

**DOES FLUORIDE IN DRINKING  
WATER AT A CONCENTRATION OF  
0.5 - 0.8 PPM CAUSE BONE  
FRACTURE AMONG ADULTS?**

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## **ABSTRACT:**

*This evidence-based report studied the existing literature in order to understand the correlation between a long term exposure of population to fluoridated drinking water and the incidence of bone fracture in adults. The review is based on studies and articles founded by a minutiae search of several electronic data base including references from the potential articles obtained, as well as knowledge and inputs from other Dentistry disciplines like the departments of Community and Preventive Dentistry. A total of 11 articles were considered relevant and were critically appraised in accordance with the "Check list for assessing causation", and the "Guide to Community Preventive Services, 2006" of Canadian Task Force. Four studies met the criteria; scoring 9/13 on the check list. Only long term exposures on adults, men and women, at levels of 0.5ppm to 0.8ppm fluoride added in drinking water were analyzed .The incident data of hip fractures had been obtained from the discharge registers of public hospitals. The relative risks and the odds ratio had been calculated for different genders and age groups, and other potential risk factors for bone fractures were taken into consideration. In conclusion, long term fluoride exposure from drinking water and containing >4.32 ppm increases the risk of overall fractures as well as hip fractures however the existing literature is contradictory on the effects of fluoride at lower ppm as was the subject of our study and further investigation is warranted in order to asses a clear cause-effect relationship between water fluoridation at low levels and bone fractures.*

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## **INTRODUCTION:**

In a world increasingly concerned with health, questions are raised on issues that seem to affect our health and lives. Fluoride which is omnipresent in our environment and is recognized as the most electronegative and reactive of all elements has been added to drinking water supplies in some geographical areas as an attempt to reduce the frequency of dental caries. Its outcomes on human health have been the subject of numerous studies. Although this benefit is widely accepted, concerns remain about possible adverse health effects, particularly on bone.

Extensive research has investigated the most potentially negative side effects other than fluorosis in populations subjected to long term excessive fluoride intake. Studies have uncovered little evidence to suggest any important health problems associated with the consumption of the drinking water, containing approximately 1ppm fluoride; however the question of effects of fluoride exposure from drinking water on fracture risk remains unresolved. It is generally accepted that excessive fluoride exposure conveys an increased risk for bone fracture; however less is understood regarding fracture risk at lower exposures.

Fluoride in drinking water originates from natural sources or is artificially added to protect dental health. Ingested fluoride is absorbed in the stomach and peak plasma fluoride concentration is reached in half an hour. Fluoride exhibits an affinity for bone but is not irreversibly bound to calcified tissues. Fluoride incorporates into bone tissue by replacing hydroxyl group of hydroxyapatite to form Fluorapatite (Kleerekoper 1998). The latter is more resistant to osteoclastic resorption which may result in an altered bone remodeling pattern; this in turn may lead to bone with impaired biomechanical properties since remodeling is an integral part of skeletal health. The degree to which Fluorapatite is mixed with hydroxyapatite is dependent on fluoride dose and exposure time. It has been found that fluoride absorbs more rapidly in growing bone, than after peak bone mass has been achieved. In higher serum concentrations fluoride is anabolic to bone in that it increases cancellous bone mass. (Kleerekoper 98, lau 98, kleerekoper94).This effect increases with time. In dose dependent manner fluoride may cause impairment in mineralization of the newly synthesized osteoid and consequently

affect biomechanical properties of the bone (Kleerekoper 98, Fejerskov 96).

The available information in the literature is limited and often contradictory as to whether the exposure to fluoride in drinking water for cariostatic purposes increases the risk of fracture. Hip fractures have been shown to be a major cause of morbidity and mortality in persons aged 65 yrs and older in many western nations that largely have good access to health care systems. This is both scientifically and politically important as on one hand there are potential risk factors that depend on an individual's personal choices, however fluoride exposure from drinking water is determined largely by public health policy, with the individual being able to make little choice, with regards to his or her consumption of publicly supplied water. With a significant portion of the population exposed to fluoride, even a small increase in the risk will yield a large increase in the number of fractures, which will have a significant and dramatic impact on public health. Clearly it is imperative that any potential risks associated with such exposure be well studied and understood.

The purpose of this study is to find evidence in literature to answer if fluoride in drinking water at concentrations of 0.5-0.8 ppm cause bone fractures among adults.

## **METHODS:**

A systematic method was applied to identify, select and critically appraise relevant studies.

