Water fluoridation, bone mass and fracture: a quantitative overview of the literature  
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Authors' objectives
To determine whether water fluoridation is associated with altered fracture risk at a population level, and whether differences between studies are consistent with confounding or chance variation between studies.

Searching
MEDLINE was searched from 1966 to November 1997 for English language studies using the following terms: 'fluoridation', 'bone mass', and/or 'fracture'. Current reviews and bibliographies were scanned. There was no clear evidence of publication bias using a funnel plot.

Study selection
Study designs of evaluations included in the review
Observational studies were eligible. Included studies were of the following designs: ecological studies, cross-sectional studies and cohort studies.

Specific interventions included in the review
Studies reporting on water fluoridation were eligible. Years of exposure to fluoride (where stated) ranged from less than 5 years to 25.9 years or a lifetime, and dose of fluoride (where stated) ranged from greater than 0.1 to 5 parts per million.

Participants included in the review
The inclusion criteria were not defined in terms of participants. The participants included both males and females from several countries including USA, Finland, Canada, Taiwan, France, New Mexico and UK.

Outcomes assessed in the review
Studies assessing bone mass or fracture were eligible. Bone mass was assessed by spinal, chest or hand X-ray, single-photon absorptiometry (SPA), or dual-energy X-ray absorptiometry (DXA); fractures studied included hip, vertebral, and all fractures.

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
Validity was assessed and scored according to the following criteria: ascertainment of fracture (not stated = 0, self-report = 1, hospital discharge data = 2, X-ray confirmation = 3) or ascertainment of bone mass (not stated = 0, other methods = 1, SPA = 2, DXA or quantitative computer tomography or dual-photon absorptiometry = 3); representativeness of population (uncertain = 0, selected group = 1, somewhat representative = 2, valid sampling procedure = 3); selection of non-exposed cohort/population (uncertain = 0, different community = 1, same community = 2); comparability of cohort populations or adjusted for in analysis (score 0 to 6, with one point for each of age, smoking, physical activity, weight, medication, migration rates or duration of residence); ascertainment of exposure (not stated = 0, water sampling from same source as community = 1, water sampling from household or direct ascertainment of water intake = 2, water sampling from household and direct ascertainment of water intake = 3). Maximum possible score was 17 points. Two reviewers scored and assessed validity separately from data extraction.

Data extraction
One reviewer, blinded to validity score, extracted data with the process being repeated after two weeks. Any
discrepancies were resolved by reference to the original paper. Tables reported in the review included the following information: author and publication year published; type of study; population; sex; years of exposure to fluoride; dose of fluoride; fracture type; and urban or rural index. The relative risk (RR) and 95% confidence interval (CI) of fracture, and difference in bone mass between populations were extracted or estimated for each study. Where possible stratified or adjusted data were included in the meta-analysis.

Methods of synthesis
How were the studies combined?
Pooled RR and 95% CIs for fracture were estimated using methods described by Fleiss, with weighting according to the inverse of the variance (see Other Publications of Related Interest). Pooled difference in bone mass between the two groups was expressed as a percentage difference with 95% CI or number of standard deviations difference for each screened site (lumbar spine, femoral neck and distal ratios). The odds ratio (OR) and 95% CI for a diagnosis of osteoporosis were also calculated.

How were differences between studies investigated?
Statistical heterogeneity was assessed using the chi-squared test. When heterogeneity was found, pooled RRs were estimated using a random-effects model and heterogeneity was investigated by exploring the influence of the following variables on the results: urban or rural index; study quality; source of fluoride exposure (natural or artificial); level of water fluoridation; gender; and duration of exposure to fluoride water.

Results of the review
Twenty-one studies were included: 10 ecological, 9 cross-sectional and 2 cohort studies.

The validity scores ranged from 2 to 14 out of a maximum 17 points.

Water fluoridation and fracture (18 studies: 10 ecological, 6 cross-sectional and 2 cohort studies with a total of over 70 million participants).

There was a large variation in study results with RR ranging from 0.22 to 2.10. Overall, there was no significant effect of fluoridation on fracture risk; RR was 1.01 (95% CI: 0.96, 1.09). Significant heterogeneity was found (p<0.000001) and demonstrated using a forest plot. Variation between studies was not explained by study design, gender, source of fluoridation, or fluoride dosage. There was a small but significant effect of fluoridation for any fracture type with a RR of 1.12 (95% CI: 1.04, 1.21); no evidence of heterogeneity was found for this group of studies (p=0.35).

After exclusion of one study due to excessive weighting (sample size was 70 million) the combination of gender, urban or rural index, and study quality explained 25% of the variation in the natural logarithm of RR (p=0.05).

Water fluoridation and bone mass (9 studies: 2 ecological, 6 cross-sectional and 1 cohort studies with a total of 10,415 participants).

Osteoporosis (4 studies with 3,351 participants): these studies tended to be older and of poorer quality. Fluoridation was associated with a significant decrease in the risk of osteoporosis; RR was 0.39 (95% CI: 0.20, 0.75).

Bone mass.

Femoral neck (3 studies): the observed change was +0.90% (95% CI: -0.14, +1.9). No significant heterogeneity was found.

Lumbar spins (3 studies): the observed change was +2.6% (95% CI: +1.6, +3.5%). No significant heterogeneity was found.

Distal radius (3 studies): the observed change was -2.2% (95% CI: -5.7, +1.3%). Significant heterogeneity was found.
Study quality.

There were no significant associations between quality and effect size.

**Authors’ conclusions**

Water fluoridation, both at levels aimed at preventing dental caries and possibly at higher naturally occurring levels, appears to have little effect of fracture risk, either protective or deleterious, at a population level. The small effect on bone mass seen in studies performed at the individual level is consistent with this finding. Variation between studies is also likely to arise from differences in the distribution of other recognised fracture risk factors between different populations. Confirmation of these findings is required in large studies performed at the individual level.

**CRD commentary**

The aims were stated, and the inclusion criteria were defined in terms of study design, intervention and outcome. Restricting primary studies to those published in the English language, and identified from one database, may have resulted in the omission of other relevant studies. Publication bias was assessed. Methods used to select primary studies were not described. Validity was formally assessed and scored using predefined criteria, and methods used to assess validity were described. Relevant data were extracted and presented in tabular format, and details of the methods used were provided. Statistical heterogeneity was assessed, and where found, potential causes were investigated. The discussion includes consideration of the following limitations of the review: poor quality of primary studies; discrepancies between studies could not be explained; bone mass was assessed using various different methods; and the possibility of publication bias.

The evidence presented supports the authors' conclusions.

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

Practice: The authors state that fluoridation has little effect on fracture risk and a small effect on bone mass.

Research: The authors state that confirmation of the findings, i.e. the lack of effect of fluoridation on fracture risk and bone mass, is required in large studies performed at the individual level, with careful assessment of and adjustment for potential confounders and effect modifiers, as well as a detailed ascertainment of exposure to fluoride.

**Bibliographic details**


**PubMedID**

10083687

**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.