

MAGNESIUM SUPPLEMENTATION IN CHRONIC DISEASES

Sylwia Lach¹  , **Kinga Kałuża**² ,
Ilona Bednarek² , **Aleksandra Kowalczyk**³ ,
Adrian Pączek⁴ , **Paweł Dyczek**⁵ ,
Julia Hofman³ , **Wiktoria Staniszevska**⁵ ,
Aleksandra Mucha³ , **Olaf Jadanowski**⁶ 

¹Independent Public Health Care Institution of the Ministry of Internal Affairs and Administration in Kielce, Poland

²Provincial Specialist Hospital in Czerwona Góra, Chęciny, Poland

³Medical University of Silesia in Katowice, Poland

⁴Zagłębiowski Clinical Hospital in Czeladź, Poland

⁵Wojewódzki Hospital in Bielsko-Biała, Poland

⁶University of Health Sciences in Bydgoszcz, Poland



[download article \(pdf\)](#)

 lachsylwia@interia.eu

ABSTRACT

BACKGROUND

Magnesium is an essential intracellular cation involved in enzymatic reactions, energy metabolism, neuromuscular transmission, and cardiovascular regulation. Hypomagnesemia is common in patients with chronic diseases, particularly type 2 diabetes, metabolic syndrome, cardiovascular disorders, and neuropsychiatric conditions, and is frequently underrecognized in clinical practice.

AIMS

The aim of this narrative review is to systematize current clinical and experimental evidence on the role of magnesium deficiency and the effects of magnesium supplementation in chronic diseases, with particular attention to metabolic, cardiovascular, and neuropsychiatric outcomes, as well as drug associated hypomagnesemia.

METHODS

A narrative review was performed based on analysis of 46 English language publications retrieved from PubMed and Google Scholar and published between 2020 and 2025. The included studies addressed magnesium homeostasis, causes of hypomagnesemia, and clinical or molecular effects of magnesium supplementation in chronic diseases. No quantitative meta analysis or formal quality assessment was conducted.

RESULTS

The reviewed evidence indicates that magnesium deficiency is associated with insulin resistance, endothelial dysfunction, inflammatory activation, and neuropsychological disturbances. Magnesium supplementation is associated with modest improvements in intermediate clinical parameters, including glycemic control, blood pressure, inflammatory markers, lipid profile, sleep quality, mood, and selected neuropsychological outcomes, particularly in individuals with low baseline magnesium status. Most available data relate to surrogate endpoints rather than hard clinical outcomes.

CONCLUSIONS

Magnesium deficiency is common in chronic diseases and may contribute to metabolic, cardiovascular, and neuropsychiatric dysregulation. Current evidence supports consideration of magnesium assessment and supplementation in selected high risk populations as an adjunctive measure. Further well-designed clinical studies are required to define optimal dosing strategies, duration of supplementation, formulation specific effects, and clinically meaningful long-term outcomes.

Keywords: magnesium supplementation; hypomagnesemia; chronic diseases; metabolic disorders; cardiovascular diseases

INTRODUCTION

Magnesium (Mg^{2+}) is an essential micronutrient and a cofactor in more than 300 enzymatic reactions, including those involved in energy metabolism, nucleic acid synthesis, neuromuscular conduction, and the regulation of the cardiovascular system. Despite its pivotal role in maintaining physiological homeostasis, magnesium deficiency remains highly prevalent, particularly among individuals with chronic non-communicable diseases.

Hypomagnesemia is frequently observed in patients with type 2 diabetes, metabolic syndrome, cardiovascular disorders, and neurological conditions. Current evidence indicates that disturbances in magnesium homeostasis may play not only a secondary but also a pathogenic role, contributing to oxidative stress and vascular tone dysregulation. Consequently, Mg^{2+} deficiency may promote the progression of numerous chronic diseases.

An increasing body of research confirms that magnesium supplementation may exert beneficial effects on glycemic control, blood pressure regulation, inflammatory processes, and the functioning of the nervous system. Assessment and correction of hypomagnesemia therefore constitute an important component of clinical management in patients with chronic conditions. Given the growing scientific evidence, further research is warranted to deepen our understanding of optimal supplementation strategies and the molecular mechanisms underlying magnesium's physiological effects.

RELEVANCE

Magnesium deficiency is widespread among patients with chronic non-communicable diseases and often remains underestimated in clinical practice. Accumulated evidence demonstrates an association between hypomagnesemia and insulin resistance, cardiovascular complications, neuropsychiatric disorders, and drug-induced electrolyte disturbances. At the same time, magnesium is rarely considered an independent clinically significant factor, and assessment of magnesium status is not routinely included in standard management algorithms for patients with chronic diseases. The absence of a unified approach to the interpretation of clinical data results in non-systematic use of magnesium supplementation without clear understanding of indications, dosage, and expected effects.

NOVELTY

The novelty of this narrative review lies in the systematization of contemporary clinical and experimental data on the role of magnesium in chronic diseases with particular attention to drug-associated hypomagnesemia and clinically relevant effects of magnesium supplementation. The article summarizes recent randomized controlled trials and meta-analyses, allowing comparison of supplementation doses and duration with observed metabolic, cardiovascular, and neuropsychiatric effects. In addition, available data on anti-inflammatory and immune-related effects of magnesium in the context of chronic diseases are reviewed.

AIM

The aim of this narrative review is to provide a systematic analysis of current evidence on the role of magnesium deficiency and the effects of magnesium supplementation in the pathogenesis and clinical management of chronic diseases, including metabolic, cardiovascular, and neuropsychiatric conditions.