### ***SEARCH STRATEGY***

Three primary strategies were followed to obtain potentially relevant articles pertaining to our area of interest.

1. An exhaustive search of **Ovid Medline, Pub med, Cochrane and Web of Science** and relevant publications in print was performed. The purpose being, to identify as many articles as possible.
2. Consultation with the Department of Community dentistry, Faculty of Dentistry, University of Toronto
3. Consultation with the Department of Preventive Dentistry, Faculty of Dentistry, University of Toronto

The following key words and combination of key words were used in the search

1. Fluoride and bone fracture
2. Water fluoride and bone fracture
3. Water fluoridation and bone fracture in adults

### ***INCLUSION CRITERION***

The articles selected for this report had to meet the following criterion:

1. Studies on humans
2. Level of fluoride in drinking water within our target range
3. Studies on adults, male/ female, 19 + yrs
4. Study design - Cohort, case control, ecological studies, clinical trials , RCTs validation studies, journal articles, legal cases and scientific integrity reviews
5. Articles published in the English, French, Hebrew, Hindi, Persian, Romanian, and Russian languages.

## **EXCLUSION CRITERION**

1. Children under the age of 18
2. Studies on animals
3. Studies which use Interview Survey and Meta-Analysis design.
4. Fluoride exposure in concentration higher than those which make the purpose of this study.

## **DETERMINATION OF RELEVANCE USING VALIDITY INSTRUMENTS**

Specific criterion for the selection of articles was included in our research. The relevant articles had to meet the following criterion

1. The study must be a primary study and not a review of other primary studies
2. Study design must be cohort, case control, cross sectional studies. Cohort studies were considered the strongest design, and therefore, the most desirable
3. The proposed study must declare, Logistic regression, relative risk, odds ratio
4. The proposed study must cover a range of water fluoride concentration pertinent to our search criterion of between 0.5-0.8ppm.

Following an initial search, 1194 articles were found meeting the inclusion criteria. From this study pool, after removing 458 duplicates 681 articles were rejected on the basis of their title. Out of the remaining articles, 44 were further discarded at the abstract stage. The remaining 11 articles were retrieved and copied for review. Those documents were further analyzed for relevance and strength of evidence and were meticulously scored using the checklists (Adapted from: Fletcher, Fletcher and Wagner. Clinical epidemiology-the essentials.3<sup>rd</sup> ed.; Sackett et. Al. evidence- based medicine: how to practice and teach EBM.1997). Finally 4 articles meeting our scoring cut offs were included in this study.

## **VALIDITY INSTRUMENT:**

The checklist for accessing causation was used to assess those final 11 selected articles. A score of **9/13** was the cut off

1. Was the study ethical?
2. Was a strong design used to access causation and risk?
3. Were cases defined validly and reliably measured?
4. Were the risks validly and reliably measured?
5. Were the risks assessed controlling for other factors and was the models predictive power strong?
6. Did the cause precede the effect?
7. Was the estimate of risk beyond chance?
8. Was there a dose-response relationship?
9. Was reversibility demonstrated?
10. Is the cause observed in different time and places?
11. Is the cause biologically plausible?
12. Is the cause specific to that disease?
13. Is the cause analogous to another disease?

Adapted from: Fletcher, Fletcher and Wagner. Clinical epidemiology-the essentials.3<sup>rd</sup> ed.  
Sackett et. Al. evidence- based medicine: how to practice and teach EBM.1997

The Highest attainable score was 13.

**TABLE:**

<i>Author, Date</i>	<i>Population [Age, Sex, Location, representative of?]</i>	<i>Exposure or test treatment, [number studied]</i>	<i>Control Treatment [number studied]</i>	<i>Outcome</i>	<i>Critical Appraisal comments</i>	<i>Conclusion , strength of evidence &amp; classification</i>
Hillier S. et al Jan 2000	1041 ,50 yrs & above, M & F ,U.K. Cleveland county , Hospital Discharge Register	1.79 ppm 514	0.15ppm 527	Hip Fractures, life time exposure [45yrs] OR: 1 [C.I. 0.7-1.5], Inconclusive	good design for causation accurate and reliable determination of exposure to fluoridated water <u>association with a biomarker(content of fluoride in femoral head)</u>	Case control, good execution, moderate design,17 months, 3 studies, consistent, large effect size, sufficient strength of evidence, C.T.F. : II-2/ C Score for causality: 9/13
Kurttio P. et al Oct 1999	144627 50--80yrs M & F, Finland, Hospital Discharge Register	2.4 ppm N.A.	0.1ppm N.A.	Hip Fracture RR(m)=0.97, life time Exposure, inconclusive	Estimate individual exposure in a large sample, no measurement of exposure to risk factor , analyze only rural population, not considered other factors that could influence the result	Retrospective Cohort, good execution moderate design, 3 studies , consistent, 13 years, large effect size, sufficient strength of evidence C.T.F.: II-2/C Score for causality: 9/13

