashkooli, and S. Moradi. 2020. The effects of magnesium supplementation on blood pressure and obesity measure among type 2 diabetes patient: A systematic review and meta-analysis of randomized controlled trials. *Biological Trace Element Research*. https://doi.org/10.1007/s12011-020-02157-0.

Barbagallo, M., and L. J. Dominguez. 2007. Magnesium metabolism in type 2 diabetes mellitus, metabolic syndrome and insulin resistance. *Archives of Biochemistry and Biophysics* 458 (1):40–7. doi: 10.1016/j.abb.2006.05.007.

Barbagallo, M., L. J. Dominguez, A. Galioto, A. Ferlisi, C. Cani, L. Malfa, A. Pineo, A. Busardo', and G. Paolisso. 2003. Role of magnesium in insulin action, diabetes and cardio-metabolic syndrome X. *Molecular Aspects of Medicine* 24 (1-3):39–52. doi: 10.1016/S0098-2997(02)00090-0.

Barbagallo, M., L. J. Dominguez, and L. M. Resnick. 2007. Magnesium metabolism in hypertension and type 2 diabetes mellitus. *American Journal of Therapeutics* 14 (4):375–85. doi: 10.1097/01.mjt.0000209676.91582.46.

Barbagallo, M., R. K. Gupta, L. J. Dominguez, and L. M. Resnick. 2000. Cellular ionic alterations with age: Relation to hypertension and diabetes. *Journal of the American Geriatrics Society* 48 (9):1111–6. doi: 10.1111/j.1532-5415.2000.tb04788.x.

Borenstein, M., L. V. Hedges, J. P. Higgins, and H. R. Rothstein. 2011. *Introduction to meta-analysis*. West Sussex, UK: John Wiley & Sons.

Brilla, L., M. Giroux, A. Taylor, and K. Knutzen. 2003. Magnesium-creatine supplementation effects on body water. *Metabolism* 52 (9):1136–40. doi: 10.1016/S0026-0495(03)00188-4.

Cappuccio, F., N. Markandu, G. Beynon, A. Shore, B. Sampson, and G. MacGregor. 1985. Lack of effect of oral magnesium on high blood pressure: A double blind study. *British Medical Journal (Clinical Research ed.)* 291 (6490):235–8. doi: 10.1136/bmj.291.6490.235.

Castellanos-Gutiérrez, A., T. G. Sánchez-Pimienta, A. Carriquiry, T. H. da Costa, and A. C. Ariza. 2018. Higher dietary magnesium intake is associated with lower body mass index, waist circumference and serum glucose in Mexican adults. *Nutrition Journal* 17 (1):114. doi: 10.1186/s12937-018-0422-2.

Cosaro, E., S. Bonafini, M. Montagnana, E. Danese, M. S. Trettene, P. Minuz, P. Delva, and C. Fava. 2014. Effects of magnesium supplements on blood pressure, endothelial function and metabolic parameters in healthy young men with a family history of metabolic syndrome. *Nutrition, Metabolism, and Cardiovascular Diseases : NMCD* 24 (11):1213–20. doi: 10.1016/j.numecd.2014.05.010.

Costello, R. B., R. J. Elin, A. Rosanoff, T. C. Wallace, F. Guerrero-Romero, A. Hruby, P. L. Lutsey, F. H. Nielsen, M. Rodriguez-Moran, Y. Song, et al. 2016. Perspective: The case for an evidence-based reference interval for serum magnesium: The time has

come–5. *Advances in Nutrition (Bethesda, Md.)* 7 (6):977–93., doi: 10.3945/an.116.012765.

Cruz, K. J. C., A. R. S. de Oliveira, D. P. Pinto, J. B. S. Morais, F. da Silva Lima, C. Colli, F. L. Torres-Leal, and D. do Nascimento Marreiro. 2014. Influence of magnesium on insulin resistance in obese women. *Biological Trace Element Research* 160 (3):305–10. doi: 10.1007/s12011-014-0044-2.

Day, R. O., W. Liauw, L. M. Tozer, P. McElduff, R. J. Beckett, and K. M. Williams. 2010. A double-blind, placebo-controlled study of the short term effects of a spring water supplemented with magnesium bicarbonate on acid/base balance, bone metabolism and cardiovascular risk factors in postmenopausal women. *BMC Research Notes* 3:180. doi: 10.1186/1756-0500-3-180.

