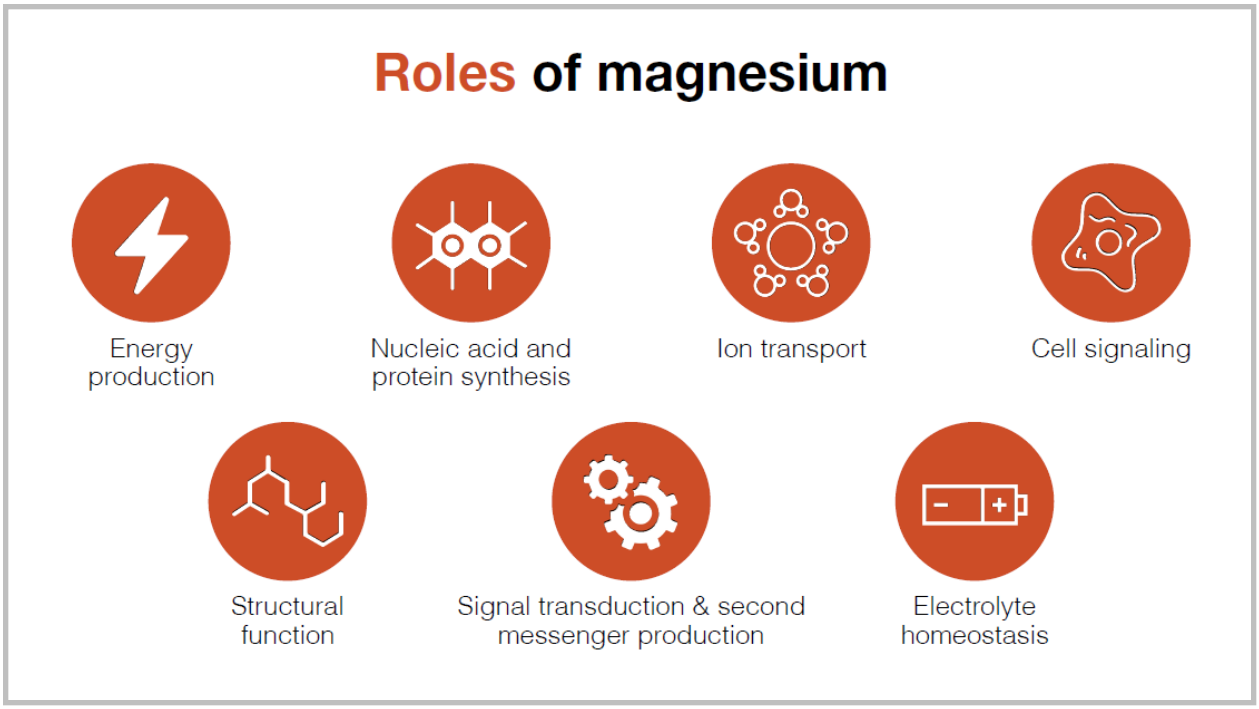
KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