<b>Author, Date</b>	<b>Population [Age, Sex, Location, representative of?]</b>	<b>Exposure or test treatment, [number studied]</b>	<b>Control Treatment [number studied]</b>	<b>Outcome</b>	<b>Critical Appraisal comments</b>	<b>Conclusion , strength of evidence &amp; classification</b>
Yiming Li et al Nov 2001	8266, >50 yrs, M & F, China, Random General Population with more than 25 yrs of Residence	Range upto 7.97ppm N.A.	0.25ppm N.A.	Overall Spinal& Hip Fracture OR =1.25 at 0-.58--0.73 ppm, Slightly preventive	good design for causation, risk assessed for other factors, some of the fracture were self-reported, no measurement of exposure to risk factor[biomarker]	Ecological cohort, good execution , moderate design, 6 studies with a good consistency, large effect size, strong evidence C.T.F.: II-2/B Score for causality: 10/13
Phipps K et al Oct 2000	7129, >65years old, White women only , U.S.A., Civil records	6.6ppm 3218	0.88ppm 2563	Spine, Wrist, Humerus, Hip, Vertebra fracture , 20 yrs exposure, Preventive [protective], For Hip Fractures R.R= 0.69[95%C.I. 0.5,0.96, For Vertebral fractures R.R.=0.73 95% C.I.0.55,0.97	good study design, Biomarker[bone density], investigated for other sites of fractures , only white women more than 65 yrs, small sample size	Retrospective study of prospective cohort, good execution , greatest design 7 studies , with good consistency, [2yrs], large effect size, strong evidence, C.T.F. : II-2/B Score for causality: 9/13

## DISCUSSION:

The ability of fluorides to induce new bone formation and their extensive evaluation in the treatment of osteoporosis have led to studies examining the relationship between water fluoridation and the occurrence of both osteoporosis and bone fractures. Each year there are an estimated 1.5 million fractures associated with osteoporosis in the United States alone with an incidence of hip fractures estimated to be around 250,000. The rapidly growing population of elderly people not only in the developed world, but also in many Asian countries, indicates that this will have a major impact on the health care systems in many parts of the world. Recently published data indicates that by the year 2020, Asian countries might bear the majority of the world's hip fracture burden. It thus becomes imperative that the identification of preventable factors that increase the risk for fractures be carried out in earnest. The increasing use of water fluoridation for the prevention of dental caries mandates that we exhaustively research the potential impact of fluoride levels used on the risk of bone fractures. For many years the studies addressing this issue were ecological comparisons. The most frequent design was the determination of the incidence in hip fractures in a geographically defined population. The results of these kinds of studies were most of the time conflicting and they were put under a collective sign of ecological fallacy. With the advancements and development of epidemiology and statistical analysis techniques, far more sophisticated study designs were available to assess the causality of complex potential risk factors. The scientist directed their attention to stronger study designs like prospective cohort and case control studies. To determine the real exposure to fluoridated water some authors used individual questionnaires, civil records and data from official sources regarding the level of fluoridation. The requirement of a better measurement marker of the risk factor, and water fluoridation, made some researchers analyze the bone mineral density, serum fluoride levels and the amount of fluoride incorporated in femoral bone. Among overall fractures, hip fractures are the most used in case definition because they usually are serious, can't pass undiagnosed and require hospitalization. Our study looked at the best evidence in the literature to try and analyze evidence linking water fluoride levels in low concentrations to the risk of fracture.

A case control study run by Hillier et al studied fluoride in drinking water and the risk of hip fracture in 1041 individuals. Both, study and control population, were interviewed and passed a mental ability test. To determine the exposure to fluoride and possible confounding factors all participants provided further detailed information about their residential history, level of physical activity, smoking and alcohol consumption, medications and dietary sources of calcium and fluoride. In 105 cases of fractures treated by arthroplasty, the femoral head was analyzed to determine the amount of fluoride in the bone, which was linked to the patients, estimated average lifetime exposure to fluoride in drinking water. The authors found low risk in population ingesting fluoride in drinking water at a concentration of about 1ppm. The adjusted odds ratio associated with an average lifetime exposure to fluoride in drinking water of 0.9ppm or higher was 1.0(95% CI 0.7-1.5). Hip fracture was strongly associated with low body-mass index and there was an increased risk reported in patients treated with oral corticosteroids.