RESEARCH OBJECTIVES

- To analyze the physiological functions of magnesium and the main mechanisms regulating its homeostasis.

- To assess the prevalence and key causes of hypomagnesemia in chronic diseases with consideration of medication related factors.
- To summarize data from clinical studies and meta analyses on the effects of magnesium supplementation on metabolic, cardiovascular, and neuropsychiatric outcomes.
- To relate reported clinical effects of magnesium to supplementation dose and duration based on published evidence.
- To identify gaps in existing research and outline directions for future clinical studies.

METHODS

STUDY DESIGN

This study is a narrative review based on analytical synthesis of published epidemiological, experimental, clinical, and molecular studies addressing magnesium homeostasis, causes of hypomagnesemia, and the effects of magnesium supplementation in chronic diseases.

DATA SOURCES

The literature search was conducted using two electronic databases: PubMed and Google Scholar.

SEARCH STRATEGY

The search was performed using combinations of the following keywords and terms: magnesium, magnesium deficiency, hypomagnesemia, magnesium supplementation, chronic diseases, type 2 diabetes, metabolic syndrome, cardiovascular diseases, neuropsychiatric disorders, inflammation, oxidative stress.

Time frame and language

Only articles published between 2020 and 2025 and written in English were considered.

Inclusion criteria

Studies were included if they met the following criteria:

- publications addressing magnesium homeostasis or hypomagnesemia in the context of chronic diseases;
- clinical studies, randomized controlled trials, meta-analyses, or experimental studies reporting effects of magnesium supplementation;
- articles providing clinical, biochemical, or molecular data relevant to metabolic, cardiovascular, or neuropsychiatric conditions discussed in the review.
- Exclusion criteria
- Studies were excluded if they met at least one of the following criteria:
 - publications not related to chronic diseases;
 - articles not addressing magnesium deficiency or magnesium supplementation;
 - non-English language publications;
 - conference abstracts, editorials, commentaries, narrative opinions without data, and publications without accessible full text;
 - studies published outside the predefined time frame.

Data extraction and synthesis

No primary data were collected. Data were extracted from the included publications and synthesized narratively through analytical comparison of reported clinical outcomes and mechanistic findings, as presented in the original sources.

Methodological considerations

The methodological approach was descriptive and analytical, consistent with the narrative review design.

RESULTS

PHYSIOLOGICAL IMPORTANCE OF MAGNESIUM

Magnesium is the second most abundant intracellular cation after potassium. Mg²⁺ ions are involved in virtually every biochemical process in the cell, including: glucose metabolism, energy storage and transfer (e.g., ATP-Mg²⁺ complexes), neuromuscular system function, DNA and RNA synthesis, activation of over 600 enzymes, with another 200 requiring Mg²⁺ as an activator [1,2]. The total magnesium content in the human body is approximately 24–30 g, of which 60–65% is found in bones, 20% in muscles, and only 1% in extracellular fluid, including blood serum, and in this part in the serum, 32% of magnesium is bound to albumin, whereas 55% is free [3].

Among other things, due to the distribution of this element in the body, it is difficult to assess the real storage. Serum magnesium level measurement is the standard but imperfect method of assessing its status, as it does not correlate well with total body magnesium levels. The reference range for serum magnesium concentration is 0.7–1.0 mmol/L. Factors influencing magnesium status include diet, age, intestinal pH, kidney function and medications [4].

CAUSES OF HYPOMAGNESEMIA

Hypomagnesemia is a significant yet frequently underrecognized electrolyte disorder that can lead to a variety of metabolic, neurological, and cardiovascular complications. It may also result from the treatment of several medical conditions. In highly developed countries, hypomagnesemia is increasingly linked to dietary magnesium deficiency, largely due to high consumption of processed foods and insufficient intake of vegetables and whole grains. Chronic diseases and iatrogenic factors also play a substantial role in its pathogenesis.

Almost 30% of adults fail to meet the estimated average daily requirement for magnesium, a crucial mineral for our health. Alarmingly, widely used medications (Table 1), exacerbate this deficiency, putting many individuals at risk [5].

Moreover, hypomagnesemia is remarkably more common-up to ten times-in people with type 2 diabetes (T2DM) than in those without the conditio [6].

Several factors contribute to this significant disparity, including insufficient dietary magnesium, alterations in the gut microbiota, the use of certain medications, and genetic factors. The association between low magnesium levels and insulin resistance is especially troubling, as it not only heightens the likelihood of developing T2DM but also impairs blood sugar regulation in individuals already diagnosed. Ensuring adequate magnesium intake is not merely advantageous-it is vital for improving health outcomes [7].

Table 1. Conditions, Medications and Mechanisms Contributing to Hypomagnesemia

Condition / Clinical Indication	Medications / Factors Causing Hypomagnesemia
Type 2 Diabetes	Metformin, insulin
Asthma, COPD	β2-agonists (salbutamol, terbutaline, rimiterol), theophylline
Gastroesophageal Reflux Disease (GERD)	Proton pump inhibitors (PPIs)
Constipation	Laxatives
Cancer (chemotherapy)	Cisplatin, carboplatin, foscarnet, EGFR monoclonal antibodies, mTOR inhibitors
Transplants, autoimmune diseases	Calcineurin inhibitors (cyclosporine, tacrolimus)
Nephrotoxic infections and drugs	Aminoglycosides, amphotericin B, pentamidine, foscarnet
Hypertension, heart failure, edema	Thiazide diuretics, furosemide
Heart disease (arrhythmias, failure)	Digoxin
Alcoholism	Alcohol

Transplants, anemia (massive transfusions)	Massive transfusions (citrate)
Resistant infections (CMV, HSV, Pneumocystis)	Foscarnet
Osteoporosis and bone diseases	Bisphosphonates, denosumab, teriparatide

As demonstrated in the Table 1, many of the agents associated with magnesium loss are widely used in routine clinical practice, particularly in outpatient care.

