Magnesium

Common Acronyms

CNS	Chinese Nutrition Society
CRN	Council for Responsible Nutrition
DRI	dietary reference intake
EC SCF	European Commission Scientific Committee on Food
EFSA	European Food Safety Authority
EVM	Expert Group on Vitamins and Minerals
ICMR-NIN	Indian Council of Medical Research - National Institute of Nutrition
IOM	Institute of Medicine
IU	international unit
KNS	Korean Nutrition Society
LOEL	lowest observed effect level
NDA	EFSA Panel on Nutrition, Novel Foods and Food Allergens
NIH	National Institute of Health
NOEL	no observed effect level
RCT	randomized clinical trial
SUL	safe upper level
UF	uncertainty factor
UL	tolerable upper intake level

Introduction

Magnesium is essential to maintaining skeletal system and immune system health, as well as a variety of biochemical and physiological processes, especially those related to energy metabolism and utilization, nucleic acid and protein synthesis, ion transport, cell signaling, and bone structure (IOM 1997; Rude 2014; Delage 2018; Razzaque and Wimalawansa 2023). Clinical consequences of magnesium deficiency include a variety of neurological and neuromuscular signs such as tremors, spasms, and altered reflexes. In addition, magnesium deficiency may cause or exacerbate alterations in vitamin D, potassium, and calcium homeostasis,

Published by Council for Responsible Nutrition (CRN), Washington, D.C.

loss of appetite, nausea, vomiting, fatigue, weakness, numbness, tingling, muscle contractions and cramps, seizures, personality changes, abnormal heart rhythms, and coronary spasms (Delage 2018; NIH 2022). These deficiency outcomes are brought on not only by dietary inadequacy but also by malabsorption of magnesium; kidney dysfunction, often as increased excretion under the influence of diuretic drugs (NIH 2022); gastrointestinal, renal, endocrine, and metabolic disorders (Delage 2018); genetic and congenital disorders; and alcoholism (Shils 1996; Delage 2018; NIH 2022). Magnesium is efficiently absorbed in the intestine, and body concentrations are controlled primarily through the regulation of urinary excretion rates. Magnesium is stored and reserved in the skeleton (Shils 1994, 1999; IOM 1997; Rude 2014).

Safety Considerations

Healthy human kidneys are capable of rapidly excreting large amounts of absorbed or intravenous magnesium. In individuals with normal kidney function, serum levels usually stay within the range of 1.8 to 2.3 mg/dL, even after large intakes of magnesium (IOM 1997; Shils 1999; Allen and Sharma 2025). In addition, consumption of nonfood magnesium in individuals with normal renal function has rarely been reported to result in elevated serum magnesium levels (IOM 1997). However, elevated magnesium serum levels may occur when consuming magnesium in an excess of 2,500 to 5,000 mg per day (SCF 2001; NIH 2022). For example, a few cases of hypermagnesemia (defined as serum levels greater than 2.5 mg/dL) have been reported and were attributed to the use of laxatives or antacids in single doses greater than 2,500 mg (SCF 2001; Allen and Sharma 2025). Increases in serum magnesium levels greater than 5.35 mg/dL can manifest symptoms such as nausea, dizziness, weakness, and confusion. Serum magnesium levels greater than 8.5 mg/dL can result in depressed reflexes, headache, flushing gastrointestinal symptoms, drowsiness, urinary complications, and blurred vision (Aal-Hamad et al. 2023). Generally, elevated serum levels of magnesium around 4.8 to 8.4 mg/dL have been associated with the onset of symptoms of hypermagnesemia, whereas serum levels greater than 6.0 mg/dL are considered to be indicative of severe hypermagnesemia (IOM 1997; Razzaque and Wimalawansa 2023).

