

Magnesium Matters

Are we getting enough?

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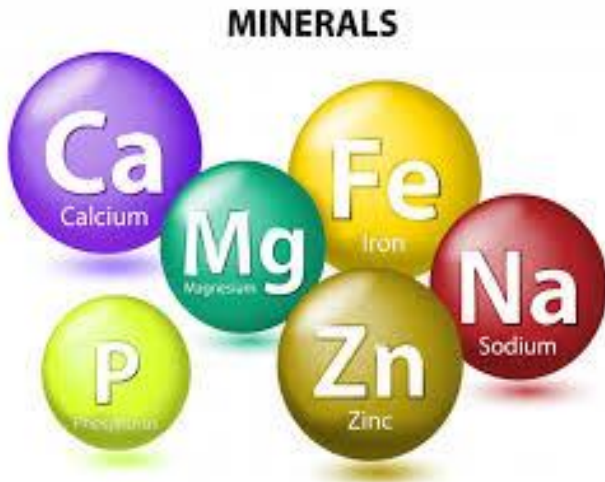
Conflict of interest

- The presenter declares no conflicts of interest
- The presenter is not employed by the particular organisation or any other
- The presenter received no funding or research grants from the organisation

Introduction



Introduction



•Calcium

•Potassium

•Sodium

•Magnesium

Introduction



Functions of Magnesium



Energy production

- Involved in oxidative phosphorylation (ATP production)



Glucose regulation

- Plays a role in glycolysis
- Involved in insulin signalling



Protein synthesis & enzyme function

- Part of 300 enzymatic processes
- Involved in DNA and RNA synthesis
- Protein synthesis
- Glutathione production



Bone structure

- Supports skeletal strength and contributes to the formation of bones and teeth
- Reservoir of exchangeable Mg^{2+}



Muscle contraction

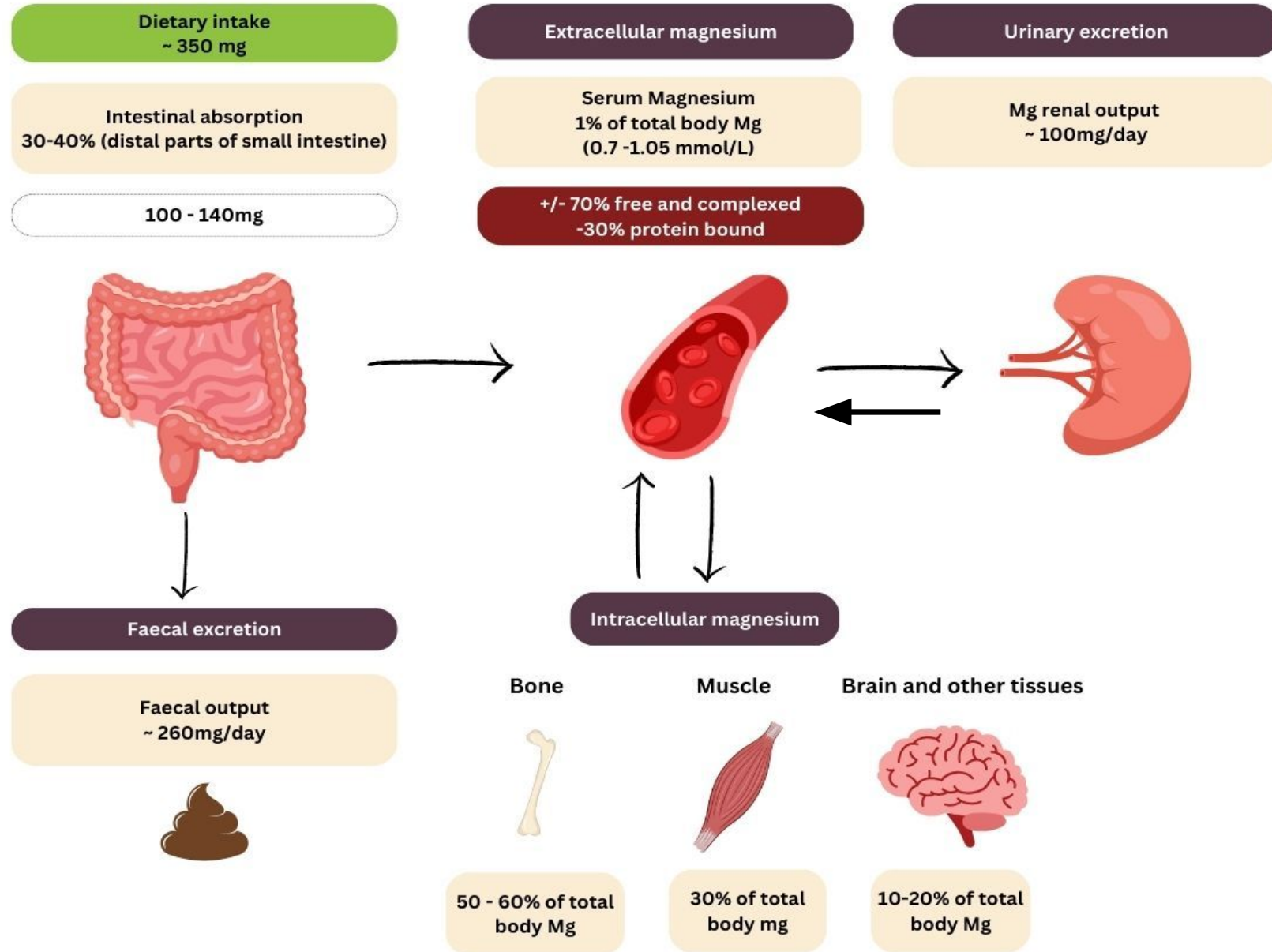
- Involved in muscle contraction > relaxant