Consequently, the risk of hypomagnesemia is substantial and should be considered a relevant clinical concern in a broad population of patients, especially those receiving long-term pharmacotherapy.

ROLE OF SUPPLEMENTATION MAGNESIUM IN SELECTED CHRONIC DISEASES

Type 2 Diabetes and Metabolic Syndrome

In 2022, an estimated 828 million adults worldwide were living with diabetes, marking an increase of 630 million cases since 1990 [8]. This alarming rise has spurred extensive research efforts aimed at optimizing treatment strategies for diabetes and its related complications.

A growing body of evidence highlights the association between magnesium deficiency, insulin resistance, and poor glycemic control [9]. Moreover, meta-analyses have demonstrated that magnesium supplementation can improve insulin sensitivity and potentially lower the risk of developing type 2 diabetes.

Table 2 below summarizes recent clinical studies evaluating the effects of magnesium supplementation in individuals with type 2 diabetes and other metabolic disorders.

Table 2. Summary of Recent Clinical Studies on Magnesium Supplementation in Metabolic and Related Conditions

Year	Authors	Condition	Comment
2024	Kisters et al.	Metabolic syndrome	Supplementation with 250 mg of magnesium improved many aspects of quality of life, including physical, emotional, social functioning, and general health [10].
2024	Khalid et al.	Type 2 diabetes, hyperlipidemia	Total cholesterol and social quality of life improved after supplementation with magnesium and potassium [11].
2022	Tan & Huang	Gestational diabetes	Meta-analysis showed magnesium supplementation positively affects glycemic control in gestational diabetes [12].
2022	Norouzi et al.	Rheumatoid arthritis	Magnesium supplementation lowered glucose, insulin, and HOMA-IR – may help prevent type 2 diabetes in RA patients [13].
2023	Halawa et al.	Diabetic nephropathy	Magnesium citrate improved microalbuminuria, lipid profile, and quality of life without serious side effects [14].
2023	Hasan et al.	Metabolic syndrome (women)	Magnesium lactate reduced blood pressure (significant decline in SBP) in women with metabolic syndrome [15].
2024	Drenthen et al.	Type 2 diabetes	Magnesium modulated CD4+ and CD8+ T-cell function; lower hs-CRP levels after magnesium supplementation compared with placebo [16].

CARDIOVASCULAR DISEASES

Cardiovascular diseases are strongly correlated with diabetes and other metabolic disorders. Magnesium plays a crucial role in regulating blood pressure, cardiac rhythm, and endothelial function. Deficiency of magnesium has been associated with a wide range of cardiovascular complications, including:

- Hypertension
- Cardiac arrhythmias [17]
- Increased platelet aggregation and thrombosis
- Atherosclerosis [18]
- Vascular and soft tissue calcification
- Heart failure
- Myocardial infarction [19]
- Sudden cardiac death.

These findings underscore the essential role of magnesium in maintaining cardiovascular homeostasis and highlight the clinical significance of magnesium deficiency in cardiovascular disease pathogenesis.

Supplementation may reduce the risk of cardiovascular events. Numerous studies have been conducted by researchers in this field, confirming the beneficial effects of magnesium supplementation on cardiovascular health. However, a current challenge remains to determine the optimal dosing strategies for supplementation. As evidenced by the studies summarized

in the table below, the positive impact of magnesium supplementation continues to be consistently supported.

Table 3. Summary of Recent Studies on Magnesium Supplementation and Cardiovascular-Related Conditions

Year	Authors	Conditions Studied	Summary of Findings
2022	Schutten et al.	Overweight/obesity, healthy individuals	450 mg magnesium citrate for 24 weeks had no effect on arterial stiffness or blood pressure; other forms were also ineffective [20].
2025	Argeros et al.,	Hypertension	Magnesium reduced DBP, but had no significant effect on the SBP [21].
2022	Rahnama Ichehsablagh et al.	Atherosclerosis	300 mg/day of magnesium sulfate for 3 months increased eNOS and decreased TP53 - suggesting a protective effect [22].
2023	Mohebi et al.	Coronary artery disease (CAD)	Supplementation of 300 mg/day for 3 months reduced IL-18 and TNF- α - suggesting anti-inflammatory effects [23].
2024	Uysal et al.	Ventricular extrasystoles (VES) in children	Oral magnesium therapy suppressed VES regardless of serum magnesium levels [24].
2024	Behers et al.	Hypertension (general population)	Magnesium \leq 360 mg/day (>3 months) reduced SBP by -3.03 to -4.31 mmHg; lower doses over longer periods were more effective [25].

2024	Kim et al.	Retinal vein occlusion (RVO)	Adequate magnesium intake was associated with significantly lower risk of RVO, especially in individuals <60 years, hypertensive, and without glaucoma [26].
2024	Alharran et al.	Hypertension (umbrella meta-analysis)	Overall reduction in SBP and DBP with magnesium supplementation, particularly at doses ≥ 400 mg/day for ≥ 12 weeks [27].