Kurtio in 1999 published a retrospective cohort study. In a remarkable effort, the authors analyzed a cohort of populations born in between 1900-1930 in rural area of Finland, who have lived in the same location at least from 1967 to 1980. Individual exposure was estimated after a "fluoride map" of Finland was set up using a nationwide database on ground water fluoride measurements in 8927 wells by the Geographical Survey of Finland. The risk estimators were calculated for men and women and for age groups, related to regions with different fluoride level in water. No association was found between hip fractures and estimated fluoride concentration in well water in either men or women when all ages' groups were analyzed together. However the risk increases for women between 50—64 years old when they are exposed to fluoride levels higher than 1.5ppm (adjusted rate ratio 2.09, 95CI 1.16, 3, 76)

The results of another significant study were published in 2001 by Li and colab. They carried out a Ecological Cohort study in order to determine the prevalence of bone fractures in six Chinese populations with water fluoride concentration ranging from 0.25 to 7.97 ppm. A study size of 8266 male and female subjects over 50 years of age were enrolled. The authors chose this location because in contrast to the US population, who use fluoride in various delivery systems, residents of rural China rarely changed residence, and most had been using the same water supply throughout their life. The risk was assessed taking into consideration other factors that could influence the outcome such as nutrition levels, tea drinking, alcohol consumption, cigarette smoking and physical activity. Data about fractures were collected from medical records or were self reported by the study subjects using a detailed questionnaire. The prevalence of bone fractures was reported low by Li et al in the population exposed long term to 1.00-1.06 ppm fluoride in drinking water. However at high levels of more than 4.32ppm the risk was significantly increased. In general the trend of the fracture prevalence in relation to the water fluoride concentration exhibited a U shaped pattern.

Phipps K et al in 1986-1988 addressed the issue of community water fluoridation, bone mineral density and fractures in older women in a retrospective study of a prospective cohort in which 7129 white women aged at least 65 years were enrolled.. Along with the incidence of hip, vertebrae, wrist and humerus fracture, the authors measured the bone mineral density and found increased value in spine and vertebrae but lower in radius among women with continuous exposure to fluoridated water. The risk estimators are calculated after adjustment for several factors known to be associated with rates of fracture, including use of estrogen, smoking, and body weight. This study pin pointed that a long term exposure to fluoride at 0.88 to 2.20ppm/day reduces the incidence of bone fracture. Moreover this daily intake of fluoride might be a very efficient method to reduce at a low cost, the incidence of hip fracture.

#### **ARE THE RESULTS APPLICABLE TO ONATRIO?**

- We found no substantive data in the literature indicating any co-relation between water fluoridation at 0.5-0.8ppm and risk of bone fractures.
- Data available indicates no evidence to discontinue fluoridation of water at the current levels in Ontario [0.6ppm].
- We conclude that further studies are required on a larger scale to further assess the impact of lower level of fluoride on bone.

#### **CONCLUSION:**

The conclusions drawn after evaluating these studies found that 0.5 to 0.8ppm fluoride in drinking water and an increase in the incidence of bone fracture were not related or if at all, this seemed to be a preventive factor for bone fractures. Since some of the studies were ecological, complete control of potential confounders and effect modifiers was not possible. In some of the studies the odds ratios were adjusted so as to take individual variables into account. Since results of most studies on water fluoridation & bone fracture are conflicting, a cause and effect relationship cannot be established. In the long run more interest should focus on the consumption of fluoride by an individual from drinking water & other potential fluoride sources. This is of particular concern especially in North America as individuals are exposed to multiple sources of fluoride throughout their life. (Drinking fluoridated water between 0.5 to 0.8 ppm eight times a day is nearly equivalent to drinking water concentrations at 4 ppm). Further studies with strong design patterns like prospective cohort studies need to be undertaken. These can assess other variables like fluoride from multivariate sources, its level and the duration of exposure, in order to accurately assess and provide systematic and compelling evidence of an effect of fluoride burden on bone at lower concentrations. This topic needs to be further delved into and researched for the overall impact that this might have on the health of many communities, at large.

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