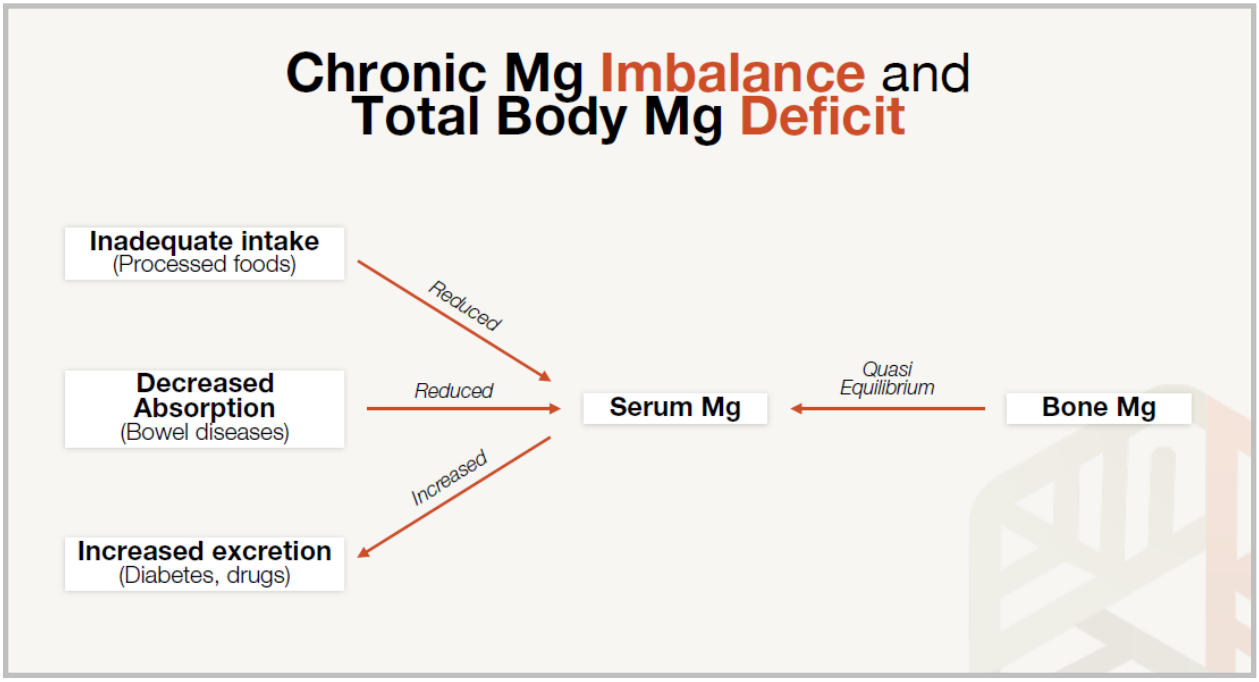
# Magnesium Deficiency - Part One

Hey, everybody. In this presentation, we're going to discuss magnesium deficiency.

