Reviewer's report

Title: Low urine pH and acid excretion do not predict bone fractures or the loss of bone mineral density: a prospective cohort study

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Reviewer: Jean-Phillipe Bonjour

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This is an important and timely study submitted by experts in the field of epidemiology in calcium-phosphate metabolism and bone health. The following points deserve to be considered by the authors.

P.2 Abstract, Methods. The first sentence specifying: “…..to examine associations between acid excretion measures in fasting morning urine pH and urine acid excretion and for the incidence of fractures…..“ is confusing; it should be clearly rewritten. Likewise, regarding the sentence describing the association between urinary pH or acid excretion and changes in BMD as evaluated by multiple linear regression.

P.5, 2nd §. The method to estimate the urinary excretion of organic acids should be briefly described for the reader not familiar with the article published by Berkemeyer and Remer (Reference 36, J Nutr 2006 ; 136 : 1203-1208). That the urinary excretion of organic acids (including citric acid, oxalic acid, malic acid, succinic acid and lactic acid, as well as anionic amino acids, glutamic and aspartic acid) can be estimated from anthropometric body surface area (with R2 varying from 0.15 to 0.39 according to reference 36, in which is reported a study carried out in children, adolescents and young adults) is not so obvious, to say the least ! However, even if this estimate can be questioned from physiological viewpoint, the authors are right to include it in the calculation, since it is used by the “defenders” of the hypothesis that considers the potential acid load of the diet as a risk factor for osteoporosis.

P.6. 1rst §. The two sentences referring to missing values and the indicator variables used to retain the sample size is not clear.

Table 1. The number of kidney diseases should be checked, since it appears odd that it would be greater in the BMD (n=119) than the Fracture study (n=118).

P.6. Results. 2nd §, as well as Table 3 and Figure 3. BMD changes do not appear to be consistent between the text on p.6, and Table 3. The time during which the BMD changes were recorded (whether one or five years ?) should be indicated. The variance whether SD or SEM should be indicated in the leghents of Table 2, and 3. Figure 3 : the Dotplot distribution of BMD changes should be better introduced so that the reader can capture the key message which is supposed to be conveyed by this illustration. If the authors cannot deem what this figure adds to the data presented in both the result section on p. 6 and in Table 3 it would be better not to maintaining it in the paper.
P.6. 3rd §. The age distribution of the subjects having experienced a fragility (and other fractures which could not be considered as probably due to bone tissue structural weakness) fracture during the follow-up observational years should be indicated, since the lowest age limit was 25 years (p.4), an early age at which fragility fractures are very unlikely to be experienced. Were the 46 “confirmed” fragility fractures (Table 3) recorded in subjects over 50 years of age? In the result section or in complement to Table 3, information on the distribution of the fractured skeletal sites (forearm, hip, spine, humerus, others?) should also be provided for both confirmed and not confirmed fragility fractures.

P.7 and Table 5. It would be of interest to document which of the various confounding variables (age, gender, family history of osteoporosis, etc) introduced in the adjusted models are particularly important to make the relationships between FN BMD changes and either urine pH or urine acid excretion no more statistically significant.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interest with the content of this manuscript