Nerve function

- Plays a role in active transport of Ca and K ions across cell membranes
- Cardiac rhythm
- Blood pressure regulation

Total Body Magnesium = 25g



What affects Mg²⁺ absorption in the gut?

- Fermentable or Non-fermentable fibre
- Low or indigestible CHO: inulin, FOS/GOS, resistant starch, mannitol, lactulose
- High calcium intakes
- Excessive alcohol, sodium, soft drinks, coffee
- Serum Vitamin D and B6
- Diuretics, Proton-pump inhibitors, Antibiotics

Magnesium and Mortality

- Definitive link between Mg^{2+} and mortality
- **Higher dietary magnesium intake (+100mg/day) = lower risk of death**

6% lower risk of all cause mortality

5% lower risk of cancer mortality

Magnesium and Mortality – How?

**Maintains genomic
stability**

Reduces inflammation

**Enhances endothelial and
heart function and lipid
metabolism**

DNA synthesis and repair

**Support glucose and
insulin balance**

Anti-platelet effect

Implications of deficiency

Asthma	Cystic Fibrosis	COPD	Liver disease	Vascular calcification	CAD
MI	Arrhythmia	HPT	Muscle cramps	Osteoporosis	Pre-eclampsia
Diabetes	Parkinson's Disease	Brain injury	Stroke	Epilepsy	Depression
Migraine					

Dietary sources of M



Per serving	mg
Pumpkin seeds, 1 TBS (12g)	33
Chia seeds, 1 TBS (10g)	33
Almonds, 10 (10g)	27
Spinach, boiled, 1/2 cup (100g)	80
Cashew nuts, 10 (18g)	50
Black beans, ½ cup (80g)	55
Avocado, ¼ unit	10
Milk, 250ml	28
Oat Bran, raw, ½ cup	55
Rice, brown, cooked, ½ cup	42

Recommended Daily Allowance (RDA) & Intakes

mg	0-6 mo	7-12 mo	1-3 yrs	4-8 yrs	9-13 yrs	14-18 yrs	19-30 yrs	31-50 yrs	> 50 yrs
Males	30	75	80	130	240	410	400	420	420
Females	30	75	80	130	240	360	310	320	320
Pregnancy	-	-	-	-	-	400	350	360	-
Lactation	-	-	-	-	-	360	310	320	-
UL	To be determined	To be determined	65	119	350	350	350	350	350

Institute of Medicine 1997: Food and Nutrition Board: dietary reference intakes for calcium, phosphorus, Vitamin D, fluoride. Washington DC: National Academic Press 1997

Dietary sources of M

RDA: 310-420mg

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Recommended Intakes For ???

