Authors' objectives
To review studies published since the 1991 National Health and Medical Research Council report on the effect of fluoride on bone strength, mass, and fracture rate (see Other Publications of Related Interest).

Searching
MEDLINE was searched from 1991 to December 1998 for studies published in the English language. The keywords used in combination with 'fluoride' were 'bone', 'osteoporosis' and 'fractures'. The reference lists of the identified studies were also examined.

Study selection
Study designs of evaluations included in the review
The studies of humans included controlled clinical trials, before-and-after studies, case-control studies, cohort studies, cross-sectional studies and ecological studies.

Specific interventions included in the review
Fluoride treatments were eligible if it was possible to separate the independent effects of fluoride from other components of the treatment. Fluoridation of the water supply was compared with non-fluoridation, while oral fluoride was compared with either placebo or no treatment control. The dose of fluoride in the community water supply ranged from 0.03 to 4 parts per million (ppm), while the fluoride content administered in clinical trials was estimated to range from 9.0 to 33.9 mg/day. The duration of fluoride exposure ranged from 12 months in a clinical trial to a mean of 25 years in a cross-sectional study.

Participants included in the review
Studies that involved patients with normal or purely osteoporotic bone were eligible for inclusion. The participants included people of both sexes living in fluoridated and non-fluoridates areas, pre- and postmenopausal women, and osteoporotic patients. The age of the participants ranged from 18 to 80 years. Animal feeding studies were also included.

Outcomes assessed in the review
Studies that assessed fracture incidence, bone mineral density (BMD) or bone strength were eligible. The actual outcomes assessed included: rates of hip, femoral neck, distal forearm, vertebral, and any fractures; the hospitalisation rate for hip fractures; and the BMD of lumbar spine, femoral neck, and anterior-posterior lumbar spine.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Study validity was not formally assessed although some aspects of validity were discussed in the text.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

The following information were tabulated: the year of publication; study design; sample size; age and gender of the participants; intervention and control details; fluoride content of preparation used; the duration of exposure; bone
measurements; the confounders addressed; and the size, units and significance of the effect.

**Methods of synthesis**

How were the studies combined?
The studies were grouped according to study design and a narrative synthesis was undertaken.

How were differences between studies investigated?
Differences between the studies were discussed in the text of the review.

**Results of the review**

Twenty-seven studies of humans were included in total. There were 12 controlled clinical trials (1,535 people), one before-and-after study (21 people), one case-control study (282 people), 3 cohort studies (6,119 people), 5 cross-sectional studies (5,101 people), and 7 ecological studies (over 70 million people).

Clinical trials (12 studies). There were no reports of reduced BMD and fracture rates in osteoporotic patients in any of the studies. Ten studies reported a significant increase in the bone density of the femoral neck, femoral condyle, and lower spine associated with daily fluoride (2 to 22.6 mg) over 1 to 4 years. Case-control study (1 study, 282 nurses). Nurses with higher toenail fluoride (greater than 5.5 ppm) had a non-statistically significant decrease in the risk of hip fracture (the odds ratio, OR, was 0.8, 95% confidence interval, CI: 0.2, 4) and a non significant increase in the risk of forearm fracture (OR 1.6, 95% CI: 0.8, 3.1), compared with those with the lowest fluoride levels (less than 0.2 ppm). Cohort studies (3 studies). One study reported no significant effect on lumbar spine or hip BMD from 20 years of fluoride exposure, after adjustment for nine potential confounding factors. Two studies reporting on fracture rates found inconsistent results: one study reported a decreased risk of hip fracture at 0.7 ppm fluoride, with no effect on non-hip fractures; the other study reported a significant increase in fracture rate associated with 4 ppm versus 1 ppm fluoridation in postmenopausal women. Cross-sectional studies (5 studies). The results were inconsistent. Three of the 5 studies found that BMD was increased among those using fluoridated water. The studies were adjusted for varying numbers of confounding factors. Ecological studies (7 studies). The results were conflicting. Two of the 7 studies did not show any significant effect in hip fracture; 2 other studies showed an increased fracture incidence; and 2 studies showed a reduction in fracture incidence. Most studies attempted to adjust for age and gender, but there was no adjustment for other potentially influential variables that may also influence the incidence of fractures.

**Authors’ conclusions**

There was a substantial body of evidence that fluoride up to 1ppm does not have an adverse effect on bone strength, BMD or the incidence of fractures.

**CRD commentary**

The aims were stated, and the exclusion criteria were defined in terms of the participants, intervention and outcome. However, the inclusion criteria were not defined in terms of the study design. By restricting the literature search to articles published in one database, other relevant studies may have been omitted. In addition, the lack of any attempts to locate unpublished material raises the possibility of publication bias. The methods used to select the studies were not described. Validity was not formally assessed although some aspects were addressed in the text of the review. Some relevant data were tabulated but the methods used to extract the data were not described. A narrative synthesis was appropriate given the diversity of the studies. The level of evidence in this review would be strengthened by the following: a more comprehensive literature search; more details of the methods used to conduct the review; and a discussion of the results from clinical trials that takes study quality into account.

The evidence presented appears to support the authors’ conclusions.

**Implications of the review for practice and research**

Practice: The authors state that there is no evidence that drinking fluoridated water has any adverse effects on bone.
Research: The authors did not state any implications for further research.

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Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.