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# Impact of Magnesium Supplementation on Blood Pressure: An Umbrella Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

*Background and aim:* Conflicting results on the effect of magnesium supplementation on blood pressure have been published in previous meta-analyses; hence, we conducted this umbrella meta-analysis of RCTs to provide a more robust conclusion on its effects.
*Methods:* Four databases including PubMed, Scopus, EMBASE, and Web of Science were searched to find pertinent papers published on international scientific from inception up to July 15, 2024. We utilized STATA version 17.0 to carry out all statistical analyses (Stata Corporation, College Station, TX, US). The random effects model was used to calculate the overall effect size ES and CI.
*Findings:* Ten eligible review papers with 8610 participants studied the influence of magnesium on SBP and DBP. The pooling of their effect sizes resulted in a significant reduction of SBP (ES = -1.25 mmHg; 95% CI: -1.98, -0.51, $P = 0.001$) and DBP (ES = -1.40 mmHg; 95% CI: -2.04, -0.75, $P = 0.000$) by magnesium supplementation. In subgroup analysis, a significant reduction in SBP and DBP was observed in magnesium intervention with dosage ≥400 mg/day (ES for SBP = -6.38 mmHg; ES for DBP = -3.71mmHg), as well as in studies with a treatment duration of ≥12 weeks (ES for SBP = -0.42 mmHg; ES for DBP = -0.45 mmHg).
*Implications:* The findings of the present umbrella meta-analysis showed an overall decrease of SBP and DBP with magnesium supplementation, particularly at doses of ≥400 mg/day for ≥12 weeks.


## Introduction

Systemic hypertension, a persistent elevation of the systemic arterial blood pressure (BP), is a highly prevalent condition and a major independent risk factor of mortality and cardiovascular disease.[1] Preventing and treating hypertension has become a significant factor in decreasing the risk and burden of various diseases, thus reducing disease-related mortality.[2,3] However, inadequate management of BP still remains one of the greatest individual risk factors of all-cause mortality globally,[4] and each 10 mmHg rise in average systolic blood pressure (SBP) has been previously associated with an increase in cardiovascular disease (CVD) and chronic kidney disease risk by up to 16%.[5] Dietary and lifestyle modifications play major role in managing BP.[6,7] For this reason, the pressure-lowering effect of natural supplements has been

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widely studied, and beneficial effects with minimal adverse effects have been discovered for many substances.[3]

Magnesium is the fourth most common cation in the human body,[8] and a deficient intake of magnesium has been associated with various diseases, including asthma, diabetes mellitus, hypertension, stroke, heart disease, hypertension, and even cancer.[9,10] Therefore, magnesium has been proposed as a treatment for hypertension.[11] By inducing the formation of nitric oxide and prostacyclin,[12] magnesium helps in modulating vasodilation, decreasing vascular tone and vascular reactivity.[13] Magnesium also possess anti-inflammatory and as antioxidant properties[14] and interacts with calcium,[12] decreasing peripheral vascular resistance[15] and decreasing blood pressure.[16]

Observational epidemiological studies have reported a negative association between dietary magnesium supplementation and BP,[17] and various clinical trials have been conducted in the past years to study the effects of magnesium on BP, with inconsistent results published.[16] Even systematic reviews conducted on RCTs provided inconclusive results on the effects of magnesium on SBP and DBP. For instance, one meta-analysis reported a significant reduction in DBP and a nonsignificant reduction in SBP,[18] while another meta-analysis reported that magnesium supplementation resulted in significant reduction of SBP and DBP,[19] and a third meta-analysis reported only a slight decrease in BP.[20] In patients with type 2 diabetes mellitus a meta-analysis reported beneficial effect of magnesium on BP,[21] while a second one showed a favorable effect on SBP but not on DBP.[22]

Conflicting results were obtained from various studies and hence we conducted this umbrella meta-analysis of RCTs to provide clear evidence and conclusion on the effect of magnesium supplementation on blood pressure.