- Obesity
- Athletes
- Elderly
- At risk populations:
 - GIT diseases: Crohn's Disease, Coeliac Disease
 - Alcohol dependency
 - T2DM
 - Drugs: PPI, Diuretics, Chemotherapeutic agents, GLP-1

Are we meeting requirements?

USUAL NUTRIENT INTAKE FROM FOOD AND BEVERAGES

What We Eat in America, NHANES

Table H 36. Magnesium (mg): Mean and Percentiles of Usual Intake from Food and Beverages, among Individuals Over 350% of Poverty Level, in the United States, 2013-2016

	N	Mean (SE)	Percentiles							<EAR	
			5th (SE)	10th (SE)	25th (SE)	50th (SE)	75th (SE)	90th (SE)	95th (SE)	EAR	% (SE)
Over 350% poverty											
Males and females:											
1-3.....	191	188 (5)	125* (4)	136 (4)	158 (5)	184 (5)	215 (6)	244 (8)	262* (9)	65	<3
4-8.....	307	221 (5)	148* (4)	161 (5)	187 (5)	217 (5)	252 (7)	286 (8)	308* (9)	110	<3
Males:											
9-13.....	159	275 (8)	164* (9)	184* (8)	221 (8)	267 (8)	321 (10)	375* (14)	412* (17)	200	16 (3.1)
14-18.....	158	298 (8)	180* (8)	202* (8)	241 (7)	289 (8)	346 (10)	407* (14)	444* (17)	340	73 (3.5)
19-50.....	743	367 (6)	199 (5)	227 (6)	283 (6)	354 (6)	438 (7)	523 (9)	579 (10)	350	46 (2.2)
51+.....	672	361 (8)	192 (6)	222 (6)	277 (7)	348 (8)	431 (9)	515 (11)	571 (13)		51 (2.7)
19+.....	1415	364 (6)	196 (6)	225 (6)	280 (6)	351 (6)	435 (7)	519 (9)	575 (11)		48 (2.2)
Females:											
9-13.....	143	249 (6)	145* (7)	164* (7)	199 (6)	242 (6)	292 (8)	344* (12)	380* (15)	200	25 (3.0)
14-18.....	155	233 (5)	133* (7)	152* (7)	184 (6)	227 (5)	274 (6)	325* (9)	357* (12)	300	84 (2.2)
19-50.....	705	301 (4)	178 (4)	199 (4)	241 (4)	293 (4)	352 (5)	413 (6)	455 (7)	265	35 (2.0)
51+.....	618	291 (5)	169 (5)	191 (5)	231 (5)	282 (5)	341 (6)	404 (7)	441 (8)		41 (2.5)
19+.....	1323	296 (4)	173 (4)	194 (4)	236 (4)	287 (4)	347 (4)	408 (6)	448 (7)		38 (1.9)

Advances in Nutrition
Volume 12, Issue 2, March
2021, P 298-304

Recommended Daily Allowance (RDA) & Intakes

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Upper Level – Time for Re-evaluation ?

- **1997 (IOM):** UL for magnesium set at **350 mg/day** from **supplements only** (not including food).
- Rational: few studies found mild GI side effects (cramping & diarrhea) on supplemental doses > 350mg/day
- **2004–2022 (FDA CAERS data):**
 - only 40 GI adverse events
 - only 1/3 involved diarrhea

Upper Level – Time for Re-evaluation

- 2023 Hawaii review

Advances in Nutrition 14 (2023) 973–982



Advances in Nutrition

AN INTERNATIONAL REVIEW JOURNAL

journal homepage: <https://advances.nutrition.org/>



Perspective

Perspective: Call for Re-evaluation of the Tolerable Upper Intake Level for Magnesium Supplementation in Adults



Rebecca Costello^{*}, Andrea Rosanoff, Forrest Nielsen, Christina West

CMER, Center for Magnesium Education and Research, Pahoa, Hawaii, United States



Upper Level – Time for Re-evaluation

- Current **UL of 350 mg/day (supplements only)** = too low, overlapping with amounts needed to **prevent chronic latent Mg deficiency**.
- Hidden **Mg deficiency** ↑ **risk of HPT, CVD, and DM**, even when intakes and serum levels appear “normal.”
- Widespread **underconsumption** flagged in the 2015–2020 U.S. Dietary Guidelines → **higher-dose supplements** often necessary.
- Preventive Mg supplementation could **lower chronic disease risk by 5%** and save >\$3 billion annually in healthcare costs.