The risk of hypermagnesemia increases in individuals with impaired renal function, especially

with excessive intake of magnesium-containing supplements or drugs, such as laxatives or antacids. The onset of hypermagnesemia associated with impaired renal function can lead to more serious neurological and cardiac symptoms, such as hypotension or disturbances in normal cardiac rhythm (IOM 1997; Delage 2018). Individuals with underlying causes resulting in renal impairment, particularly older adults (> 50 years old), are at higher risk for adverse effects from excess supplemental magnesium intake (IOM 1997). Some recent studies conducted in patients with chronic kidney disease have reported isolated cases of diarrhea at doses ranging from 104-365 mg magnesium per day (e.g., Toprak et al. 2017; Van Laecke et al. 2017; Sakaguchi et al. 2019; Oka et al. 2019); however, at least two of these clinical studies determined this effect not to be statistically significant (Toprak et al. 2017; Van Laecke et al. 2017). Nevertheless, given the increased risk for adverse effects in individuals with kidney related disease, this patient population is excluded from the target population for deriving a UL.

Aside from osmotic diarrhea related to unabsorbed magnesium, there is no evidence that large quantities of oral magnesium are harmful to people with normal kidney function (IOM 1997). Average total dietary intakes of magnesium by U.S. adults range from 234 to 350 mg per day and average total intakes from diet and supplements range from 387 to 449 mg per day (NIH 2022). As IOM (1997) previously discussed, some published clinical studies have reported a low incidence of diarrhea with supplemental intakes of magnesium, especially in the elderly population. More recently published clinical trial studies have also shown only isolated incidences of diarrhea in a variety of populations (e.g., healthy individuals and those with prediabetes, metabolic syndrome, and hypomagnesaemia); furthermore, the incidences reported in each of these studies were not statistically[1] significantly different between magnesium intervention and control groups (Salehidoost et al. 2018; Rodríguez-Morán et al. 2018; Guerrero-Romero et al. 2015).[2] Of note, one recent clinical study reported that "50% assigned to magnesium and 7% assigned to placebo commented on GI [gastrointestinal] changes at any point in the study" following intervention with 241 mg magnesium per day as magnesium oxide

[1] As reported by the study author(s), where relevant. For studies in which statistical analysis was not performed, standard statistical analysis was conducted according to the methodology included in CRN's Methodology for 4th Edition Nutrient Chapter Updates.

[2] One such study lacked a concurrent control group (Pouteau et al. 2018).

for 12 weeks. However, such changes included all gastrointestinal observations (e.g., transient nausea, "upset stomach") and there was variation in the self-reporting, often associated with confounders, such as recent colorectal surgery or increased stress (Lutsey et al. 2018).

IOM (1997) cited two clinical studies demonstrating no onset of diarrhea at doses of 400 mg magnesium or higher (IOM 1997). In the first study, no diarrhea was found in postmenopausal women who were given up to 750[3] mg magnesium per day as magnesium hydroxide for six months (Stendig-Lindberg et al. 1993). In the second study, diabetic subjects supplemented with 400 mg magnesium per day as an oxide or chloride, for eight weeks, experienced no diarrhea (Nadler et al. 1992). More recent clinical trials have shown a lack of any serious adverse effects and no statistically significant increases in the incidence of diarrhea following intervention with magnesium at levels of 400-500 mg per day for durations ranging from 8 weeks up to 23 weeks (Rooney et al. 2020; Khalid et al. 2024; Afitska et al. 2021; Vázquez-Lorente et al. 2020; Bullarbo et al. 2018; Schutten et al. 2022). Schutten et al. (2022) reported "mild diarrhea" in healthy patients in control and magnesium treatment groups (450 mg magnesium per day; as either magnesium citrate, magnesium oxide, or magnesium sulfate) during this 24-week study. While the study authors did not report on the statistical significance of diarrhea, the incidences in all magnesium groups were found not to be significantly different from that of the control group based on separate analysis.[4] However, the authors did show the overall self-reported gastrointestinal symptoms (e.g., nausea, gas, bloating, diarrhea, etc.) to be statistically significantly higher in the magnesium sulfate group compared to controls.[5] One study was identified that administered magnesium higher than 500 mg per day (0, 482, or 724 mg magnesium per day as magnesium oxide) for 8 weeks to postmenopausal women (Park et al. 2015). The authors concluded that there "were no [statistically] significant toxicity differences, measured by Common Terminology Criteria for Adverse Events (CTCAE)" between groups based on "symptom experience data", including for diarrhea. Symptoms recorded for diarrhea