## Methods

This study was implemented based on the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines.[23]

### *Search strategy and study selection*

Four databases including PubMed, Scopus, EMBASE, and Web of Science were searched to find pertinent papers published on international scientific journals from inception up to July 15, 2024. The search strategy was established using the following keywords and MeSH terms: (((((“Magnesium”[Mesh]) OR “Magnesium”[tiab])))) AND (((((((((Blood Pressure [Title/Abstract] OR Systolic Blood Pressure[Title/Abstract]) OR diastolic Blood Pressure[Title/Abstract]) OR “Blood Pressure”[Mesh]) OR SBP[Title/Abstract]) OR DBP[Title/Abstract])))) AND ((((“systematic review” [Title/Abstract] OR “meta-analyses” [Title/Abstract] OR “meta-analysis” [Title/Abstract])))) (Supplementary Table 1).

### *Inclusion and exclusion criteria*

We included articles in the present umbrella meta-analysis according to PICO criteria: Population/Patients (P: subjects treated with magnesium); Intervention (I: magnesium); Comparison (C: control or placebo group); and Outcome (O: SBP and DBP). Meta-analysis articles examining the effects of magnesium on blood pressure (SBP and DBP) in humans with reported effect sizes (ESs) and confidence intervals (CI), were included in the current umbrella meta-analysis. Moreover, observational studies, case reports, controlled clinical trials, prospective studies, studies with a “low quality” score, and articles in languages other than English were excluded.

### *Methodological quality assessment and grading of the evidence*

Two independent researchers utilized the A Measurement Tool to Assess Systematic Reviews (AMSTAR)2 questionnaire to evaluate the methodological quality of eligible meta-analyses.[24] This tool contains 16 items that require referees to answer “Yes,” “Partial Yes,” “No,” or “No Meta-analysis.” The AMSTAR2 list was categorized into “high quality,” “moderate quality,” “low quality,” and “critically low quality.” We appraised the general strength and quality of evidence using GRADE based on the Cochrane Handbook of systematic reviews of interventions.[25]

### *Study selection and data extraction*

Two independent investigators reviewed the papers to select those fulfilling the eligibility criteria and discrepancy was resolved by the corresponding author. The following items were extracted from the included articles: year of publication, first author’s name, study location, sample size, magnesium supplementation dosage, and effect sizes and CIs for SBP and DBP.

### *Data synthesis and statistical analysis*

We utilized STATA version 17.0 to carry out all statistical analyses (Stata Corporation, College Station, TX, US). To calculate the overall ES and Cis, the random-effects model was used. Heterogeneity among studies was assessed using the $I^2$ statistic and Cochrane’s Q-test, with a $P < 0.1$ or $I^2$ value $>50\%$ regarded as significant. Subgroup analyses were conducted to detect potential sources of heterogeneity based on the reported median predetermined variables, namely duration of intervention and magnesium supplementation dosage. We applied sensitivity analyses to survey the influence of any particular effect size removal on the combined results. Formal Egger’s tests and funnel plots visual checking were also performed to detect publication bias, with a $P$-value $< 0.05$ regarded as meaningful.

## Results

### *Study characteristics*

Figure 1 shows the flow diagram of the literature search process. 507 papers were recovered in the electronic database searches, out of which 178 were excluded for being duplications. After screening the titles and abstracts of the remaining 329 publications, 315 articles were removed. Ultimately, 10 meta-analyses published between 2002 and 2021 were included in the umbrella meta-analysis, amounting to a total of 8610 participants.[21,22,26–29,19,30–32] Mean magnesium dose varied from 364 to 440 IU/day, and intervention duration ranged between 8.85 and 14.54 weeks. Detailed characteristics of the included meta-analyses are outlined in Table 1. Most of the included meta-analyses in this umbrella review were graded as having moderate to high quality; the results of the quality assessment of every article in each of the AMSTAR2 questionnaire items are presented in Table 2.

### *The effects of magnesium supplementation on systolic blood pressure*

10 eligible review papers with 8610 participants studied the effect of magnesium on SBP. Pooling their effect sizes based on the random effects model, a significant reduction in SBP after magnesium supplementation was discovered (ES = -1.25 mmHg; 95% CI: -1.98, -0.51, $P = 0.001$) (Figure 2). However, a significant heterogeneity among studies was detected ($I^2 = 92\%$, p= 0.000). In subgroup