Assessment of Mg²⁺ status

- Total serum magnesium (Se-Mg)
 - “Normal”: 0.7 – 1.05mmol/L
 - > 0.85 mmol/L
- Mg excretion in urine (24 hour)
- Red blood cell Mg (RBC-Mg)
 - < 2.5 mmol/L
- Intracellular magnesium?



Assessment of Mg²⁺ status

Other tests

- Oral & IV magnesium loading test
- Hair magnesium content
- Muscle content (biopsy)
- Bone magnesium content
- Ration of ionized to total Mg



Signs of Magnesium Deficiency



Loss of appetite



Peripheral neuropathy



Nausea & Vomiting



Muscle cramps & spasms



Headache



Depression, Anxiety, Irritability



Fatigue



Fibromyalgia



Muscle weakness



Malaise

More serious complications



Seizures



Tremors



Nausea & Vomiting



Personality changes



Ataxia



ECG abnormalities



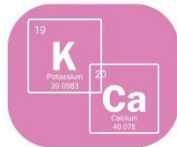
Vertigo



Arrhythmias



Muscle weakness



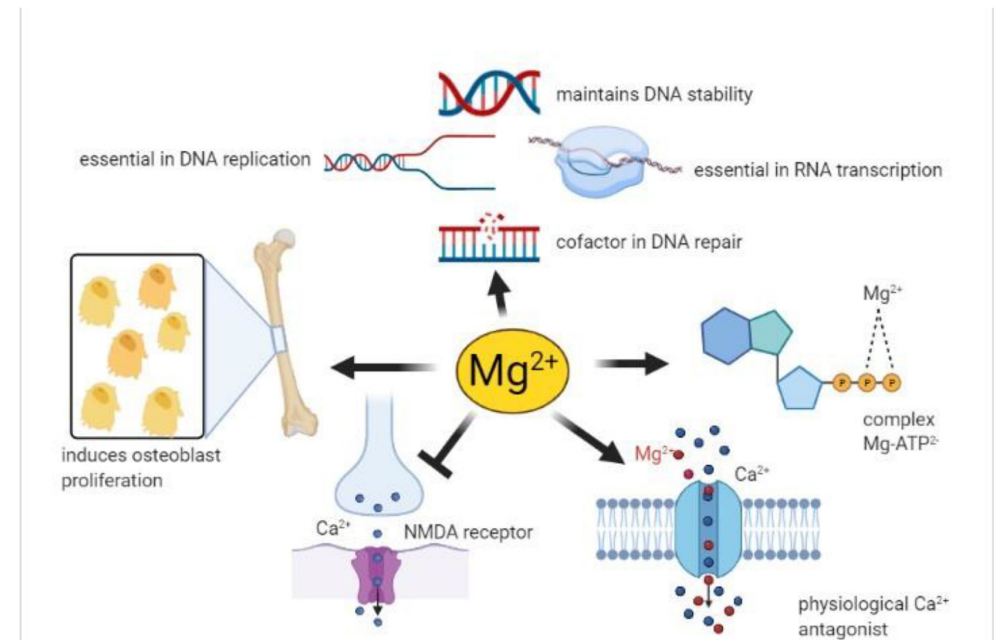
Hypokalemia & Hypocalcemia

At risk groups



Magnesium and Health

- Habitual low intakes of magnesium induce changes in biochemical pathways that increase the risk of illness over time