Devaux, S., M. Adrian, P. Laurant, A. Berthelot, and A. Quignard-Boulangé. 2016. Dietary magnesium intake alters age-related changes in rat adipose tissue cellularity. *Magnesium Research* 29 (4):175–83. doi: 10.1684/mrh.2016.0406.

Dong, J.-Y., P. Xun, K. He, and L.-Q. Qin. 2011. Magnesium intake and risk of type 2 diabetes: Meta-analysis of prospective cohort studies. *Diabetes Care* 34 (9):2116–22. doi: 10.2337/dc11-0518.

Duval, S., and R. Tweedie. 2000. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 56 (2):455–63. doi: 10.1111/j.0006-341x.2000.00455.x.

Dwyer, J. T., D. B. Allison, and P. M. Coates. 2005. Dietary supplements in weight reduction. *Journal of the American Dietetic Association* 105 (5):80–6. doi: 10.1016/j.jada.2005.02.028.

Farsinejad-Marj, M., L. Azadbakht, F. Mardanian, P. Saneei, and A. Esmaillzadeh. 2020. Clinical and metabolic responses to magnesium supplementation in women with polycystic ovary syndrome. *Biological Trace Element Research* 196 (2):349–10. doi: 10.1007/s12011-019-01923-z.

Fatahi, S., E. Daneshzad, H. Kord-Varkaneh, N. Bellissimo, N. R. Brett, and L. Azadbakht. 2018. Impact of diets rich in whole grains and fruits and vegetables on cardiovascular risk factors in overweight and obese women: A randomized clinical feeding trial. *Journal of the American College of Nutrition* 37 (7):568–77. doi: 10.1080/07315724.2018.1444520.

Guerrero-Romero, F., C. Bermudez-Pena, and M. Rodriguez-Moran. 2011. Severe hypomagnesemia and low-grade inflammation in metabolic syndrome. *Magnesium Research* 24 (2):45–53. doi: 10.1684/mrh.2011.0281.

Guerrero-Romero, F., and M. Rodriguez-Moran. 2009. The effect of lowering blood pressure by magnesium supplementation in diabetic hypertensive adults with low serum magnesium levels: A randomized, double-blind, placebo-controlled clinical trial. *Journal of Human Hypertension* 23 (4):245–51. doi: 10.1038/jhh.2008.129.

Guerrero-Romero, F., L. Simental-Mendía, G. Hernández-Ronquillo, and M. Rodriguez-Morán. 2015. Oral magnesium supplementation improves glycaemic status in subjects with prediabetes and hypomagnesaemia: A double-blind placebo-controlled randomized trial. *Diabetes & Metabolism* 41 (3):202–7. doi: 10.1016/j.diabet.2015.03.010.

Guerrero-Romero, F., H. Tamez-Perez, G. e González-González, A. Salinas-Martinez, J. Montes-Villarreal, J. Trevino-Ortiz, and M. Rodriguez-Moran. 2004. Oral magnesium supplementation improves insulin sensitivity in non-diabetic subjects with insulin resistance. A double-blind placebo-controlled randomized trial. *Diabetes & Metabolism* 30 (3):253–8. doi: 10.1016/S1262-3636(07)70116-7.

Guerrero-Romero, F., and M. Rodríguez-Morán. 2011. Magnesium improves the beta-cell function to compensate variation of insulin sensitivity: Double-blind, randomized clinical trial. *European Journal of Clinical Investigation* 41:405–10.

Hadjistavri, L. S., P. A. Sarafidis, P. I. Georgianos, I. M. Tziolas, C. P. Aroditis, A. Hitoglou-Makedou, P. E. Zebekakis, M. I. Pikilidou, and A. N. Lasaridis. 2010. Beneficial effects of oral magnesium supplementation on insulin sensitivity and serum lipid profile. *Medical Science Monitor* 16:CR0–CR0.

Hassabou, N. F., and A. F. Farag. 2020. Anticancer effects induced by artichoke extract in oral squamous carcinoma cell lines. *Journal of the Egyptian National Cancer Institute* 32 (1):1–10. doi: 10.1186/s43046-020-00026-4.