Separately, we highlighted the findings of a 2023 meta-analysis by L. Xu et al. provided critical insights into the dose-dependent effects of magnesium supplementation on metabolic parameters in individuals with type 2 diabetes mellitus [28]. By systematically reviewing 24 clinical trials, the researchers identified specific dosage thresholds associated with clinically significant improvements in glycemic control, lipid metabolism, and blood pressure regulation.

The dose-response analysis revealed the following optimal supplementation ranges:

- 279 mg/day for 116 days - to improve glycemic control,
- 429 mg/day for 88 days - to enhance lipid profile,
- 300 mg/day for 120 days - to reduce arterial blood pressure.

These findings emphasize the therapeutic potential of magnesium supplementation

as an adjunctive strategy in the management of type 2 diabetes. When appropriately dosed, magnesium may support better regulation of blood glucose, improve cardiovascular risk markers, and contribute to the correction of metabolic dysregulation.

A summary of the key outcomes from this meta-analysis is provided in the following table.

Table 4. Clinical Effects of Magnesium Supplementation on Diabetes and Cardiovascular Risk Factors

Parameter	Effect of Magnesium Supplementation	Subgroup / Notes	Optimal Dose & Duration
Fasting Plasma Glucose	Significant reduction	Patients with hypomagnesemia or supplementation	≥ 90 days
Insulin Resistance (HOMA-IR)	Greater improvement	T2D patients with BMI ≤ 30 kg/m ² , baseline HbA1c $> 8\%$, or diabetes ≤ 10 years	≥ 400 mg/day or duration ≥ 90 days
LDL Cholesterol (LDL-C)	Lower plasma levels	Patients with BMI ≤ 30 kg/m ² or diabetes diagnosed < 10 years	-
HDL Cholesterol (HDL-C)	Increased levels	American T2D patients	300–399 mg/day
Systolic Blood Pressure (SBP)	More pronounced reduction	Younger populations with T2D; inorganic magnesium supplements	-
Glycemic Control	Clinically relevant improvement	-	~ 279 mg/day for 116 days

Lipid Profile	Improvement in circulating lipids	-	~429 mg/day for 88 days
Blood Pressure Control	Effective reduction	-	~300 mg/day for 120 days

NEUROPSYCHIATRIC DISORDERS

As previously noted, magnesium plays a crucial role in the proper functioning of the nervous system, being indispensable for maintaining neurophysiological balance and supporting synaptic transmission, neurotransmitter regulation, and neuromuscular excitability.

Magnesium deficiency can impair hypothalamic-pituitary-adrenal (HPA) axis function

and neurotransmission, thereby increasing the risk of depression, anxiety, and migraines. Studies have demonstrated that magnesium supplementation provides therapeutic benefits in patients suffering from depression and migraines [29].

Given the high prevalence of mental health disorders globally, these findings highlight the potential role of magnesium supplementation as an adjunctive treatment in neuropsychiatric conditions.

The table below demonstrates the wide range of diseases for which magnesium supplementation may provide therapeutic support.

Table 5. Summary of Magnesium Supplementation Effects on Neurological, Psychological, and Musculoskeletal Conditions

Year	Authors	Condition/ Disease	Summary of Findings
2020	Reno et al.,	Muscle soreness and recovery	10-day magnesium supplementation reduced muscle soreness and improved recovery in physically active individuals [30].
2021	Byram et al.,	Acute low back pain	Adding magnesium to standard treatment did not significantly improve clinical outcomes [31].
2021	Afsharfar et al.,	Depression	Daily intake of 500 mg magnesium oxide for 8 weeks improved Beck's depression scores and serum magnesium levels [32].
2022	Saba et al.,	Anxiety and depression post-cardiac surgery	Magnesium supplementation reduced anxiety and depression levels and improved sleep quality in post-cardiac surgery patients [33].
2023	Wang et al.,	Depression and anxiety	Intake of antioxidant supplements, including magnesium, associated with improved depression and anxiety states [34].
2023	Jadidi et al.,	Restless Legs Syndrome (RLS)	Magnesium and vitamin B6 supplementation reduced severity of RLS symptoms and improved sleep quality [35].
2024	Gorantla et al.,	Restless Legs Syndrome (RLS)	Magnesium citrate monotherapy improved RLS symptoms and multiple suggested immobilization test scores [36].
2024	Khalid et al.,	Insomnia in diabetic patients	Magnesium and potassium supplementation reduced intensity and duration of insomnia in diabetic patients [37].

2024	Hausenblas et al.,	Sleep quality and daytime functioning	Magnesium-L-threonate improved sleep quality, mood, energy, alertness, and daily activity in adults with non-clinical [38].
2024	Tarsitano et al.,	Muscle soreness and recovery	Magnesium sulfate supplementation reduced muscle soreness, improved performance, recovery, and protected against muscle damage [39].
2025	Rawji et al.,	Sleep quality, anxiety	Meta-analysis showed moderate positive effects on sleep and anxiety [40].
2023	Moabedi et al.,	Depression	Meta-analysis: Magnesium supplementation significantly reduced depression symptoms [41].
2024	Khalid et al.,	Insomnia in diabetes patients	Mg and K significantly affected cortisol, melatonin, and reduced insomnia severity [42].

As detailed in the table, recent studies show that magnesium supplementation provides benefits in alleviating symptoms of conditions such as depression, anxiety disorders, insomnia, and restless legs syndrome, as well as supporting muscle recovery.

Meta-analyses confirm moderate positive effects of magnesium on improving sleep quality and reducing depressive symptoms.