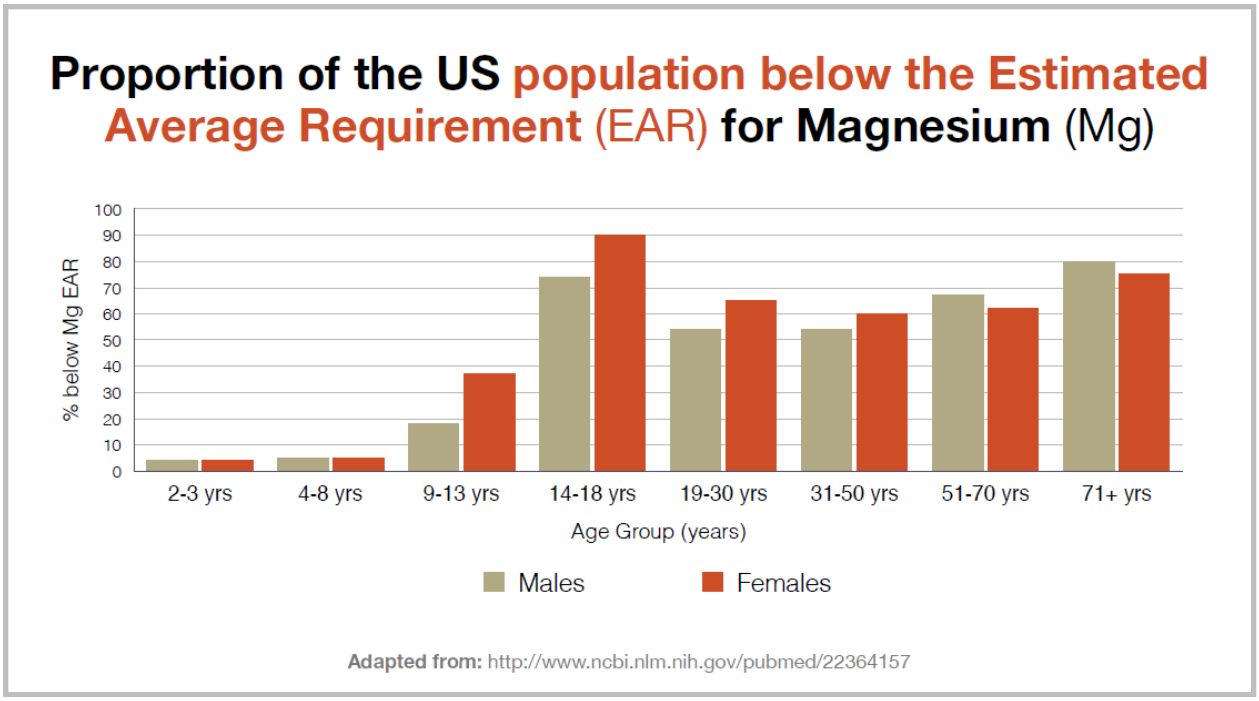



Magnesium is an essential mineral and cofactor for hundreds of enzymes. It's involved in many physiological pathways, including energy production, nucleic acid and protein synthesis, ion transport, and cell signalling, and it also has structural functions. It's the fourth most abundant mineral in the body after calcium, potassium, and sodium. It's required for the function of kinases. It's necessary for phosphorylation. It turns many protein enzymes on and off, thereby altering their function and activity, and over 30 percent of body proteins are activated by magnesium-dependent kinases.

Magnesium is crucial for regulating cell cycles and growth, as well as apoptosis, cell death. It plays a vital role in signal transection and the production and action of second messengers such as cAMP and cGMP, and it plays an important role in electrolyte homeostasis. For example, chronic magnesium deficiency may lead to refractory hypokalemia and hypocalcemia, and these won't improve with potassium or calcium supplementation alone.

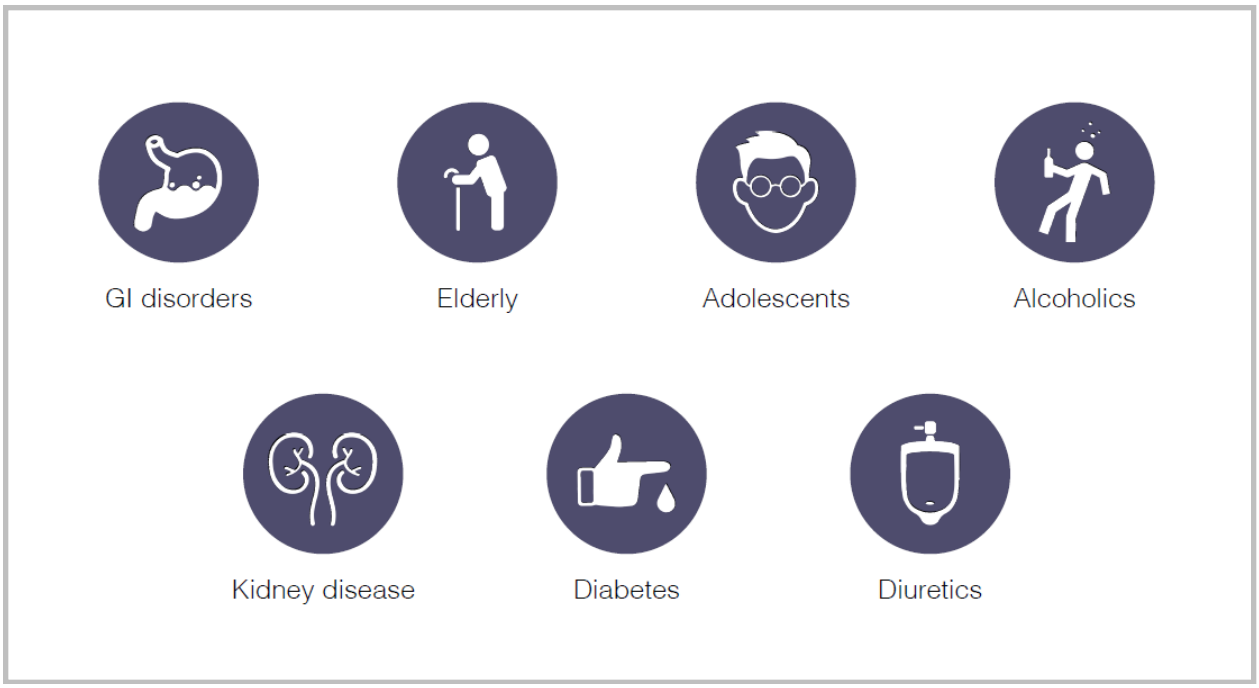



Magnesium deficiency is one of the most common nutrient deficiencies in the U.S. and likely in the industrialized world. Almost half of the U.S. population consumed less than the required amount of magnesium from food in 2005 and 2006, and such findings along with lab results, as we'll see, suggest that marginal magnesium deficiency may be more common than not in the U.S. There are three primary causes of magnesium deficiency: inadequate intake, decreased absorption, and increased excretion.