He, K., K. Liu, M. L. Daviglus, S. J. Morris, C. M. Loria, L. Van Horn, D. R. Jacobs, Jr, and P. J. Savage. 2006a. Magnesium intake and incidence of metabolic syndrome among young adults. *Circulation* 113 (13):1675–82. doi: 10.1161/CIRCULATIONAHA.105.588327.

He, K., Y. Song, R. J. Belin, and Y. Chen. 2006b. Magnesium intake and the metabolic syndrome: Epidemiologic evidence to date. *Journal of the Cardiometabolic Syndrome* 1 (5):351–5. doi: 10.1111/j.1559-4564.2006.05702.x.

Huerta, M. G., J. N. Roemmich, M. L. Kington, V. E. Bovbjerg, A. L. Weltman, V. F. Holmes, J. T. Patrie, A. D. Rogol, and J. L. Nadler. 2005. Magnesium deficiency is associated with insulin resistance in obese children. *Diabetes Care* 28 (5):1175–81. doi: 10.2337/diacare.28.5.1175.

Inoue, I. 2005. [Lipid metabolism and magnesium]. *Clinical Calcium* 15 (11):65–76.

Itoh, K., T. Kawasaka, and M. Nakamura. 1997. The effects of high oral magnesium supplementation on blood pressure, serum lipids and related variables in apparently healthy Japanese subjects. *The British Journal of Nutrition* 78 (5):737–50. doi: 10.1079/BJN19970191.

Jose, B., V. Jain, N. K. Vikram, A. Agarwala, and S. Saini. 2012. Serum magnesium in overweight children. *Indian Pediatrics* 49 (2):109–12. doi: 10.1007/s13312-012-0024-6.

Ju, S.-Y., W.-S. Choi, S.-M. Ock, C.-M. Kim, and D.-H. Kim. 2014. Dietary magnesium intake and metabolic syndrome in the adult population: Dose-response meta-analysis and meta-regression. *Nutrients* 6 (12):6005–19. doi: 10.3390/nu6126005.

Karandish, M., M. Tamimi, A. A. Shayesteh, M. H. Haghighizadeh, and M. T. Jalali. 2013. The effect of magnesium supplementation and weight loss on liver enzymes in patients with nonalcoholic fatty liver disease. *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences* 18:573.

Kerkhoffs, G. M., E. Servien, W. Dunn, D. Dahm, J. A. Bramer, and D. Haverkamp. 2012. The influence of obesity on the complication rate and outcome of total knee arthroplasty: A meta-analysis and systematic literature review. *The Journal of Bone and Joint Surgery. American Volume* 94 (20):1839–44. doi: 10.2106/JBJS.K.00820.

Lu, L.,. C. Chen, K. Yang, J. Zhu, P. Xun, J. M. Shikany, and K. He. 2020. Magnesium intake is inversely associated with risk of obesity in a 30-year prospective follow-up study among American young adults. *European Journal of Nutrition*:1–9. https://doi.org/10.1007/s00394-020-02206-3.

Matsuda, M., and I. Shimomura. 2013. Increased oxidative stress in obesity: Implications for metabolic syndrome, diabetes, hypertension, dyslipidemia, atherosclerosis, and cancer. *Obesity Research & Clinical Practice* 7 (5):e330–e341. doi: 10.1016/j.orcp.2013.05.004.

Moher, D., A. Liberati, J. Tetzlaff, and D. G. Altman. 2009. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Annals of Internal Medicine* 151 (4):264–9. doi: 10.7326/0003-4819-151-4-200908180-00135.

Mooren, F., K. Krüger, K. Völker, S. Golf, M. Wadepuhl, and A. Kraus. 2011. Oral magnesium supplementation reduces insulin resistance in non-diabetic subjects–a double-blind, placebo-controlled, randomized trial. *Diabetes, Obesity & Metabolism* 13 (3):281–4. doi: 10.1111/j.1463-1326.2010.01332.x.

Mooren, F. C. 2015. Magnesium and disturbances in carbohydrate metabolism. *Diabetes, Obesity & Metabolism* 17 (9):813–23. doi: 10.1111/dom.12492.