ANTIOXIDANT PROPERTIES OF MAGNESIUM AND FUTURE RESEARCH DIRECTIONS

It is also important to highlight recent studies investigating the antioxidant properties of magnesium. Emerging evidence suggests that magnesium supplementation may have protective effects against carcinogenesis and the aging process. So far, most of these findings are based on preclinical studies conducted on animal models. However, one significant epidemiological study involving over 11,000 participants from the United States reports that magnesium supplementation may have a beneficial impact on factors related to the aging process [43].

Table 6. Recent Research on Magnesium Supplementation and Its Effects on Oxidative Stress and Related Diseases

Year	Authors	Condition/ Disease	Summary
2022	El-Domiaty et al.,	Memory deficit in aged rats	Magnesium supplementation and treadmill exercise improved memory in aged rats by enhancing hippocampal neurogenesis and plasticity [44].
2024	Huang et al.,	Cancer	Magnesium deficiency is associated with tumor development; supplementation may inhibit tumor growth via mitochondrial regulation and oxidative stress modulation [45].
2025	Ma X et al.,	Aging and Klotho expression	Magnesium supplementation may enhance Klotho expression, benefiting aging and age-related diseases [43].
2024	Laragione et al.,	Rheumatoid arthritis (mouse model)	Magnesium inhibited inflammatory gene expression, oxidative stress response, and aging processes – suggesting therapeutic potential for RA and autoimmune diseases [46].

DISCUSSION

The present review emphasizes the central role of magnesium as a key intracellular cation involved in enzymatic

reactions, energy metabolism, nucleic acid synthesis, and neuromuscular and cardiovascular regulation [1,2]. Despite this fundamental physiological importance, reliable assessment of total body magnesium status remains problematic, as serum magnesium concentrations represent only a small fraction of the total magnesium pool and do not accurately reflect intracellular or skeletal stores [3,4]. Against the background of the increasing prevalence of magnesium deficiency in industrialized countries, the data reviewed highlight the need for greater clinical awareness of hypomagnesemia and its systematic evaluation in patients with chronic diseases [5].

Available evidence indicates that magnesium deficiency has a multifactorial etiology, resulting from insufficient dietary intake, altered intestinal absorption, renal losses, chronic disease states, and medication related effects, including diuretics, proton pump inhibitors, and antidiabetic drugs [5,7]. Of particular clinical relevance is the strong association between hypomagnesemia and insulin resistance, which likely contributes to the markedly higher prevalence of magnesium deficiency observed in patients with type 2 diabetes mellitus [6,7]. This relationship has important metabolic implications, as low magnesium levels may not only predispose to the development of diabetes but also aggravate glycemic dysregulation in established disease. Meta analyses and controlled trials provide evidence that magnesium supplementation can modestly improve insulin sensitivity and glycemic parameters, supporting its role as an adjunctive component of metabolic therapy rather than a primary treatment strategy [12,13,28].

Magnesium deficiency has a clinically relevant impact on the cardiovascular system and should be considered in the context of chronic disease prevention and management. Available evidence indicates that magnesium participates in the regulation of vascular tone, cardiac electrophysiology, endothelial function, and hemostatic balance [17,18]. Observational studies and clinical investigations associate low magnesium status with increased prevalence of hypertension, cardiac arrhythmias, endothelial dysfunction, and atherosclerotic processes [19,22]. Interventional studies and meta analyses show modest but consistent effects of magnesium supplementation on blood pressure reduction and inflammatory markers [20,21,25,27]. At the same time, the majority of available data concern intermediate cardiovascular endpoints, while evidence linking magnesium supplementation to reductions in cardiovascular mortality or major adverse cardiovascular events remains limited and requires confirmation in large scale randomized controlled trials [21,27].

In the neuropsychiatric domain, available evidence indicates a potential supportive role of magnesium supplementation. Experimental and clinical studies suggest that magnesium is involved in regulation of the hypothalamic pituitary adrenal axis, synaptic transmission, and neurotransmitter balance, mechanisms that are relevant to stress response, mood regulation, and pain perception [29]. Clinical trials and meta analyses report modest but consistent reductions in the severity of depressive symptoms, anxiety, sleep disturbances, and migraine frequency following magnesium supplementation, particularly in individuals with low baseline magnesium status [32,33,40,41]. Given the high prevalence of neuropsychiatric disorders and the generally favorable safety profile of magnesium, these findings support its consideration as an adjunctive, but not standalone, component of supportive therapy [29,41].

Data on the antioxidant and cytoprotective properties of magnesium are emerging, but at present remain largely based on experimental and preclinical studies. Available evidence suggests that magnesium deficiency may be associated with enhanced oxidative stress, mitochondrial dysfunction, and dysregulation of cellular aging pathways, while supplementation can modulate these processes in animal models and selected observational settings [43–46]. Epidemiological data indicate a potential association between adequate magnesium intake and markers of healthy aging; however, evidence supporting a direct protective effect against cancer development is preliminary and insufficient to draw clinical conclusions [43,45]. These observations should therefore be interpreted as hypothesis generating rather than clinically actionable.

Overall, the accumulated evidence indicates that adequate magnesium status is an important component of metabolic, cardiovascular, and neurological health. Nevertheless, hypomagnesemia remains underrecognized in routine clinical practice, particularly among patients receiving long term pharmacotherapy. Current data are insufficient to support uniform supplementation strategies, underscoring the need for further well designed clinical studies to improve assessment of magnesium status, define evidence based supplementation protocols, and identify patient populations most likely to benefit from targeted magnesium interventions.

