

Review of: "Magnesium and Longevity"

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Potential competing interests: No potential competing interests to declare.

Comments on Qeios Review Magnesium and Longevity

by **Patrick Chambers**

Overall

Overall, an excellent and thoughtful review of the wide and complex functionality of Mg and its relationship with longevity, including the involvement of Ca and Ca:Mg, which, as the author says, is not often discussed or measured but is crucial. It was also good to see detail on the role of Mg in relation to vitamin D synthesis and perhaps more crucially, for both key stages of vitamin D activation.

One topic that was not discussed is the role of Mg as a cofactor for the enzymes necessary for the synthesis of the bone matrix and its role in bone formation. This was possibly due to the outcome of these processes not being directly related to longevity, but through its impact on bone health/strength, it certainly has an impact on the healthspan since the major psychological and physical impacts that bone breakages have on the old can hasten mortality. The suggestion to include something on this topic is obviously the author's decision but would perhaps be of interest to many readers.

Another related topic which was only touched on briefly is that concerning dietary recommendations for Mg and Ca. Simply put, are the current recommendations for these nutrients satisfactory, or do they need to be increased or adjusted with more attention to Ca:Mg? As mentioned, dietary intake targets are frequently not achieved for a variety of reasons. So, some comment on current recommendations would be valuable (see below re p.7 and 8)

General comments or queries on parts of the text

Page 1. Heart rate variability: Confirm that this is resting rate variability and if greater variability is associated with reduced lifespan?

Page 2. Half of Americans are deficient in Mg; this partly relates to my comment above on dietary recommendations, but do the data indicate any influence of age/sex? In the UK, we have great concern about Mg intake by adolescent females, where more than 50% have Mg intakes less than the Lower Reference Nutrient Intake, which satisfies the requirement of only the bottom 2.5% of the population. Any such information in US data would be useful.

Page 2: In the microbiome paragraph 1, references for the preservation of insulin sensitivity and the impact of insulin resistance on cancer, T2 diabetes, and dementia would be useful.

Page 2. The last but one line of the secondary bile acids last paragraph refers to 'Mg levels,' which also appears throughout the text. The meaning of this can be confusing. It can refer to status, dietary intake, or serum concentrations (which may indicate status). The context on page 2 suggests it is serum concentration, which declines with age, but more specific terms would be helpful.

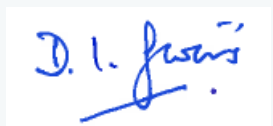
Page 4. Figure 2 is great, but since haem Fe is also a cofactor for enzymes (Cyto P450 family) involved in both hydroxylation stages, are there any indications of an interaction between Mg and Fe?

Page 5. Most journals now ask for the generic use of 'calorie' to be replaced with 'energy.' This coincides with energy being expressed in SI units (kJ/MJ).

Page 6, second line. 'Mg level is positively related to HRV.' As above, does Mg level mean serum Mg concentration or Mg nutritional status? But a positive relationship implies that higher Mg status is associated with greater HRV. But is greater HRV not related to a shorter lifespan? Apologies if I misunderstand.

Page 7, the penultimate sentence indicates that intake of Ca:Mg has increased substantially in recent times, with the implication that this is primarily due to increased Ca intake. However, on page 8, the penultimate sentence of the Ca:Mg section states that 42% of Americans do not meet their EAR for Ca. This seems contradictory to the previous statement. It would be helpful to clarify the current situation of Ca and Mg intake relative to recommended intakes. Also, if the outcome of this (or serum data) highlights a need to reduce the Ca:Mg ratio, indicate whether this should be done by increasing Mg intake, reducing Ca intake, or a combination of both. This would also have relevance in the conclusion.

I hope these comments are helpful.

A handwritten signature in blue ink, reading "D. I. Givens", is centered within a white rectangular box. This box is itself centered within a larger, light gray rectangular area.

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