Morais, J. B. S., J. S. Severo, L. R. Dos Santos, S. R. de Sousa Melo, R. de Oliveira Santos, A. R. S. de Oliveira, K. J. C. Cruz, and D. do Nascimento Marreiro. 2017. Role of magnesium in oxidative stress in individuals with obesity. *Biological Trace Element Research* 176 (1):20–6. doi: 10.1007/s12011-016-0793-1.

Moslehi, N., M. Vafa, A. Rahimi-Foroushani, and B. Golestan. 2012. Effects of oral magnesium supplementation on inflammatory markers in middle-aged overweight women. *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences* 17:607.

Moslehi, N., M. Vafa, J. Sarrafzadeh, and A. Rahimi-Foroushani. 2013. Does magnesium supplementation improve body composition and muscle strength in middle-aged overweight women? A double-blind, placebo-controlled, randomized clinical trial. *Biological Trace Element Research* 153 (1-3):111–8. doi: 10.1007/s12011-013-9672-1.

Navarrete-Cortes, A., J. L. Ble-Castillo, F. Guerrero-Romero, R. Cordova-Uscanga, I. E. Juárez-Rojop, H. Aguilar-Mariscal, C. A. Tovilla-Zarate, and M. del Rocio Lopez-Guevara. 2014. No effect of magnesium supplementation on metabolic control and insulin sensitivity in type 2 diabetic patients with normomagnesemia. *Magnesium Research* 27 (2):48–56. doi: 10.1684/mrh.2014.0361.

Niranjan, G., D. Anitha, A. Srinivasan, V. K. Velu, C. Venkatesh, M. S. Babu, R. Ramesh, and S. Saha. 2014. Association of inflammatory sialoproteins, lipid peroxides and serum magnesium levels with cardiometabolic risk factors in obese children of South Indian population. *International Journal of Biomedical Science: IJBS* 10:118.

Pi-Sunyer, X. 2009. The medical risks of obesity. *Postgraduate Medicine* 121 (6):21–33. doi: 10.3810/pgm.2009.11.2074.

Pokan, R., P. Hofmann, S. P. von Duvillard, G. Smekal, M. Wonisch, K. Lettner, P. Schmid, M. Shechter, B. Silver, and N. Bachl. 2006. Oral magnesium therapy, exercise heart rate, exercise tolerance, and myocardial function in coronary artery disease patients. *British Journal of Sports Medicine* 40 (9):773–8. doi: 10.1136/bjsm.2006.027250.

Rajizadeh, A., H. Mozaffari-Khosravi, M. Yassini-Ardakani, and A. Dehghani. 2017. Effect of magnesium supplementation on depression status in depressed patients with magnesium deficiency: A randomized, double-blind, placebo-controlled trial. *Nutrition (Burbank, Los Angeles County, Calif.)* 35:56–60. doi: 10.1016/j.nut.2016.10.014.

Rashvand, S., M. Mobasseri, and A. Tarighat-Esfanjani. 2019. The effects of choline and magnesium co-supplementation on metabolic parameters, inflammation, and endothelial dysfunction in patients with type 2 diabetes mellitus: A randomized, double-blind, placebo-controlled trial. *Journal of the American College of Nutrition* 38 (8):714–21. doi: 10.1080/07315724.2019.1599745.

Razzaghi, R., F. Pidar, M. Momen-Heravi, F. Bahmani, H. Akbari, and Z. Asemi. 2018. Magnesium supplementation and the effects on wound healing and metabolic status in patients with diabetic foot ulcer: A randomized, double-blind, placebo-controlled trial. *Biological Trace Element Research* 181 (2):207–15. doi: 10.1007/s12011-017-1056-5.

Rodríguez-Moran, M., and F. Guerrero-Romero. 2014. Oral magnesium supplementation improves the metabolic profile of metabolically obese, normal-weight individuals: A randomized double-blind placebo-controlled trial. *Archives of Medical Research* 45 (5):388–93. doi: 10.1016/j.arcmed.2014.05.003.

Rodríguez-Morán, M., and F. Guerrero-Romero. 2003. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: A randomized double-blind controlled trial. *Diabetes Care* 26 (4):1147–52. doi: 10.2337/diacare.26.4.1147.