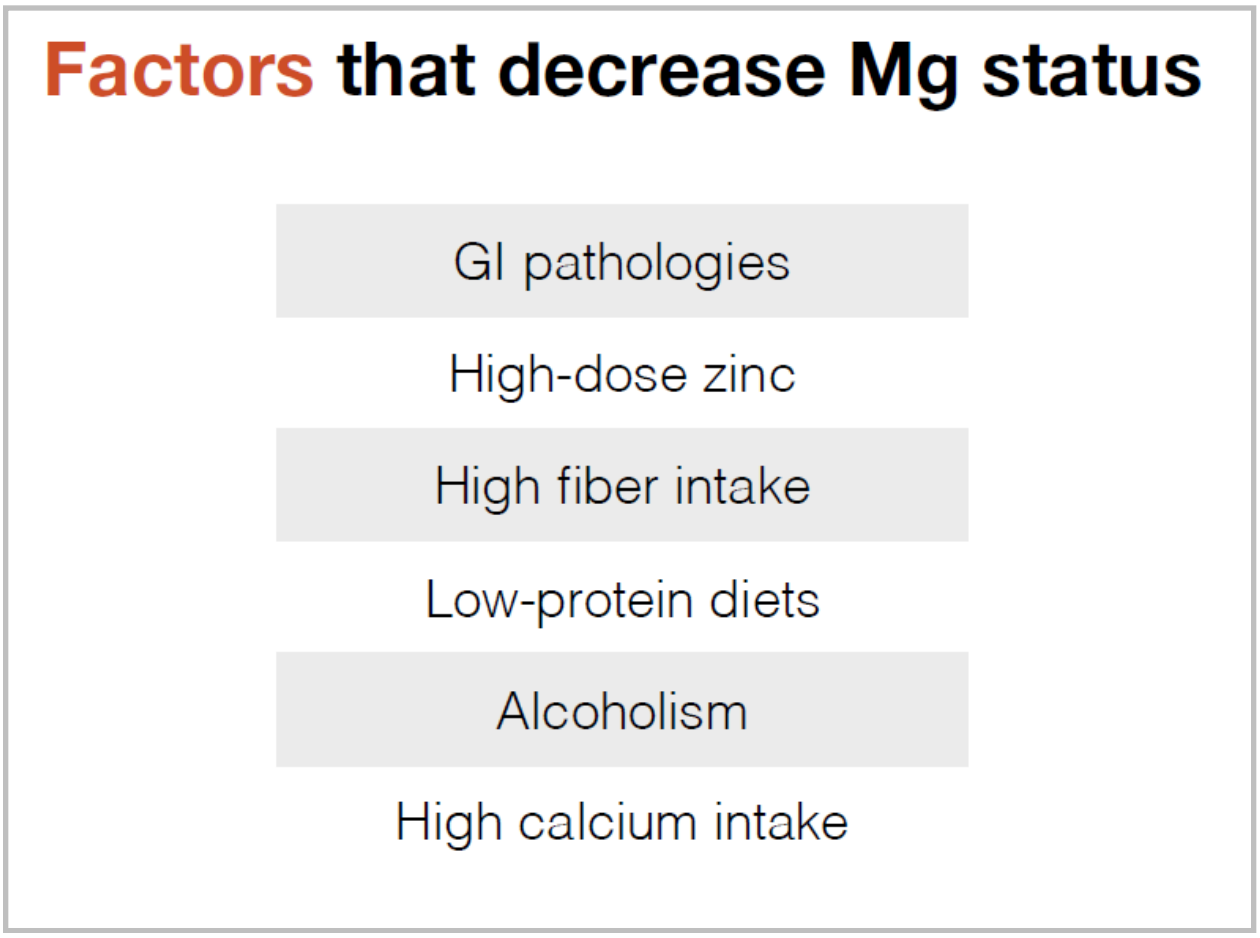


The recommended daily intake is 320 to 420 mg per day for adults, or 6 mg/kg of body weight for both genders. A large U.S. national survey indicated that average magnesium intake is about 350 mg per day for men and about 260 mg per day for women, which is significantly below the current recommended dietary allowance. Magnesium intake was even lower in men and women over 50 years of age. Another study of 37,000 Americans found that 39 percent ingested less than 70 percent of the RDA, and 10 percent of women over 70 years old consumed less than 42 percent of the RDA. Finally, three USDA surveys over five years found that between 50 and 90 percent of adolescent boys and girls and adult men and women fall below the average requirement for dietary intake of magnesium.

In part, this is due to soil depletion, but in part, it's also due to a reduction in the consumption of nutrient-dense wild plant foods. The cultivated plants that we eat today don't contain as much magnesium as the wild plants that our ancestors ate.




Populations that are at risk for magnesium deficiency seemingly include just about everybody. It includes people with GI disorders, which, as we know, is a large number of people; the elderly; adolescents; alcoholics; people with kidney disease; people with diabetes; and people who are taking diuretics. If you look at the chart on the last slide, you see that nearly everybody, except young kids, doesn't get enough magnesium in their diet, but you need to pay special attention to the populations that are listed on this slide.




Magnesium absorption may be decreased by GI pathologies such as IBD, celiac, and SIBO. Very high-dose zinc, very high-fiber intake, and low-protein diets below 30 g per day also decrease magnesium absorption. Magnesium absorption is decreased in alcoholics. Studies have shown that high dietary calcium-to-magnesium ratios above 2.8 can be detrimental to magnesium status. Between 1977 and 2012, U.S. calcium intake increased at a rate 2 to 2.5 times that of magnesium intake, resulting in a dietary calcium-to-magnesium ratio of above 3.0.