Cardiovascular Health



Cardiovascular Health



Endothelial NO
synthetase activation
→ boost NO
production

Calcium antagonism
→ reduces smooth
muscle contraction

Anti-inflammatory
and anti-oxidant
effect

Vasodilatory effect

Regulate vascular tone

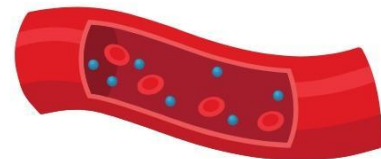
Reduce arterial stiffness

Regulate and enhance
endothelial function

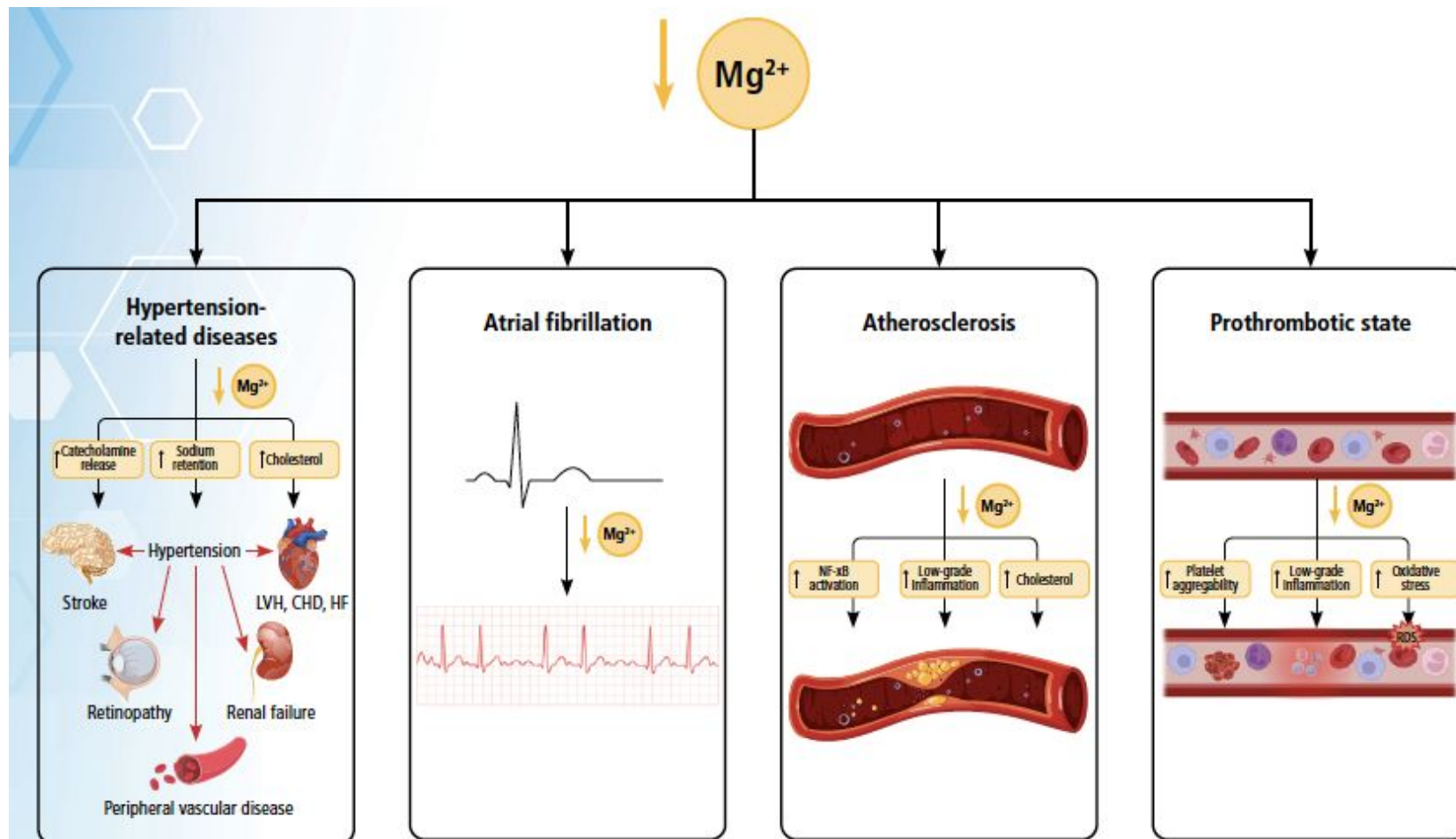
Lower blood pressure

Improved cardiovascular function

Prevents CVA



Cardiovascular Health



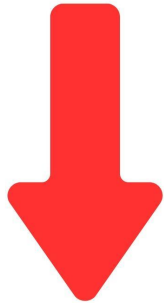
Cardiovascular Health

- **IV** Magnesium: Pre-eclampsia, eclampsia, malignant hypertension
- Oral Mg supplementation: **less clear**
- Inverse relationship between **dietary Mg intake and HPT** prevalence & incidence
- ? Optimal dosage and duration
- Dietary intake: **300 – 600mg**
- Individualised assessment & take CVD medication into consideration