Rodríguez-Morán, M.,. L. E. Simental-Mendía, C. I. Gamboa-Gómez, and F. Guerrero-Romero. 2018. Oral magnesium supplementation and metabolic syndrome: A randomized double-blind placebo-controlled clinical trial. *Advances in Chronic Kidney Disease* 25 (3):261–6. doi: 10.1053/j.ackd.2018.02.011.

Rodríguez-Ramírez, M., M. Rodríguez-Morán, M. A. Reyes-Romero, and F. Guerrero-Romero. 2017. Effect of oral magnesium supplementation on the transcription of TRPM6, TRPM7, and SLC41A1 in individuals newly diagnosed of pre-hypertension. A randomized, double-blind, placebo-controlled trial. *Magnesium Research* 30 (3):80–7. doi: 10.1684/mrh.2017.0426.

Rude, R. K. 1992. Magnesium deficiency and diabetes mellitus. Causes and effects. *Postgraduate Medicine* 92 (5):217–24. doi: 10.1080/00325481.1992.11701494.

Ryan, D. H., and S. R. Yockey. 2017. Weight loss and improvement in comorbidity: Differences at 5%, 10%, 15%, and over. *Current Obesity Reports* 6 (2):187–94. doi: 10.1007/s13679-017-0262-y.

Ryschon, T. W., D. L. Rosenstein, D. R. Rubinow, J. E. Niemela, R. J. Elin, and R. S. Balaban. 1996. Relationship between skeletal muscle intracellular ionized magnesium and measurements of blood magnesium. *Journal of Laboratory and Clinical Medicine* 127 (2):207–13. doi: 10.1016/S0022-2143(96)90080-3.

Sadeghian, M., L. Azadbakht, N. Khalili, M. Mortazavi, and A. Esmaillzadeh. 2020. Oral magnesium supplementation improved lipid profile but increased insulin resistance in patients with diabetic nephropathy: A double-blind randomized controlled clinical trial. *Biological Trace Element Research* 193 (1):23–35. doi: 10.1007/s12011-019-01687-6.

Shamnani, G., C. A. Rukadikar, V. Gupta, S. Singh, S. Tiwari, S. S. Bhartiy, and P. Sharma. 2018. Serum magnesium in relation with obesity. *National Journal of Physiology, Pharmacy and Pharmacology* 8:1–1077. doi: 10.5455/njppp.2018.8.0104016022018.

Simental-Mendía, L. E., M. Rodríguez-Morán, and F. Guerrero-Romero. 2014. Oral magnesium supplementation decreases C-reactive protein levels in subjects with prediabetes and hypomagnesemia: A clinical randomized double-blind placebo-controlled trial. *Archives of Medical Research* 45 (4):325–30. doi: 10.1016/j.arcmed.2014.04.006.

Simental-Mendía, L. E., M. Rodríguez-Morán, M. A. Reyes-Romero, and F. Guerrero-Romero. 2012. No positive effect of oral magnesium supplementation in the decreases of inflammation in subjects with prediabetes: A pilot study. *Magnesium Research* 25 (3):140–6. doi: 10.1684/mrh.2012.0322.

Solati, M., L. Kazemi, N. S. Majd, M. Keshavarz, N. Pouladian, and N. Soltani. 2019. Oral herbal supplement containing magnesium sulfate improve metabolic control and insulin resistance in non-diabetic overweight patients: A randomized double blind clinical trial. *Medical Journal of the Islamic Republic Of Iran* 33:2.

Solati, M., E. Ouspid, S. Hosseini, N. Soltani, M. Keshavarz, and M. Dehghani. 2014. Oral magnesium supplementation in type II diabetic patients. *Medical Journal of the Islamic Republic Of Iran* 28:67.

Song, C., W. Choi, H. Oh, and K. Kim. 2007. Associations of serum minerals with body mass index in adult women. *European Journal of Clinical Nutrition* 61 (5):682–5. doi: 10.1038/sj.ejcn.1602568.

Song, Y., J. E. Manson, J. E. Buring, and S. Liu. 2004. Dietary magnesium intake in relation to plasma insulin levels and risk of type 2 diabetes in women. *Diabetes Care* 27 (1):59–65. doi: 10.2337/diacare.27.1.59.