LIMITATIONS

This review has several limitations that should be acknowledged. First, the work is based on a narrative review design, which does not follow a predefined systematic protocol and is therefore subject to selection bias. Second, no formal assessment of study quality, risk of bias, or strength of evidence was performed, limiting the ability to compare results across studies with differing methodologies. Third, the included literature is heterogeneous with respect to study design, population characteristics, magnesium formulations, dosages, and duration of supplementation, which restricts direct comparability of outcomes. Fourth, most available clinical data address intermediate endpoints such as biochemical markers, blood pressure, or symptom scores, while evidence for effects on hard clinical outcomes remains limited. Finally, only English language publications from a restricted time frame were included, which may have resulted in omission of relevant data published earlier or in other languages.

CONCLUSIONS

Magnesium deficiency is common in patients with chronic diseases and is associated with disturbances in metabolic, cardiovascular, and neuropsychiatric regulation. Available clinical and experimental data indicate that hypomagnesemia is linked to insulin resistance, endothelial dysfunction, inflammatory activation, and impaired neuromuscular and neuropsychological function. Evidence from randomized controlled trials and meta analyses shows that magnesium supplementation can result in modest improvements in glycemic control, blood pressure, inflammatory markers, lipid parameters, and selected neuropsychological outcomes, primarily affecting intermediate clinical endpoints.

Despite its essential physiological role, magnesium status is often not assessed in routine clinical practice, particularly in patients receiving long term pharmacotherapy and those with chronic metabolic or cardiovascular conditions. Current evidence supports consideration of magnesium assessment and supplementation in selected high risk populations rather than universal screening or routine supplementation.

The role of magnesium in disease prevention and early intervention remains insufficiently defined. Further well designed clinical studies are required to establish optimal dosing strategies, duration of supplementation, formulation specific effects, and clinically meaningful outcomes before magnesium supplementation can be incorporated into standardized clinical guidelines for chronic disease management.

AUTHORS' CONTRIBUTIONS

Conceptualization: Sylwia Lach;

Methodology: Aleksandra Kowalczyk;

Software: Ilona Bednarek, Paweł Dyczek;

Validation: Sylwia Lach;

Formal analysis: Adrian Pączek;

Investigation: Julia Hofman;

Resources: Ilona Bednarek;

Data curation: Aleksandra Mucha;

Writing - rough preparation: Olaf Jadanowski;

Writing - review and editing: Julia Hofman;

Visualization: Kinga Kałuża;

Supervision: Wiktoria Staniszevska;

Project administration: Julia Hofman.

All authors have read and agreed with the published version of the manuscript.

USE OF AI

In preparing this work, the authors used ChatGPT for the purpose of improving language and readability. After using this tool the authors have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

REFERENCES

1. de Baaij JHF, Hoenderop JGJ, Bindels RJM. Magnesium in man: Implications for health and disease. *Physiol Rev.* 2015;95(1). <https://doi.org/10.1152/physrev.00012.2014>
2. Gröber U, Schmidt J, Kisters K. Magnesium in Prevention and Therapy. *Nutrients* 2015, Vol 7, Pages 8199-8226. 2015;7(9):8199-8226. <https://doi.org/10.3390/NU7095388>
3. DiNicolantonio JJ, O'Keefe JH, Wilson W. Subclinical magnesium deficiency: a principal driver of cardiovascular disease and a public health crisis. *Open Heart.* 2018;5(1):668. <https://doi.org/10.1136/OPENHRT-2017-000668>
4. Workinger JL, Doyle RP, Bortz J. Challenges in the diagnosis of magnesium status. *Nutrients.* 2018;10(9).