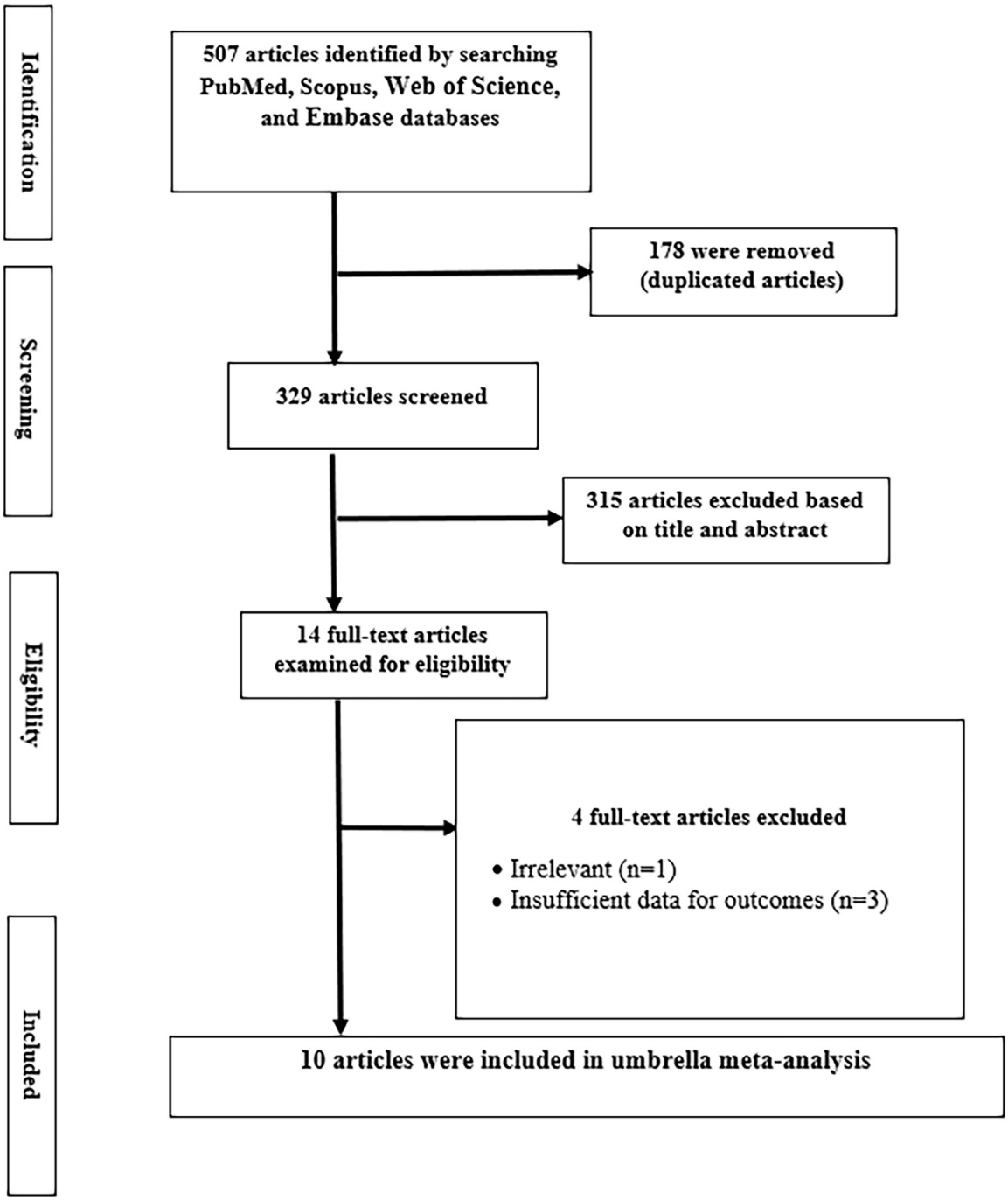


**Figure 1.** Flow chart of the study selection process for the umbrella meta-analysis.

analysis, a significant reduction in systolic blood pressure was observed in magnesium intervention with doses ≥400 mg/day (ES = -6.38 mmHg; 95% CI: -11.56, -1.19, $P = 0.016$) and treatment duration ≥12 weeks (ES = -0.42 mmHg; 95% CI: -0.78, -0.06, $P = 0.020$) (Supplementary Figure 1).