[3] Based on the publication reporting 125 mg magnesium per tablet, for a maximum of 750 mg per day. Of note, IOM (1997) reported this as magnesium hydroxide, citing the elemental magnesium as up to 678 mg per day.
[4] Standard statistical analysis was conducted according to the methodology included in CRN's Methodology for 4th Edition Nutrient Chapter Updates.
[5] Differences between magnesium oxide and magnesium citrate compared to controls, respectively, were not significant.

using a 100-pt scale[6] were reported to be (mean [standard deviation]): +0.4 (12.6), -4.5 (11.7), and -14.3 (25.8) for the placebo, low, and higher intervention groups, respectively. While the authors noted "an increased incidence" of diarrhea in the groups given magnesium compared to placebo, no incidence data for individuals or statistical analysis thereof was provided in this publication.

Costello et al. (2023) performed a review of available studies (published 1997-2022) reporting gastrointestinal adverse effects to evaluate the previously set UL by IOM, which provides additional context around the available data regarding diarrhea. Costello et al. reviewed five meta-analyses and five randomized controlled trials and determined that seven of these studies showed no significant differences in diarrhea occurrence between the intervention and control groups at supplemental magnesium intakes of 128-1,200 mg per day. The three remaining publications reported minor differences in gastrointestinal disturbances, such as diarrhea, between the treatment arms and the placebo group; however, these incidences were either not statistically significant or the reported effects were not clearly associated with the treatment arm. Based on their review, Costello et al. concluded that a re-evaluation of the IOM UL for magnesium is warranted, suggesting that the current value is too conservative.

As reviewed by Delage (2018), potential nutrient interactions between magnesium and fiber, protein, vitamin D, zinc and calcium have also been observed. For example, zinc intervention has been shown to decrease magnesium absorption, experimental studies have suggested that dietary fiber can decrease magnesium utilization, and one study showed that dietary protein intake could potentially affect magnesium absorption. Calcitriol, the active form of vitamin D, may minimally increase the intestinal absorption of magnesium, while inadequate blood concentrations of magnesium resulted in low calcium blood concentrations (Delage 2018).

Official Reviews

IOM (1997). The IOM concluded that the magnesium found in foods has not been shown to

[6] Positive change denotes decrease in symptoms.

produce adverse effects and that "the primary initial manifestation of excessive magnesium intake from other oral nonfood sources is diarrhea." The physiological effects of longer-term high intakes of oral magnesium have been observed only in persons with abnormal kidney function. Thus, the critical adverse effect identified as the appropriate basis for the magnesium UL is diarrhea. In its dose-response evaluation, the IOM identified a few studies, mainly in the elderly, that found an increase in the incidence of diarrhea with supplemental intakes of magnesium chloride or other soluble salts in the range of 360 to 460 mg of magnesium per day (Marken et al. 1989; Ricci et al. 1991; Bashir et al. 1993), but noted that foods enriched with 452 mg of magnesium as magnesium oxide did not cause diarrhea (Altura et al. 1994). The IOM described the Stendig-Lindberg et al. (1993) study, which reported no diarrhea in postmenopausal women who were given up to 678 mg[7] magnesium per day for six months as magnesium hydroxide and the Nadler et al. (1992) study in which diabetic subjects supplemented with 400 mg magnesium per day as magnesium oxide or chloride for eight weeks reported no diarrhea. In another study discussed, elderly subjects given 372 mg[8] of magnesium per day for four weeks did not have any increase in diarrhea or gastrointestinal complaints (Paolisso et al. 1992). Based on these studies, in particular that of Bashir and colleagues (1993), the IOM identified a LOAEL of 360 mg for nonfood magnesium. To derive the UL, the IOM selected a UF of 1.0, even though it was being applied to a LOAEL, because of "the very mild, reversible nature of osmotic diarrhea caused by ingestion of magnesium salts." CRN notes that the Bashir et al. (1993) study was conducted on individuals with congestive heart failure taking multiple medications; as such, the relevance of this study to the general population should be considered in the derivation of an UL.

European Commission, Scientific Committee on Food (EC SCF 2001). The EC SCF agreed that osmotic diarrhea is the critical effect for identification of a UL for magnesium. The Committee identified a LOAEL of 360 mg with a small percentage of adult subjects reporting mild diarrhea effects at oral doses of 360-365 mg per day (Fehlinger et al. 1988; Spätling and Spätling 1988; Gullestad et al. 1991; Rasmussen et al. 1989). A NOAEL of 250 mg per day for

[7] IOM (1997) reported this as magnesium hydroxide, citing the elemental magnesium as up to 678 mg per day.