Type 2 Diabetes Mellitus

-  Lower risk of T2DM with higher Mg intake
-  Supports glucose transport & insulin signalling
-  Cofactor in enzymes for glucose metabolism
-  Improves insulin sensitivity & control
-  Supplementation supports metabolic health

Type 2 Diabetes Mellitus



-  Insulin resistance & poor glucose control
-  Reduced insulin sensitivity
-  Chronic low-grade inflammation
-  Increased oxidative stress
-  Linked to T2DM progression & complications

Type 2 Diabetes Mellitus



Low dietary Mg intake



Increased urinary Mg loss
(hyperglycemia,
hyperinsulinemia)



Disrupted Mg transport from
insulin resistance

Despite normal serum magnesium, patients with T2DM often show lower cellular or ionized Mg levels, mainly due to urinary losses and impaired transport.

Magnesium supplementation in T2DM

- Improves **insulin sensitivity, glycemic control,** and **metabolic parameters.**
- Evidence links Mg deficiency with insulin resistance and T2DM development.
- Proposed as a **non-pharmacologic, cost-effective, safe approach.**

Magnesium supplementation in T2DM

- RCTs show modest improvements, though results are inconsistent.
- Meta-analysis of 18 RCTs: **beneficial effects on glucose and insulin sensitivity.**
- Umbrella review: higher Mg intake associated with **reduced T2DM risk.**
- Maintaining adequate Mg (diet or supplements) supports prevention and management.
- Dosage: 300 – 600mg

Bone Health & Osteoporosis

- 🦴 Involved in bone formation & mineralization.
- ⚖️ Regulates osteoblast & osteoclast activity.
- ☀️ Influences parathyroid hormone & vitamin D (calcium homeostasis).
- 📉 Mg deficiency → impaired bone matrix, low BMD, higher fracture risk.
- 🔗 Adequate Mg intake → improved bone density & reduced osteoporosis risk.



Bone Health & Osteoporosis

-  Population studies: Higher Mg intake → higher BMD (men & women).
-  Postmenopausal women: 290 mg/day Mg citrate ↓ bone turnover vs placebo.
-  2024 study: Higher Mg concentration → ↑ compressive strength & fracture toughness.
-  Mg deficiency → skeletal fragility, ↑ bone resorption, ↓ bone formation

Bone Health & Osteoporosis

- 🎯 Recommended intake: 400–800 mg/day Mg for bone health.
- 💊 Supplementation: Shown to ↑ BMD & reduce fracture risk (esp. postmenopausal women).
- 🌱 Works synergistically with calcium & vitamin D.
- 🥗 Best from diet: leafy greens, nuts, seeds, legumes, whole grains.
- 👩 Supplementation should be tailored

Migraine



Migraine

-  Small placebo-controlled trials: up to 600 mg/day Mg modestly reduced headache frequency.
-  Review on migraine prophylaxis: 300 mg Mg twice daily may help prevent migraines.
-  American Academy of Neurology & American Headache Association: Mg is “probably effective” for migraine prevention (under medical supervision).
-  Meta-analysis (789 participants): Oral Mg reduced frequency & intensity of attacks

Sport & Exercise

- Higher amounts commonly recommended
- Chronic inflammatory response
- Inadequate dietary intake & excessive losses
 - Sweat: 1.25 – 15 mmol/L
 - 1L sweat increase requirements 15 – 30%
 - Increased urinary excretion



Sport & Exercise

Healthy adults
Mg glycinate
350mg/daily



10 days



Reduction in
muscle
soreness

GLP-1 receptor agonists

- Growing utilization & efficacy
- Challenges and side effects:
 - Gastro-intestinal side effects: diarrhea, nausea, vomiting, GOR, constipation
 - Risk of inadequate nutrient intake & micronutrient deficiencies
 - Insufficient patient counseling and guidance



GLP-1 receptor agonists

- Nutritional deficiencies
 - Calorie reductions of 16 – 39%
 - Micronutrient deficiencies of concern iron, calcium, magnesium, zinc, and vitamins A, D, E, K, B1, B12, and C
 - Impact of obesity per se on micro-nutrient status
- Bone loss and affected bone density