<https://doi.org/10.3390/nu10091202>

5. Pitzer Mutchler A, Huynh L, Patel R, et al. The role of dietary magnesium deficiency in inflammatory hypertension. *Front Physiol.* 2023;14:1167904. <https://doi.org/10.3389/FPHYS.2023.1167904/FULL>
6. Xu J, Xu W, Yao H, Sun W, Zhou Q, Cai L. Associations of Serum and Urinary Magnesium with the Pre-Diabetes, Diabetes and Diabetic Complications in the Chinese Northeast Population. *PLoS One.* 2013;8(2). <https://doi.org/10.1371/JOURNAL.PONE.0056750>
7. Oost LJ, Tack CJ, de Baaij JHF. Hypomagnesemia and Cardiovascular Risk in Type 2 Diabetes. *Endocr Rev.* 2022;44(3):357. <https://doi.org/10.1210/ENDREV/BNAC028>
8. Zhou B, Rayner AW, Gregg EW, et al. Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants. *Lancet.* 2024;404(10467):2077. [https://doi.org/10.1016/S0140-6736\(24\)02317-1](https://doi.org/10.1016/S0140-6736(24)02317-1)
9. Johnson S. The multifaceted and widespread pathology of magnesium deficiency. *Med Hypotheses.* 2001;56(2). <https://doi.org/10.1054/mehy.2000.1133>
10. Kisters S, Kisters K, Werner T, et al. Positive effects of magnesium supplementation in metabolic syndrome. *Int J Clin Pharmacol Ther.* 2024;62(12):569-578. <https://doi.org/10.5414/CP204677>
11. Khalid S, Mehboob R, Bokhari SS, et al. Comparative Efficacy of Magnesium and Potassium Towards Cholesterol and Quality of Life in Patients With Type 2 Diabetes Mellitus: A Randomised Single-Blinded Controlled Clinical Trial. *Endocrinol Diabetes Metab.* 2024;7(6):e511. <https://doi.org/10.1002/EDM2.511>
12. Tan X, Huang Y. Magnesium supplementation for glycemic status in women with gestational diabetes: a systematic review and meta-analysis. *Gynecological Endocrinology.* 2022;38(3):202-206. <https://doi.org/10.1080/09513590.2021.1988558>
13. Norouzi M, Rezvankhah B, Haeri MR, et al. Magnesium supplementation and insulin resistance in patients with rheumatoid arthritis. *Eur J Transl Myol.* 2022;32(3):10622. <https://doi.org/10.4081/EJTM.2022.10622>
14. Halawa N, Elsaid TW, El Wakeel LM, Shawki MA. Impact of magnesium supplementation on clinical outcome and disease progression of patients with diabetic nephropathy: a prospective randomized trial. *Ther Adv Chronic Dis.* 2023;14. <https://doi.org/10.1177/20406223231214641>
15. Hasan EK, Mshimesh BAR, Rzoqi SS, et al. EFFECT OF MAGNESIUM L-LACTATE SUPPLEMENT ON BLOOD PRESSURE AND CORRECTED QT INTERVAL IN A SAMPLE OF IRAQI WOMEN WITH METABOLIC SYNDROME. *Wiad Lek.* 2023;76(2):360-369. <https://doi.org/10.36740/WLEK202302117>
16. Drenthen LCA, Ajie M, de Baaij JHF, Tack CJ, de Galan BE, Stienstra R. Magnesium Supplementation Modulates T-cell Function in People with Type 2 Diabetes and Low Serum Magnesium Levels. *J Clin Endocrinol Metab.* 2024;109(12). <https://doi.org/10.1210/CLINEM/DGAE097>
17. Orlov MY, Brodsky MA, Douban S. A review of magnesium, acute myocardial infarction and arrhythmia. *J Am Coll Nutr.* 1994;13(2). <https://doi.org/10.1080/07315724.1994.10718384>
18. Maier JAM. Low magnesium and atherosclerosis: An evidence-based link. *Mol Aspects Med.* 2003;24(1-3). [https://doi.org/10.1016/S0098-2997\(02\)00095-X](https://doi.org/10.1016/S0098-2997(02)00095-X)
19. Rooney MR, Lutsey PL, Alonso A, et al. Serum magnesium and burden of atrial and ventricular arrhythmias: The Atherosclerosis Risk in Communities (ARIC) Study. *J Electrocardiol.* 2020;62. <https://doi.org/10.1016/j.jelectrocard.2020.07.008>
20. Schutten JC, Joris PJ, Groendijk I, et al. Effects of Magnesium Citrate, Magnesium Oxide, and Magnesium Sulfate Supplementation on Arterial Stiffness: A Randomized, Double-Blind, Placebo-Controlled Intervention Trial. *Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease.* 2022;11(6):e021783. <https://doi.org/10.1161/JAHA.121.021783>
21. Argeros Z, Xu X, Bhandari B, Harris K, Touyz RM, Schutte AE. Magnesium Supplementation and Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Hypertension.* 2025 Nov;82(11):1844-1856. <https://doi.org/10.1161/HYPERTENSIONAHA.125.25129>
22. Rahnema Inchehsablagh B, Ghadiri Soufi F, Koochakkhani S, et al. Magnesium Supplementation Affects the Expression of Sirtuin1, Tumor Protein P53 and Endothelial Nitric Oxide Synthase Genes in Patients with Atherosclerosis: A Double-Blind, Randomized, Placebo-Controlled Trial. *Indian Journal of Clinical Biochemistry.* 2022;38(1):59. <https://doi.org/10.1007/S12291-022-01032-0>
23. Mohebi F, Ostadhadi S, Vaziri M sadegh, et al. The effect of magnesium sulfate on gene expression and serum level of inflammatory cytokines in coronary artery disease patients. *Inflammopharmacology.* 2023;31(5):2421-2430. <https://doi.org/10.1007/S10787-023-01328-4>
24. Uysal F, Turkmen H, Genc A, Bostan OM. Effect of Magnesium on Ventricular Extrasystoles in Children. *Clin Pediatr (Phila).* 2024;63(10). <https://doi.org/10.1177/00099228231223780>
25. Behers BJ, Behers BM, Stephenson-Moe CA, et al. Magnesium and Potassium Supplementation for Systolic