[8] As reported by IOM (1997).

nonfood magnesium was selected due to "mild, transient laxative effect, without pathological sequelae, which is readily reversible and for which considerable adaptation can develop within days." Selecting a UF of 1.0 for application to the 250 mg NOAEL identified by the Committee, the SCF derived a UL of 250 mg per day.

Expert Group on Vitamins and Minerals (EVM 2003). The UK's EVM determined that the data were insufficient to establish an SUL value at the time of its review. Although diarrhea was not observed in the majority of studies of individuals consuming 384-470 mg magnesium per day, a few studies reported mild and reversible diarrhea in a small percentage of patients and healthy volunteers. The EVM used this effect to set the guidance level but noted this dose range needs to be addressed in further studies for vulnerable groups such as infants and older adults. The EVM established a guidance level of 400 mg per day for nonfood magnesium and noted that "it would not be expected to result in any significant adverse effects."

Chinese Nutrition Society (CNS 2023). The CNS does not appear to have set an UL for magnesium. However, recommended nutrient intake (RNI) levels of 300-330 mg per day were derived for adults depending on age, plus an additional 40 mg per day during pregnancy.

Indian Council of Medical Research - National Institute of Nutrition (ICMR-NIN 2020). The ICMR-NIN does not appear to have set an UL for magnesium.

Korean Nutrition Society (KNS 2020). The KNS published its general approach to evaluating data for setting DRI values. Based on this approach, an UL of 350 mg per day was derived for adults.

The reviews by IOM (1997), EC SCF (2001), and EVM (2003) found no evidence that magnesium intake from food causes osmotic diarrhea but that nonfood sources such as supplements, laxatives, and antacids have the potential to produce these mild, reversible adverse effects. Thus, the SUL or guidance values identified were applied to nonfood sources only.

CRN Recommendations

The goal of the current update to CRN's supplemental UL for magnesium was to determine whether more recent human clinical data are available that might impact the conclusions published in the 3rd edition, which derived a supplemental UL value of 400 mg/day for magnesium for adults. While not all human clinical trials reviewed were specifically designed to evaluate adverse effects, no new trials were identified following CRN's updated methodology that reported statistically significant associations between magnesium intervention and diarrhea[9] in healthy volunteers, as well as in most trials involving unhealthy populations. As with any assessment in which not all available data are reviewed, inherent uncertainties with the risk assessment and selection of the UL are recognized.

CRN's safety methodology for deriving a supplemental intake UL prioritizes data from human studies, when available. The table below summarizes the key human clinical studies considered in deriving an updated UL for supplemental intakes by CRN according to its principal points of departure for risk assessment (as described in the Methods).

Approximately 68 human clinical trials published since the 3rd edition of the book (i.e., starting in 2014) were identified that met the inclusion criteria for the current update.[10] A full literature review is outside the scope of this chapter; therefore, only studies identified in the updated search with magnesium intake levels greater than approximately 400 mg per day, and therefore pertinent to assessing a revised UL based on CRN's methodology, are summarized below together with key studies already summarized in the 3rd edition.

[9] Or any serious adverse effects
[10] Literature search conducted February 2025.

Key Studies Considered for the CRN UL for Magnesium in Adults

Reference	Study Design	Participant Description	No. of Subjects	Dose(s) (mg/day)[a]	Duration	NOEL (mg/day)
Key studies from 3rd edition						
Nadler et al. 1992	Clinical trial	Patients with diabetes	20	400 (as Mg oxide or Mg chloride)	8 weeks	400
Stendig-Lindberg et al. 1993	Open, controlled trial	Postmenopausal women	31	250-750[b] (as Mg hydroxide)	2 years	750
Key studies identified in update						
Rooney et al. 2020	Double blind, randomized	Healthy (> 55 years)	59	0, 400 (as Mg oxide)	10 weeks	400
Afitska et al. 2021	Double blind, placebo controlled, randomized	Patients with metabolic syndrome	24	0, 400 (as Mg citrate)	12 weeks	400
Bullarbo et al. 2018	Double blind, placebo controlled, multicenter study	Nulliparous women in gestational weeks 12–14	199	0, 400 (as Magnesium Extra, Diasporal)	21-23 weeks	400
Schutten et al. 2022	Double blind, placebo controlled, randomized	Patients that were overweight and slightly obese, expected to have arterial stiffness	58	0, 450 (as Mg citrate, Mg oxide, or Mg sulfate)	24 weeks	450
Khalid et al. 2024	Single blind, randomized	Patients with diabetes	290	0, 500	60 days	500
Vázquez-Lorente et al. 2020	Double blind, placebo controlled, randomized	Healthy, postmenopausal women	52	0, 500	8 weeks	500