In addition, magnesium is a cofactor for vitamin D biosynthesis, transport, and activation. When you put together increasing calcium-to-magnesium intake ratios, along with an increase in calcium supplementation and vitamin D supplementation, which affects calcium levels, with suboptimal magnesium intake, that is not a good combination. It's a growing problem because oral vitamin D supplements are increasingly recommended, and many people are still taking calcium supplements despite the fact that more recent research has shown them to be not only not beneficial but probably harmful. This is just another example of how important nutrient balance is and why it is better to get nutrients from food than supplements whenever possible.

Increased excretion of magnesium occurs primarily with diabetes and diuretic drugs that cause increased urination.

Magnesium deficiency is associated with a wide variety of pathologies and diseases from type 2 diabetes to metabolic syndrome to elevated C-reactive protein, hypertension, atherosclerotic vascular disease, sudden cardiac death, osteoporosis, migraine headache, asthma, and colon cancer. One recent study showed that among women with breast cancer, those with higher dietary intake of magnesium had 50 percent lower mortality rates. Inadequate blood magnesium levels are known to result in low blood calcium levels, resistance to parathyroid hormone, and resistance to some of the effects of vitamin D.

Magnesium supplements have been shown to reduce pregnancy complications such as preeclampsia, reduce blood pressure, decrease risk of death after heart attack, improve endothelial function, improve insulin sensitivity, reduce migraines, and improve lung function in asthmatics. This is just a partial list of the benefits of magnesium.

## Signs & symptoms of Mg deficiency

| Early | Late | |
|---|---|---|
| Loss of appetite | Hypomagnesia | Hypertension |
| Headache | Hypocalcemia | CVD |
| Nausea | Hypokalemia | Pregnancy complications |
| Fatigue | Sodium retention | Infertility |
| Weakness | Low serum PTH | Neurological/muscular |
| | Osteoporosis | Personality changes |
| | Diabetes | Vomiting |

Early signs of magnesium deficiency include loss of appetite, headache, nausea, fatigue, and weakness. As magnesium deficiency progresses, you may see decreased serum magnesium levels below the lab range; decreased serum calcium levels even with adequate calcium intake; low serum potassium levels, hypokalemia; retention of sodium; low circulating levels of parathyroid hormone; osteoporosis; diabetes; hypertension; cardiovascular disease; pregnancy complications; infertility; neurological and muscular symptoms; vomiting; and personality changes.

