

Reviewer's report

Title: Phosphate decreases urine calcium and increases calcium balance: A meta-analysis of the osteoporosis acid-ash diet hypothesis

Version: 1 **Date:** 15 May 2009

Reviewer: Michael Huncharek

Reviewer's report:

Thank you for allowing me to review this manuscript and I'm sorry for the delay in getting it back to you.

The authors discuss an important topic, the paper is well written and generally well structured although I think there are some changes needed in the Methods and Results section.

I also need to make several initial important points. I am an oncologist/cancer epidemiologist and NOT an expert in bone metabolism/bone health. In my career, I've published only a single paper dealing with issues of dietary intake and bone health (see Huncharek, BONE, 2007). For the cited analysis, I had the assistance of several consultant experts in calcium and bone metabolism since none of my co-authors had the necessary relevant background.

Because of the above noted lack of expertise, it simply is not possible for me to comment on the most important aspects of the submitted paper. The issues are simply not within my knowledge-base. I can suggest a number of reviewers that would be quite capable in addressing the physiological issues discussed in the manuscript, if necessary.

Here, I will make some general comments and then some more specific ones regarding meta-analysis.

MINOR ESSENTIAL REVISIONS

On page 6 of the paper, the "Description of Studies" section, in my opinion, should be in the RESULTS section of the paper and not in the METHODS. The authors are describing the results of the literature search and this clearly should not be in the METHODS section.

On pages 4-5, the authors describe their selection of studies/search strategy etc. On page 5 they state that the lit search was not limited by study design and then under "Selection criteria for the literature" they subsequently state, "...studies with an observational design were not included since they were likely to have confounded effects...". This is inconsistent and the authors need to clarify exactly what was included and the justification for their choices.

MAJOR COMPULSORY REVISIONS

On page 7, the “Regression analysis methods” section is inadequate. I’ve pasted a reference below that the authors should review regarding the use of meta-regression from AHRQ.

Meta-Regression is complicated and not without multiple methodological issues that need to be assessed when interpreting results using these techniques. A far more complete description of what the authors did, and why, is needed. The AHRQ document helps flesh some of these out and there are other relevant references that the authors could use as well. There is no discussion of heterogeneity, for instance, in the manuscript nor is there any discussion of specific statistical models used etc. I feel this is a major shortcoming that needs to be addressed since it brings into question the validity of the presented results.

In my own work, I do not employ regression techniques. There are numerous reasons for this although the major reason is the nature of the data-sets I analyze. Meta-regression is also an evolving field that is, to some extent, still in its infancy and not all investigators are fully comfortable with its theoretical basis and its practical application.

I can suggest some experts in this field that would be able to provide a more in depth discussion of these issues. Jesse Berlin, for instance, would be a major figure that comes to mind.

I feel that lack of description and discussion of the statistical methods used by the authors is a major limitation of the manuscript and makes interpretation of the results difficult. I personally feel, that, in its present form, the manuscript should be substantially revised in this respect before it could be suitable for publication. Having the paper reviewed by some one such as Berlin, or others, could be useful and would be helpful to both the editors and the authors.

I regret that I cannot comment in more detail on the physiological arguments presented in the paper. These issues are simply outside my area of training and expertise. I think the statistical methods issues are important ones and need to be addressed before the journal should move ahead with making any decision on suitability for publication.

I hope these comments are helpful.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.