*The effects of magnesium supplementation on diastolic blood pressure*

Ten eligible review papers with 8610 participants scrutinized the influence of magnesium on DBP. The effect size pooling according to the random effects model discovered that magnesium supplementation significantly decreased DBP (ES = -1.40 mmHg; 95% CI: -2.04, -0.75, $P = 0.000$) (Figure 2), with a significant heterogeneity among studies ($I^2 = 93\%$, $P = 0.000$). In subgroup analysis, a significant reduction in diastolic blood pressure was found in magnesium intervention with doses ≥400 mg/day (ES = -3.71 mmHg; 95% CI: -6.88, -0.53, $P = 0.022$) and treatment duration ≥12 weeks (ES = -0.45 mmHg; 95% CI: -0.76, -0.14, $P = 0.004$) (Supplementary Figure 1).

**Meta-regression**

Subsequent analysis of the relationship between intervention duration (week) and magnesium supplementation dosage (mg/day) with SBP and DBP alterations revealed a significant correlation (Supplementary Figure 2) (Figure 3).

**Table 1**
Study characteristics of included studies.

| Citation (First author et al., year) | No. of studies in meta-analysis | Mean BMI | No. of participants in meta-analysis | Study duration (weeks) | Type of population | Mean age | Mean dosage (mg/day) | Outcomes |
|---|---|---|---|---|---|---|---|---|
| Asbaghi (2021)[21] | 7 | 28.33 | 357 | 11.42 | Type 2 diabetes patient | 59.75 | 364 | SBP, DBP |
| Zhao (2020)[26] | 16 | 29.2 | 1105 | 13.25 | Different | 48.14 | 383.18 | SBP, DBP |
| Verma (2017)[22] | 19 | 28.2 | 1296 | 12.63 | Different | 49.54 | 412 | SBP, DBP |
| Dibaba (2017)[27] | 11 | nr | 543 | 14.54 | Different | 54.85 | 401 | SBP, DBP |
| Zhang (2016)[28] | 34 | nr | 1999 | 12.31 | Different | 55.84 | 399 | SBP, DBP |
| Rosanoff (2013)[29] | 7 | nr | 135 | 8.85 | Hypertensive subjects | nr | 340 | SBP, DBP |
| Kass (2012)[19] | 23 | nr | 1173 | 11.3 | Different | 50.1 | 410 | SBP, DBP |
| Song (2006)[30] | 4 | nr | 237 | 12.5 | Type 2 diabetes patient | 59.41 | 440 | SBP, DBP |
| Dickinson (2006)[31] | 12 | nr | 545 | 11 | Hypertensive subjects | 54 | 413 | SBP, DBP |
| Jee (2002)[32] | 20 | nr | 1220 | 12.95 | Different | 52.2 | 443 | SBP, DBP |

**Table 2**
Results of the assessment of the methodological quality of meta-analysis.

| Study | A priori design | Selection and data extraction | Literature search | Publication type | List of studies | Characteristics of the included studies | Assessed scientific quality | Scientific quality formulating conclusions | Methods used to combine the findings | Assessed publication bias | Conflict of interest stated | Quality score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Asbaghi, O., 2021[21] | + | + | + | + | + | + | + | + | + | + | + | 11 |
| Zhao, B., 2020[26] | + | + | + | + | + | + | + | + | + | + | + | 11 |
| Verma, H., 2017[22] | + | + | + | + | + | + | + | - | + | + | + | 10 |
| Dibaba, D. T., 2017[27] | + | + | + | + | + | + | + | + | + | + | + | 11 |
| Zhang, X., 2016[28] | + | + | + | + | + | + | - | - | + | - | + | 8 |
| Rosanoff, A., 2013[29] | + | + | + | + | + | + | - | - | + | - | + | 8 |
| Kass, L., 2012[19] | + | + | + | + | + | + | - | - | + | - | + | 8 |
| Song, Y., 2006[30] | + | + | + | + | + | + | + | - | + | + | + | 10 |
| Dickinson, H. O., 2006[31] | + | + | + | + | + | + | + | + | + | + | + | 11 |
| Jee, S. H. A., 2002[32] | + | + | + | + | + | + | - | - | + | - | + | 8 |