**Less than 1% of magnesium is found in serum.**

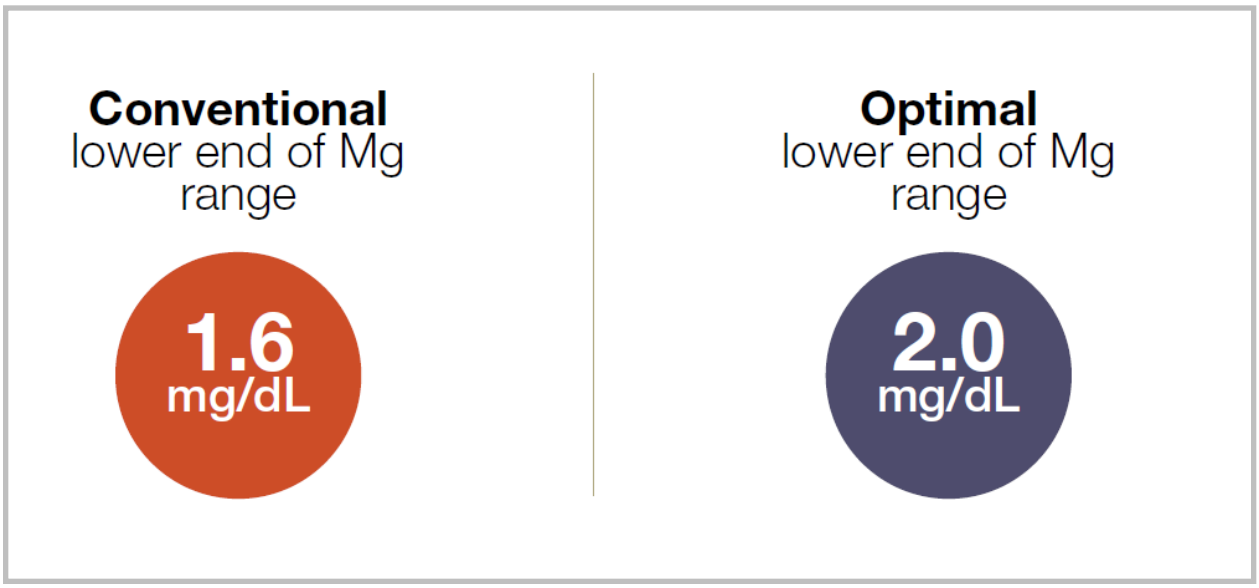
As has been the case with many other markers discussed in blood chemistry sections so far, the lab range for magnesium is not accurate. Over 60 percent of the magnesium in the body is found in the skeleton, about 27 percent is found in the muscle, 6 to 7 percent is found in other cells, and less than 1 percent is found outside of the cells in the serum. Therefore, serum magnesium is not necessarily an accurate representation of what is in the soft tissue and inside of the cells where it is used and needed. The reference range was determined in a U.S. population of 15,820 individuals aged 18 to 74 in the NHANES I cohort, and it resulted in a lab reference range of 1.8 to 2.3. LabCorp's reference range, Kaiser, and many other labs' ranges are much broader now. LabCorp's is 1.6 to 2.5 at the time of this recording. There is no explanation that I know of for making the range even broader than it was in that original study, especially because we know that the majority of adults in the U.S. do not consume enough magnesium, and defining a reference range from a population with an intake of magnesium below the RDA is not a very good idea.

## Clinical Mg deficiency at various serum Mg levels

| **Serum Mg level** (mg/dL) | **% with clinical Mg deficiency** |
|---|---|
| **1.7** | 90 |
| **1.85** | 50 |
| **1.95** | 10 |
| **2.2** | 1 |

