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## Meta-analysis of the effect of the acid-ash hypothesis of osteoporosis on calcium balance

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### CRD summary

This review evaluated the effects of diet manipulation on urine calcium, calcium balance and bone health in healthy adults. The authors concluded that increasing diet acid load did not promote skeletal bone mineral loss or osteoporosis. The review had several potential methodological limitations, including unclear quality of included studies, and so the reliability of the authors' conclusion is uncertain.

### Authors' objectives

To evaluate the effects of diet manipulation on urine calcium, calcium balance and bone health in healthy adults.

### Searching

MEDLINE, EMBASE, CINAHL, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (CENTRAL) were searched without language restrictions from inception to January 2009. Search terms were reported. Reference lists were scanned for additional studies.

### Study selection

Studies of healthy adults randomised to receive dietary manipulation (based on the acid-ash hypothesis) of acid-base intake through foods or supplemental salts to change urine net acid excretion were eligible for inclusion in the review. The eligible outcome was calcium balance, defined as calcium intake minus excretion. Interventions had to comply with recommendations from the Institute of Medicine Panel on Calcium and Related Nutrients for calcium studies. Participants with chronic conditions (such as renal diseases, diabetic ketoacidosis and any other condition that could alter calcium excretion) were excluded.

Most study participants were women. All included studies manipulated the amount and/or type of protein and compared adequate intakes with higher intakes. The calcium balance methodology for each study was reported in the paper. Urine net acid excretion (mEq/day), urine calcium (mmol/day), calcium balance (mmol/day) and a marker of bone metabolism (percentage change of N-terminal telopeptides) were measured.

The authors did not state how many reviewers selected the studies.

### Assessment of study quality

The authors did not state that they assessed validity.

### Data extraction

Data were extracted on changes in urine net acid excretion, urinary calcium, calcium balance, and the marker of bone metabolism (percentage change of N-telopeptides). Outcome measures were not specified. Study investigators were contacted for clarification, where necessary.

The authors did not state how many reviewers carried out data extraction.

### Methods of synthesis

A regression analysis was conducted, weighted by sample size, to explore the dose-response relationship between changes in urine net acid excretion and urinary calcium, calcium balance and the marker of bone metabolism. Results were presented as  $B_1$  (the slope coefficient) and the 95% confidence interval (CI).

### Results of the review

Five randomised cross-over design studies (133 participants) were included in the review. There were 77 balance study crossover comparisons.

Change in urine net acid excretion ranged from a decrease of 24mEq/day to an increase of 29mEq/day (range 54mEq/day). Regression analysis showed that while there was a statistically significant linear relationship between urine net acid excretion and urine calcium ( $B_1$  0.029, 95% CI 0.023 to 0.035), there was no relationship between net acid excretion and change in calcium balance or change in the marker of bone metabolism.

### Authors' conclusions

Increased urine calcium associated with increased urine net acid excretion did not represent loss of whole body calcium. Therefore, increasing the diet acid load did not promote skeletal bone mineral loss or osteoporosis.

### CRD commentary

The review question was clear and inclusion criteria were detailed for all aspects. A number of relevant data sources were accessed and attempts were made to minimise language bias. There was no apparent search for unpublished material and publication bias was not formally assessed, which meant that some bias in this respect was a possibility. The review process was poorly reported, which made it difficult to judge whether there were attempts to minimise error and bias. The absence of any systematic method of assessing risk of bias meant that the reliability of the included studies was unclear. It is unclear to what extent the chosen method of synthesis took account of the potential breakdown of randomisation and possible confounding/interactions over time periods arising from the inclusion of cross-over study designs. Given the various potential methodological limitations, the reliability of the authors' conclusion is uncertain.

### Implications of the review for practice and research

Practice: The authors stated that promotion of the acid-ash "alkaline diet" to prevent calcium loss was not justified.

Research: The authors stated that a robust methodological study was required to investigate the association between urine net acid excretion and osteoporosis, using direct measures of bone strength.

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