N/A, not applicable
[a] Presented as mg elemental magnesium
[b] Based on the publication reporting 125 mg magnesium per tablet, for a maximum of 750 mg per day. Of note, IOM (1997) reported this as magnesium hydroxide, citing the elemental magnesium as up to 678 mg per day.

As described above, there is no evidence that large quantities of oral magnesium are associated with serious adverse effects in people with normal kidney function. While not defined as a *true hazard* according to CRN's methodology, osmotic diarrhea related to unabsorbed magnesium

has been identified as the critical endpoint for deriving CRN's supplemental UL for adults. An UL value of 400 mg per day was derived in the 3rd edition based on the studies available at that time (Nadler et al. 1992). More recently, several studied have reported no increased incidence of diarrhea associated with magnesium at supplemental levels up to 500 mg per day (Rooney et al. 2020; Khalid et al. 2024; Afitska et al. 2021; Vázquez-Lorente et al. 2020; Bullarbo et al. 2018; Schutten et al. 2022). While a separate analysis of diarrhea incidence in the Schutten et al. (2022) study demonstrated no statistically significant difference, the authors concluded the overall self-reported gastrointestinal symptoms to be statistically significantly higher in the magnesium sulfate group (450 mg elemental magnesium per day) compared to controls (but not in the magnesium oxide or magnesium citrate groups). However, given that these side effects, including diarrhea, are considered *nuisance* effects as defined by CRN's methodology, the results of this study were determined not to be impact the derivation of a UL value for magnesium. Therefore, 500 mg per day is identified as the NOAEL for magnesium for healthy adults following the CRN process. As described in CRN's Methods, if the supplemental intake dose-response relationship is identified from the strongest data and assessed conservatively, no additional uncertainty factor is needed (that is, the implicit UF is 1.0). Consistent with CRN's methodology, an UF of 1 is applied to yield an UL of 500 mg per day for adults for supplemental magnesium.[11]

Factors such as individual diet and health status, as well as form of magnesium, have been shown to affect bioavailability of magnesium. For example, Schutten et al. (2022) observed that magnesium oxide was "better tolerated" than magnesium citrate and magnesium sulfate. Self-reported cases of diarrhea tended to be mild to moderate but infrequent and easily reversible, consistent with the observations of IOM (1997). In addition to inherent challenges with self-reporting of symptoms in clinical trials, there were no scoring guidelines followed to accurately characterize stool consistency in most studies reporting diarrhea. The CRN supplemental UL value is therefore considered to be conservative, as it is based on studies across broad populations, using various forms of magnesium and self-reporting of symptoms.

[11] Includes all potential sources of supplemental magnesium, such as antacids and laxatives.

CRN notes that the available data suggest individuals with known risk factors related to kidney impairment are excluded from the target population for the UL and should consult with their healthcare provider.

Quantitative Summary for Magnesium in Adults

CRN (2025) UL, supplemental intake	500 mg/day[a]
IOM (1997) UL, nonfood sources	350 mg/day
EC SCF (2001) UL, nonfood sources	250 mg/day
EVM (2003), guidance level, supplemental intake	400 mg/day
CNS (2023), total intake	Not determined[a]
ICMR-NIN (2020), total intake	Not determined
KNS (2020), total intake	350 mg/day

[a] Excludes those with known risk factors related to kidney impairment; such individuals should consult with their healthcare provider.
[b] Recommended nutrient intake (RNI) levels of 300-330 mg per day for adults depending on age, plus an additional 40 mg/day during pregnancy.

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