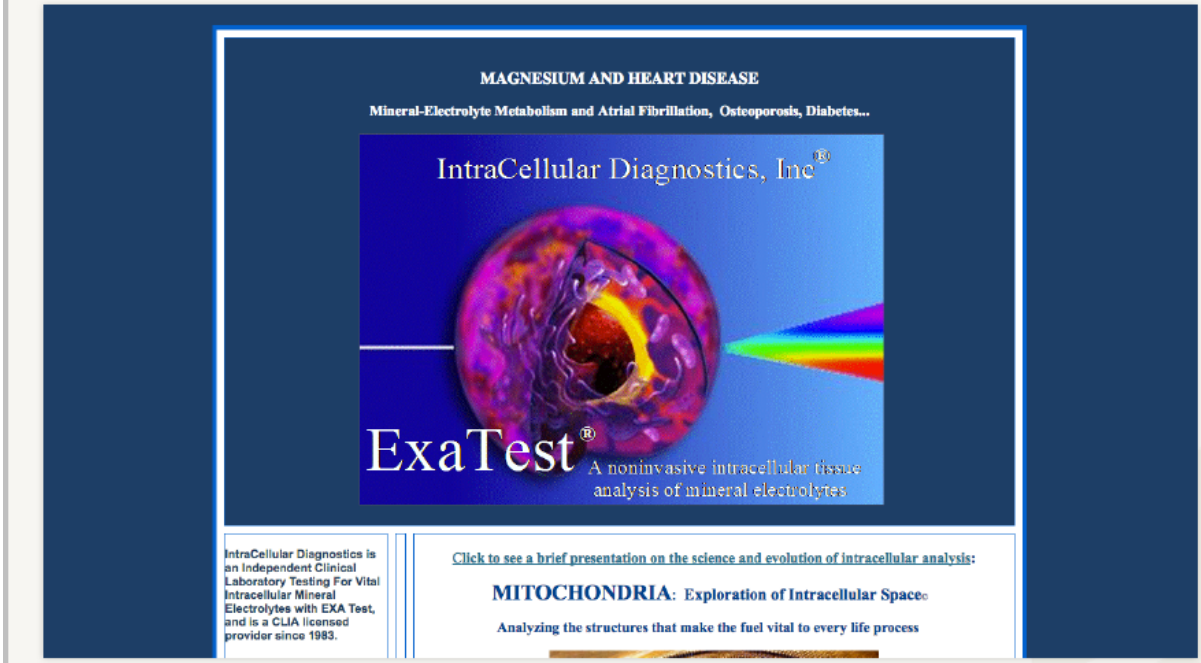
**Reference:** http://www.ncbi.nlm.nih.gov/pubmed/20736141

This explains why a study in Europe found that 90 percent of people with a serum magnesium concentration of 1.7 mg/dL had clinical magnesium deficiency. At 1.85, 50 percent were deficient. At a cutoff of 1.95, only 10 percent had deficiency, and at a cutoff of 2.2, only 1 percent had deficiency. This suggests that a lower end of the range for magnesium of maybe 2.0 or 2.1 is best from a functional perspective.




A cohort of nearly 10,000 participants in the NHANES I study was followed for 18 years, and 690 participants developed type 2 diabetes. Those with magnesium between 1.95 and 2.04 had a 20 percent higher risk of developing diabetes than those with a magnesium above 2.04. Those with a serum magnesium below 1.95 had a 50 percent higher risk of developing diabetes.

In another study, individuals between the ages of 20 and 65 were screened with a fasting blood glucose, glucose tolerance test, and a serum magnesium and were excluded from the study if any of those tests were abnormal. In the 817 people with normal glucose control who remained, there was a greater risk of impaired fasting glucose 10 years later with a serum magnesium of below 2.04 and a greater risk of future impaired glucose tolerance test with a serum magnesium below 1.95. Both of these studies support the lower end of magnesium range of 2.0 that I proposed earlier, and this is what I've chosen as my functional range.




Unfortunately, there are no other great markers that are commercially available for magnesium status. There is a urine magnesium loading test where IV magnesium is given, and the excretion of magnesium is measured in urine over a 24-hour period. That's the gold standard, but it's not available widely and not very practical. Red blood cell magnesium has not been shown to be more accurate than serum magnesium. Again, only about 6 percent of magnesium is in blood cells, and the rest is in tissue and bone. There is one test, the ExaTest, that measures magnesium concentration in sublingual epithelial cells using a cheek swab, but the results correlate with heart, muscle, and deep organ tissue, so this is probably a more accurate result, but it's not widely available, and it's pretty expensive. It's over $200 for just one test at the time of this recording. I think it's better to just use the serum magnesium cutoffs that I discussed and do therapeutic trials of magnesium supplementation.