GLP-1 receptor agonists

- No official guideline- to date – on Mg supplementation alongside GLP-1
- Early trials show Mg intake < DRI
- Magnesium supplementation may support glycemic control and CVD health along-side GLP-1s



Magnesium and other conditions

- Mental health & Psychiatric conditions
- Hormone Health: PMS, Dysmenorrhea, Menopause
- Sleep & Melatonin production
- Constipation
- Oncology

Supplements

Soluble Organic compounds		Inorganic salts	
Salts	Amino Acids Chelates	Soluble	Insoluble
Magnesium Citrate	Magnesium Bis-glycinate	Magnesium Chloride	Magnesium Oxide
Magnesium Glycerophosphate	Magnesium L-Threonate	Magnesium Sulphate	Magnesium Carbonate
Magnesium Malate			Magnesium Hydroxide
Magnesium Gluconate			
Magnesium Lactate			
Magnesium Fumerate			

Supplements

Inorganic Salts

- Low solubility in water
- Low Bioavailability
- 4% absorption in GIT

- Most common
- Provides high amount of elemental Mg
- Use has natural laxative

Mg Oxide

- Insoluble
- Extremely low bioavailability

Mg Carbonate

- High solubility in water
- Good bioavailability
- 20% absorption GIT absorption

Mg Chloride

- Epsom salts
- Commonly used for pre-eclampsia (IV)

- 4% oral absorption
- Moderately soluble in water
- Toxic in RF via IV

Mg Sulphate

- Practically insoluble

Mg Hydroxide

Supplements

Organic Compounds

- Good bioavailability and solubility
- 30% absorption

Mg Citrate

- Good solubility & good bioavailability
- 20% oral absorption
- Higher dose supplements

Mg Bis-Glycinate

- Newest compound
- Crosses the blood brain barrier
- Research is limited

Mg L-Threonate

Supplements

- Transdermal magnesium
 - Cream
 - Spray
 - Oil
 - Magnesium salt baths (abdominal pain, constipation, sore muscles)
 - (not to be ingested orally)

Supplements

- Dosage
- Label reading
- Directions
- Bio-availability
- Other supplements or nutrients



GRAXCELL
PHARMACEUTICAL, LLC.

NDC 70795-1151-2

Magnesium Oxide
400 mg

Magnesium Supplement

Supplement Facts

Serving Size: 1 tablet
Servings Per Container: 120

Amount per serving	% Daily Value*
Magnesium 241.5 mg (from 400 mg of Magnesium Oxide)	60%

*Percent daily value according to USRDI.

OTHER INGREDIENTS: Microcrystalline Cellulose, Corn Starch, Magnesium Stearate

USES: Helps maintain muscle and nerve function and normal heart rhythm & blood pressure. Helps absorption of calcium and potassium