Song, Y., P. M. Ridker, J. E. Manson, N. R. Cook, J. E. Buring, and S. Liu. 2005. Magnesium intake, C-reactive protein, and the prevalence of metabolic syndrome in middle-aged and older US women. *Diabetes Care* 28 (6):1438–44. doi: 10.2337/diacare.28.6.1438.

Sterne, J. A. C, J. Savović, M. J. Page, R. G. Elbers, N. S. Blencowe, I. Boutron, C. J. Cates, H.-Y. Cheng, M. S. Corbett, and S. M. Eldridge. 2019a. RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ* 366:l4898.

Sterne, J. A. C., J. Savović, M. J. Page, R. G. Elbers, N. S. Blencowe, I. Boutron, C. J. Cates, H.-Y. Cheng, M. S. Corbett, S. M. Eldridge, et al. 2019b. RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ (Clinical Research ed.)* 366:l4898. doi: 10.1136/bmj.l4898.

Talari, H. R., M. Zakizade, A. Soleimani, F. Bahmani, A. Ghaderi, N. Mirhosseini, M. Eslahi, M. Babadi, M. A. Mansournia, and Z. Asemi. 2019. Effects of magnesium supplementation on carotid intima-media thickness and metabolic profiles in diabetic haemodialysis patients: a randomised, double-blind, placebo-controlled trial. *British Journal of Nutrition* 121 (7):809–17. doi: 10.1017/S0007114519000163.

Thompson, S. G., and S. J. Sharp. 1999. Explaining heterogeneity in meta-analysis: A comparison of methods. *Statistics in Medicine* 18 (20):2693–708. doi: 10.1002/(SICI)1097-0258(19991030)18:20<2693::AID-SIM235>3.0.CO;2-V.

Toprak, O., H. Kurt, Y. Sarı, C. Şarkış, H. Us, and A. Kırık. 2017. Magnesium replacement improves the metabolic profile in obese and pre-diabetic patients with mild-to-moderate chronic kidney disease: A 3-month, randomised, double-blind, placebo-controlled study. *Kidney and Blood Pressure Research* 42 (1):33–42. doi: 10.1159/000468530.

Veronese, N., S. Watutantrige-Fernando, C. Luchini, M. Solmi, G. Sartore, G. Sergi, E. Manzato, M. Barbagallo, S. Maggi, and B. Stubbs. 2016. Effect of magnesium supplementation on glucose metabolism in people with or at risk of diabetes: A systematic review and meta-analysis of double-blind randomized controlled trials. *European Journal of Clinical Nutrition* 70 (12):1354–9. doi: 10.1038/ejcn.2016.154.

Walti, M., M. Zimmermann, G. Spinas, S. Jacob, and R. Hurrell. 2002. Dietary magnesium intake in type 2 diabetes. *European Journal of Clinical Nutrition* 56 (5):409–14. doi: 10.1038/sj.ejcn.1601327.

Witteman, J., D. E. Grobbee, F. Derkx, R. Bouillon, A. M. de Bruijn, and A. Hofman. 1994. Reduction of blood pressure with oral magnesium supplementation in women with mild to moderate hypertension. *The American Journal of Clinical Nutrition* 60 (1): 129–35. doi: 10.1093/ajcn/60.1.129.

Yamamoto, M. E., W. B. Applegate, M. J. Klag, N. O. Borhani, J. D. Cohen, K. A. Kirchner, E. Lakatos, F. M. Sacks, J. O. Taylor, and C. H. Hennekens. 1995. Lack of blood pressure effect with calcium and magnesium supplementation in adults with high-normal blood pressure: Results from phase I of the Trials of Hypertension Prevention (TOHP). *Annals of Epidemiology* 5 (2):96–107. doi: 10.1016/1047-2797(94)00054-W.

Zhang, X., Y. Li, L. C. Del Gobbo, A. Rosanoff, J. Wang, W. Zhang, and Y. Song. 2016. Effects of magnesium supplementation on blood pressure: A meta-analysis of randomized double-blind placebo-controlled trials. *Hypertension* 68 (2):324–33. doi: 10.1161/HYPERTENSIONAHA.116.07664.