- Blood Pressure Reduction in the General Normotensive Population: A Systematic Review and Subgroup Meta-Analysis for Optimal Dosage and Treatment Length. *Nutrients* . 2024;16(21). <https://doi.org/10.3390/NU16213617>
26. Kim J, Kim M, Lee CS, Choi EY. Sufficient Magnesium Intake Reduces Retinal Vein Occlusion Risk: National Health and Nutrition Examination Survey Analysis. *Nutrients* . 2025;17(7):1285. <https://doi.org/10.3390/NU17071285/S1>
 27. Alharran AM, Alzayed MM, Jamilian P, et al. Impact of Magnesium Supplementation on Blood Pressure: An Umbrella Meta-Analysis of Randomized Controlled Trials. *Curr Ther Res Clin Exp*. 2024;101. <https://doi.org/10.1016/j.curtheres.2024.100755>
 28. Xu L, Li X, Wang X, Xu M. Effects of magnesium supplementation on improving hyperglycemia, hypercholesterolemia, and hypertension in type 2 diabetes: A pooled analysis of 24 randomized controlled trials. *Front Nutr*. 2023;9:1020327. <https://doi.org/10.3389/FNUT.2022.1020327/FULL>
 29. Dominguez LJ, Veronese N, Barbagallo M, Domitrz I, Cegielska J. Magnesium as an Important Factor in the Pathogenesis and Treatment of Migraine—From Theory to Practice. *Nutrients*. 2022;14(5):1089. <https://doi.org/10.3390/NU14051089>
 30. Reno AM, Green M, Killen LG, Oneal EK, Pritchett K, Hanson Z. Effects of Magnesium Supplementation on Muscle Soreness and Performance. *J Strength Cond Res*. 2022;36(8):2198-2203. <https://doi.org/10.1519/JSC.0000000000003827>
 31. Bayram S, Şahin K, Anarat FB, et al. The effect of oral magnesium supplementation on acute non-specific low back pain: Prospective randomized clinical trial. *American Journal of Emergency Medicine*. 2021;47:125-130. <https://doi.org/10.1016/j.ajem.2021.03.078>
 32. Afsharfard M, Shahraki M, Shakiba M, Asbaghi O, Dashipour A. The effects of magnesium supplementation on serum level of brain derived neurotrophic factor (BDNF) and depression status in patients with depression. *Clin Nutr ESPEN*. 2021 Apr;42:381-386. <https://doi.org/10.1016/j.clnesp.2020.12.022>
 33. Saba S, Faizi F, Sepandi M, Nehrir B. Effect of short-term magnesium supplementation on anxiety, depression and sleep quality in patients after open-heart surgery. *Magnes Res*. 2022;35(2):62-70. <https://doi.org/10.1684/MRH.2022.0503>
 34. Wang H, Jin M, Xie M, et al. Protective role of antioxidant supplementation for depression and anxiety: A meta-analysis of randomized clinical trials. *J Affect Disord*. 2023;323:264-279. <https://doi.org/10.1016/j.jad.2022.11.072>
 35. Jadidi A, Rezaei Ashtiani A, Khanmohamadi Hezaveh A, Aghaepour SM. Therapeutic effects of magnesium and vitamin B6 in alleviating the symptoms of restless legs syndrome: a randomized controlled clinical trial. *BMC Complement Med Ther*. 2022;23(1):1. <https://doi.org/10.1186/S12906-022-03814-8>
 36. Gorantla S, Ravisankar A, Trotti LM. Magnesium citrate monotherapy improves restless legs syndrome symptoms and multiple suggested immobilization test scores in an open-label pilot study. *Journal of Clinical Sleep Medicine*. 2024;20(8):1357-1361. <https://doi.org/10.5664/JCSM.11206>
 37. Khalid S, Bashir S, Mehboob R, et al. Effects of magnesium and potassium supplementation on insomnia and sleep hormones in patients with diabetes mellitus. *Front Endocrinol (Lausanne)*. 2024;15:1370733. <https://doi.org/10.3389/FENDO.2024.1370733>
 38. Hausenblas HA, Lynch T, Hooper S, Shrestha A, Rosendale D, Gu J. Magnesium-L-threonate improves sleep quality and daytime functioning in adults with self-reported sleep problems: A randomized controlled trial. *Sleep Med X*. 2024;8:100121. <https://doi.org/10.1016/J.SLEEPX.2024.100121>
 39. Tarsitano MG, Quinzi F, Folino K, et al. Effects of magnesium supplementation on muscle soreness in different type of physical activities: a systematic review. *J Transl Med*. 2024;22(1):629. <https://doi.org/10.1186/S12967-024-05434-X>
 40. Rawji A, Peltier MR, Mourtzanakis K, et al. Examining the Effects of Supplemental Magnesium on Self-Reported Anxiety and Sleep Quality: A Systematic Review. *Cureus*. 2024;16(4):e59317. <https://doi.org/10.7759/CUREUS.59317>
 41. Moabedi M, Aliakbari M, Erfanian S, Milajerdi A. Magnesium supplementation beneficially affects depression in adults with depressive disorder: a systematic review and meta-analysis of randomized clinical trials. *Front Psychiatry*. 2023;14. <https://doi.org/10.3389/FPSYT.2023.1333261/PDF>
 42. Khalid S, Bashir S, Mehboob R, et al. Effects of magnesium and potassium supplementation on insomnia and sleep hormones in patients with diabetes mellitus. *Front Endocrinol (Lausanne)*. 2024;15:1370733. <https://doi.org/10.3389/FENDO.2024.1370733>
 43. Ma X, Yang Y, Yan K, et al. Association between magnesium depletion score and Klotho levels among U.S. adults: Findings from NHANES 2007–2016. *Heliyon*. 2025;11(4). <https://doi.org/10.1016/j.heliyon.2025.e42809>

44. El-Domiaty HF, El-Roghy ES, Salem HR. Combination of magnesium supplementation with treadmill exercise improves memory deficit in aged rats by enhancing hippocampal neurogenesis and plasticity: a functional and histological study. *Applied Physiology, Nutrition and Metabolism*. 2022;47(3):296-308. <https://doi.10.1139/APNM-2021-0133>
45. Huang L, Lin R, Chen J, Qi Y, Lin L. Magnesium Ion: A New Switch in Tumor Treatment. *Biomedicines*. 2024;12(8):1717. <https://doi.org/10.3390/BIOMEDICINES12081717>
46. Laragione T, Harris C, Gulko PS. Magnesium Supplementation Modifies Arthritis Synovial and Splenic Transcriptomic Signatures Including Ferroptosis and Cell Senescence Biological Pathways. *Nutrients* . 2024;16(23). <https://doi.org/10.3390/NU16234247>

[back](#)