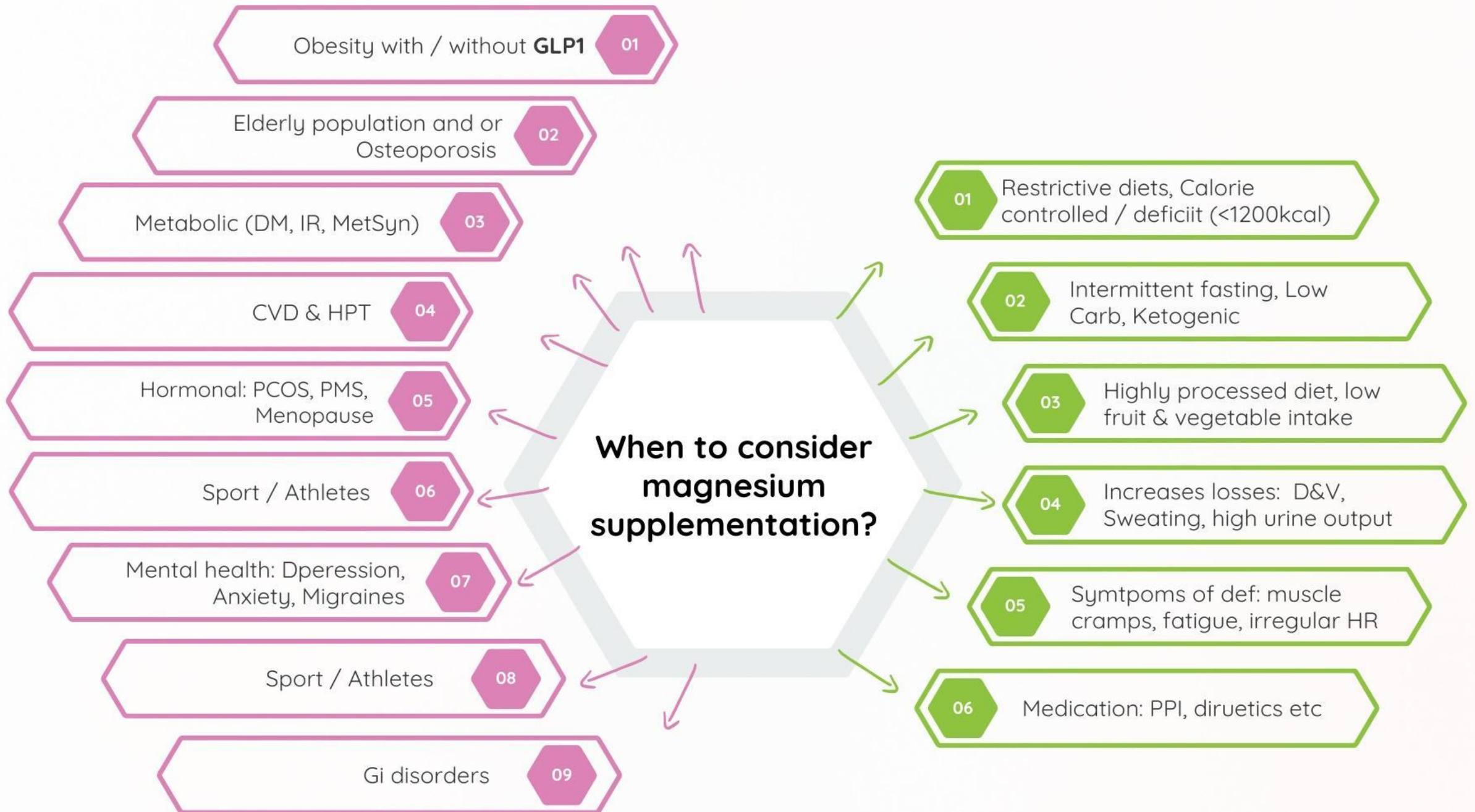
DRUG INTERACTION PRECAUTIONS: This product may interact with certain prescription drugs. If you are presently taking a prescription drug, do not take this product without consulting your doctor or other health professional.

WARNINGS: Not recommended for use in amounts over the recommended daily intake of 400 mg per day (1 tablet). Ask a doctor or pharmacist before use if you have a known allergy to this product. Stop use and contact a doctor if allergic reaction.

Side-effects and health risks

- Efficient kidney excretion
- Diarrhea
- Magnesium toxicity





Practicalities

- Common dosages in clinical trials: **200-600mg per day**
- Can be given in **split dosages** if GI side effects
- Form matters:
 - **Glycinate and Citrate** yield higher bioavailability
 - Oxide, hydroxide, citrate when osmotic effect is desired (i.e constipation)
- **Timing:** separate by 2+hours from levothyroxine, tetracyclines, bisphosphonates to avoid chelation

Practicalities

- **Caution:**

- eGFR < 30mL/min/1.73m², significant CKD
- Chronic use of laxatives, antacids
- Potassium-sparing diuretics

- **Pregnancy:**

- not to conflate oral Mg with IV for pre-eclampsia
- Generally safe, start with lower dosages

- **Children**

- Generally safe in lower dosages
- Best avoid in children < 2 years
- Magnesium salt baths for muscle cramps, sleep issues, constipation
- Active older children

Summary

- Magnesium plays a key role in almost all biological processes
- Numerous factors can give rise to magnesium deficiency, which is associated with increased morbidity and mortality risk
- Hypomagnesemia has been associated with many diseases especially in at risk populations
- Adequate dietary consumption and supplementation of Mg²⁺ have demonstrated beneficial effects on various comorbidity risk factors and may have practical importance for public health

Thank you

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