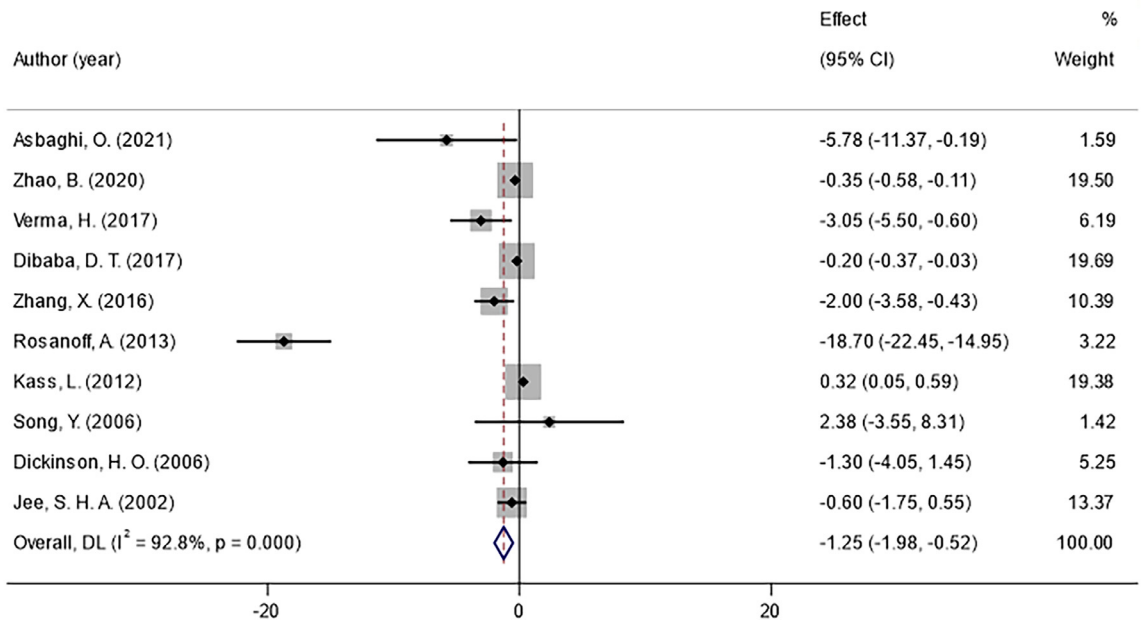


**Figure 2.** Forest plot of the umbrella review on the effects of magnesium intervention on systolic blood pressure.

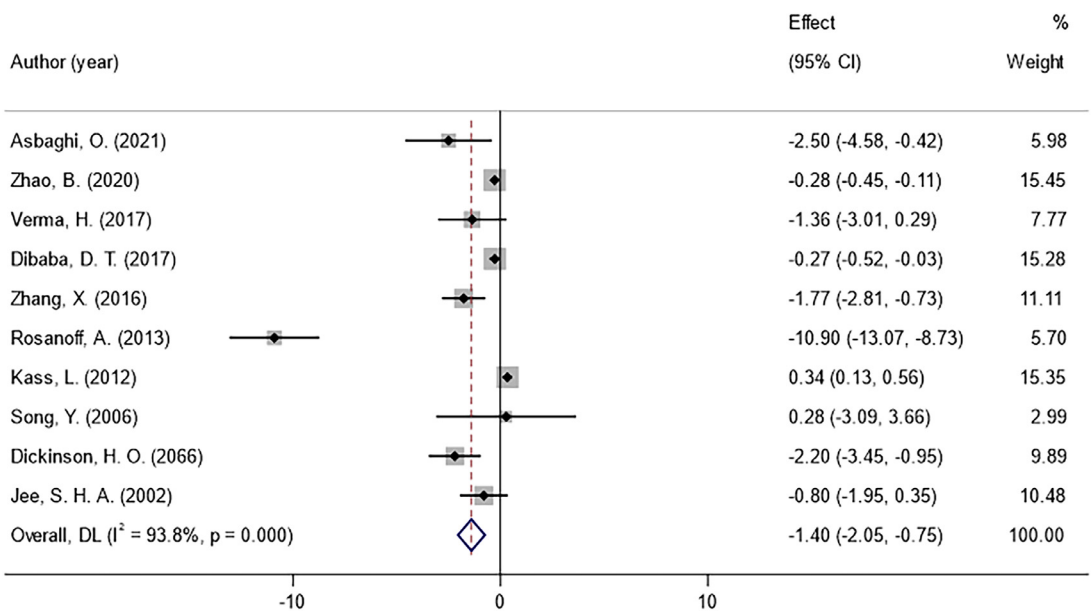


**Figure 3.** Forest plot of the umbrella review on the effects of magnesium intervention on diastolic blood pressure.

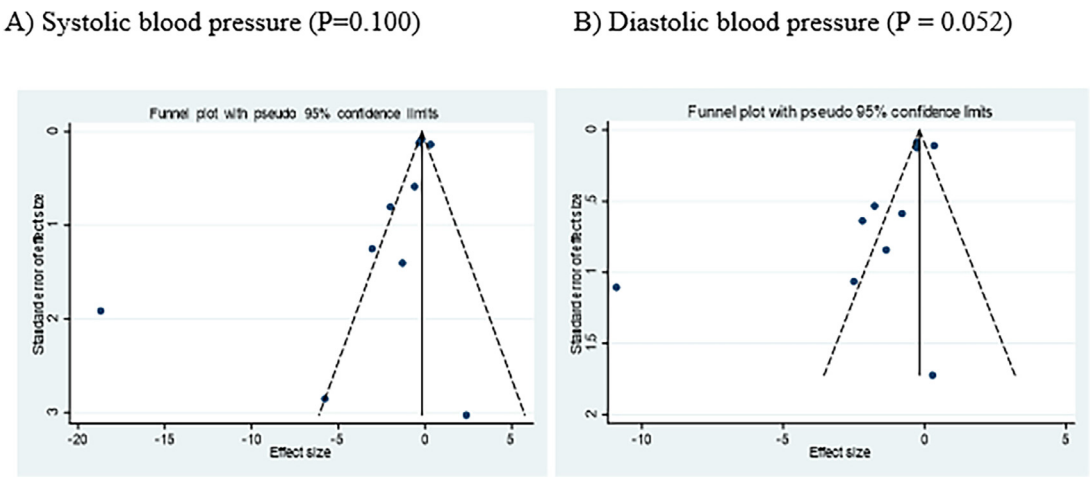


**Figure 4.** Funnel plot of the WMD versus the SE of the WMD. WMD, weighted mean difference; CI, confidence interval; SE, Standard error.

## Sensitivity analysis and publication bias

After sensitivity analysis, no special arm was found to affect the combined effect size (Supplementary Figure 3). Egger's tests and visual inspection of the funnel plots showed no sign of publication bias (Figure 4).

## Discussion

The present umbrella meta-analysis on the effect of magnesium supplementation on blood pressure summarized the results of 10 meta-analyses. The findings of this assessment support the evidence that magnesium supplementation lowers DBP and SBP in a statistically significant manner, although the effect size is small, hence, suggesting the potential use of magnesium as part of the dietary interventions for the management of hypertension. Although cost-utility analyses are lacking, magnesium supplementation could potentially reduce the economic costs of hypertension treatment. Sufficient evidence demonstrates the link between hypertension and various chronic diseases,[33] but further investigations are warranted to study the effects of magnesium supplementation on other chronic diseases.

