

**IS WATER FLUORIDATION A RISK FACTOR  
FOR HIP FRACTURE?**

**A Review of Current Evidence**

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## **INTRODUCTION**

### **Public Health Importance of Hip Fractures Among the Older Adults**

The incidence of hip fractures in industrialised countries increases with age. In the population group 55 years and over these injuries represent a significant public health problem<sup>1,2</sup>. In the United States each year more than 300,000 elderly people suffer hip fractures<sup>1,3,4</sup>, while in Canada they accounted for 355,313 hospital admissions between 1972 and 1990 and were the major consumer of hospital days of stay during that period<sup>2</sup>.

The lifetime risk of hip fracture for women who live to the age of 90 is 30%, and for men 15%<sup>5</sup>. With the projected increase in the population aged 65 years and over in Western countries, it is expected that the current number of hip fracture cases could double by the year 2000.

Hip fractures are an important cause of morbidity, disability and mortality among the elderly and pose a significant threat to the quality of their life<sup>1,2</sup>. Of those who were living independently before suffering hip fracture, 15%-25% become institutionalized for at least one year, and another 25%-35% require permanent help of other people or mechanical aids for their mobility<sup>5</sup>. In the United States hip fractures are the second leading cause of admissions to nursing homes<sup>6</sup>.

Hip fractures occurring among the elderly contribute significantly to health care costs in Western countries. The cost of providing acute hospital care for hip fractures in the United States is estimated to be \$7 billion annually<sup>3,6</sup>. The long-term

care and institutionalization of persons with hip fracture increase this cost significantly.

### **Osteoporosis - the Underlying Cause of Age-related Hip Fractures**

The vast majority of hip fractures in the elderly is the result of minimal trauma associated with osteoporosis. Osteoporosis is a metabolic bone disease which leads to a reduction in bone mass<sup>5</sup>, which occurs when resorption of bone tissue exceeds its production in a process of constant bone remodelling. It lowers injury thresholds to the level at which trauma no more severe than falling from a standing height can result in hip fracture<sup>1,4,6</sup>.

Osteoporosis may be considered an almost universal phenomenon of aging. It affects progressively both males and females after the age of 40<sup>1,2,3,5</sup>, resulting in the exponential increase in the incidence of hip fractures with age. The most rapid development occurs among women during the first few years following either natural or surgical menopause due to reductions in estrogen levels<sup>1,2,3,5</sup>.

Beside age and the occurrence of menopause, epidemiological studies have indicated many other risk factors for osteoporosis, and, via osteoporosis, for age-related hip fractures. These factors are numerous and very diverse (Appendix 1)<sup>1-7</sup>.

### **Fluoride in the Prevention of Osteoporosis**

There is plenty of evidence that fluoride is very potent in stimulating bone formation and increasing the mineral density of bone tissue<sup>8-14</sup>.

With reference to these results, it has been hypothesized that life-time and long-term exposure to water fluoridated to the level recommended for dental caries prevention (0.7ppm - 1.2ppm) may protect against osteoporosis, and, thereby, hip fractures in the elderly by increasing peak adult bone mass and by transforming hydroxyapatite to less resorptive fluorapatite.

However, the concern that protracted exposure to water with an adjusted fluoride level may have adverse effects on bone tissue and increase the risk for hip fractures has been present since fluoridation of public water supplies was introduced in 1945. This is because of many unknowns that exist in the relationship between long time fluoride ingestion and the quality of bone tissue. A number of studies have indicated that fluoride has a cumulative effect on bone tissue, and that the duration-response relationship between fluoride exposure and bone quality is very complex. While it is not biologically plausible for fluoride to have a negative effect at the levels recommended for caries prevention, a study by Alhava *et al*<sup>11</sup> has suggested that fluoride may reach toxic bone levels in a person's lifetime when its content in drinking water is 0.97 ppm.

The results from the studies examining the efficacy of fluoride in the treatment of osteoporosis<sup>15-17</sup> have also raised concerns that water fluoridation may increase the risk of hip fractures among the elderly.

Over the past few decades a number of epidemiologic studies have been conducted in an attempt to determine the effect of fluoride added to community water supplies for caries prevention on the quality of bone tissue and hip fracture rates.

## **OBJECTIVE**

The purpose of this paper is to present and evaluate epidemiologic studies concerning the relationship between exposure to drinking water fluoridated at the levels conventionally used for the prevention of dental caries (0.7ppm - 1.2ppm), and the incidence of hip fractures occurring among the elderly as a result of a minimal or moderate trauma.