Magnesium is one of the most common minerals in the human body, with 99% of it distributed intracellularly.[34] The role of magnesium in reducing hypertension has been attributed to multiple mechanisms of action, including acting as a calcium channel blocker, competing with sodium binding sites on vascular smooth muscle cells, decreasing intracellular sodium and calcium, enhancing prostaglandin E, binding cooperatively with potassium, inducing vasodilation, improving endothelial dysfunction in diabetic and hypertensive patients.[35] Moreover, magnesium induces nitric oxide release from endothelial cells, which acts as vasoactive mediator and produces a synergistic effect with antihypertensive medications.[36] The effect of magnesium on osteopontin has also been proposed to be one of the mechanisms involved in inhibiting vascular calcification and reducing BP.[37]

According to our umbrella meta-analysis, magnesium supplementation resulted in a statistically significant decrease in SBP (ES = -1.25 mmHg; 95% CI: -1.98, -0.51, $P = 0.001$) and DBP (ES = -1.40 mmHg; 95% CI: -2.04, -0.75, $P = 0.000$). Similar results have been obtained by several meta-analyses, including a meta-analysis of 11 RCTs conducted by Asbaghi et al. with magnesium doses ranging from 36.49 to 500 mg/day and intervention duration of 4 to 24 weeks, which reported a significant reduction of SBP and

DBP,[21] as well as one by Dibaba et al. which reported that administration of 365 to 450 mg/day of elemental magnesium resulted in a reduction of SBP by 4.18 mmHg and DBP by 2.27 mmHg,[27] and other meta-analyses.[38]

In contrast with our study results, Verma et al. reported that magnesium supplementation provides a moderate beneficial impact on SBP but not on DBP,[22] which could be because their meta-analysis on hypertension included only four studies, with a high heterogeneity among those studies. Song et al. reported that magnesium supplementation did not provide beneficial effects on SBP and DBP,[30] however, the study population of the meta-analysis included only patients with type 2 diabetes mellitus, which could be the reason for this conflicting result; moreover, the main focus of the study was the effect of magnesium on glycemic control rather than blood pressure.

According to The American Food and Nutrition Board, the recommended dietary magnesium intake for people aged 31–70 years is 420 mg/day for males and 320 mg/day for females.[39] In our subgroup analysis, a significant reduction in SBP and DBP was observed in magnesium supplementation with doses ≥400 mg/day and treatment duration ≥12 weeks. In line with our results, a meta-analysis conducted by Asbaghi et al. reported in their subgroup analysis that magnesium supplementation at a dose of >300 mg/day or with a duration of >12 weeks provided significant beneficial effects on both SBP and DBP.[21] In another meta-analysis, magnesium supplementation of >370 mg/day resulted in SBP reduction by 0.66 mmHg and DBP reduction by 0.57 mmHg.[19]

The reduction in BP due to magnesium supplementation could have beneficial effects on cardiovascular outcomes. A clinical trial reported that 0.8 to 2 mmHg reduction of SBP could help in decreasing the risks of coronary artery disease, stroke, and heart failure, with a 2 to 3 mmHg decrease of BP reducing the risk of stroke by up to 6 to 12%.[40] Hence, the reduction of BP by magnesium supplementation, although not enough to recommend magnesium as an antihypertensive monotherapy, could have clinical significance when used as a dietary supplement in addition to other antihypertensive medications in subjects with hypertension.

## Clinical Implications

Our umbrella meta-analysis of randomized controlled trials revealed that magnesium supplementation significantly reduced SBP and DBP. Hence, magnesium supplementation can be used in conjunction with antihypertensive medications to cause a significant decrease in blood pressure.

## Strengths and Limitations

To the best of our knowledge, this is the first umbrella meta-analysis to find the effect of magnesium supplementation on BP. We performed subgroup analysis based on the dose and duration of magnesium. Since our review included only meta-analyses of RCTs, bias was significantly reduced. In addition, Egger's test and visual inspection of the funnel plot revealed no publication bias.

However, our review is not without limitations. Significant heterogeneity was found among the included meta-analysis, and the dose and duration of magnesium interventions in patients with specific comorbidities were not reported. Thus, we recommend that future studies focus on the effects of magnesium supplementation on blood pressure in patients with comorbidities. Moreover, overlapping is unavoidable in any umbrella review which is another limitation of this review.

## Conclusion

The findings of the present umbrella meta-analysis showed a small but statistically significant decrease of SBP and DBP with magnesium supplementation, with significant effects with doses ≥400 mg/day and duration ≥12 weeks. Although the reduction of BP by magnesium supplementation is not enough to recommend its use as monotherapy for hypertension, it could have clinical significance when used as a dietary supplement in addition to other antihypertensive medications in patients with hypertension. Further studies are required to determine the effects of magnesium supplementation on BP in patients with comorbidities.

## Declaration of competing interest

No conflict of interest to declare.

## Funding

None.

## Author Contributions

A.M.A., P.J., H.K.-V., and A.A.-Z. carried out the concept, design, and drafting of this study. K.P. and H.K.-V. searched databases and screened articles. M.M.A., A.H.K., M.N.A., O.E.E., M.A., M.D.M., B.H.-W., and R.S. contributed to literature review, data collection, data interpretation, and reviewing of manuscript for editorial and intellectual contents. B.H.-W., H.K.-V., and A.A.-Z. supervised the study and performed statistical analysis. All authors approved the final version of the manuscript.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.curtheres.2024.100755.

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