## **METHODS**

To identify papers pertaining to the relationship between exposure to fluoridated water and age-related hip fractures, the medical and dental literature from the years 1965 to 1995 was searched using the Medline and Medical Index bibliographic databases. The Medical Subject Headings (MeSH) used were: fluoridation, fluorides, fractures, osteoporosis and bone density. The search was limited to the English-language literature involving human subjects.

The reference lists from the papers retrieved by this search were screened and any relevant references followed-up. Hand searching of journals was not involved.

All papers were subjected to a preliminary evaluation. According to the objective of this paper, the following were excluded: reviews, editorials, papers reporting on studies examining the effect of fluoride present in drinking water at a level higher than that suggested for caries prevention, and studies where outcome measures were different from hip fracture (e.g. fractures of other bones, bone density). Papers presenting the results of studies examining the efficacy of fluoride

in the treatment of osteoporosis were also excluded.

The review was limited to studies examining the effect of optimal (0.7ppm - 1.2ppm) versus low water fluoride content because communities face this choice of fluoride adjustment and not the choice of water fluoridation versus high (>1.2ppm) fluoride concentrations.

## RESULTS

Following these criteria, eleven papers were retained<sup>19-22,24-27,29-31</sup>. All studies presented in these papers used an **ecological design**. Case-control and cohort studies did not meet inclusion criteria, since they examined the effect of optimal versus high fluoride exposure measuring bone mass.

According to ecologic study design<sup>18</sup>, the majority of the studies (seven) selected for this review are **comparison ecologic studies**<sup>19-26 (a)</sup>, two are **multiple group comparison (correlation) ecologic studies**<sup>27,28,29 (b)</sup>, and two are **time-trend ecological studies**<sup>30,31</sup> (Table 1). The latter two can be also considered as comparison studies as they contrast the incidence of hip fracture in a community before and after the initiation of water fluoridation. Appendix 2 provides the main characteristics and objectives of these three types of ecological studies.

**Comparison ecologic studies** - All these studies compared the incidence of hip fracture in communities with public water supplies fluoridated to the level

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<sup>a</sup> 23 - editorial supplemental to Arnala et al, 1986

<sup>b</sup> 28 - editorial supplemental to Cooper et al, 1990

recommended for prevention of dental caries and those with traces of fluoride in drinking water. Four of these studies were conducted in the United States (North Dakota<sup>19</sup>, Utah<sup>24</sup>, and two national studies<sup>20,25</sup>), two in Finland<sup>21,22</sup>, and one in Canada<sup>26</sup>.

In a study conducted in North Dakota, R.Korns<sup>19</sup> compared hip fracture incidence rates in two areas, one with water fluoride levels at 1.0 ppm to 1.2 ppm since 1945, and the other below 0.05 ppm, in white populations, for the years 1964 through 1966. Danielson *et al*<sup>24</sup> have studied the incidence rates in a population 65 years and older in three communities in Utah for the years 1984 through 1990. One of the communities had received fluoridated water (1 ppm) for approximately 20 years, while the control communities had fluoride levels under 0.03 ppm. In two national studies in the United States<sup>20,25</sup>, hip fracture rates were compared between counties classified as fluoridated or unfluoridated depending on the proportion of the population receiving fluoridated water.

In Finnish studies<sup>21,22</sup> the incidence rates were determined in two cities, one with the fluoridation of drinking water (1.0 ppm - 1.2 ppm) introduced in 1959, and the other with trace quantities of fluoride in drinking water (0.0 ppm - 0.1 ppm). In a study by Simonen *et al*<sup>21</sup> hip fracture cases were identified in the population aged 50 years and over during the period 1967-1978. Arnala *et al*<sup>22</sup> studied populations in the same areas between 1972 and 1981.

In a Canadian study Suarez-Almazor *et al*<sup>26</sup> compared the hip fracture hospitalisation rates of persons aged 45 years or older during the period 1981-1987, in Edmonton and Calgary. Edmonton has had fluoridated (1.0 ppm) drinking water



since 1967, while Calgary has minimal fluoride water content ( $\approx 0.3$  ppm).

**Correlation ecologic studies** - Cooper *et al*<sup>27,28</sup> have examined correlation between hip fracture hospital discharge rates among men and women aged 45 years and over, and water fluoride content (0.005 ppm - 0.93 ppm) in 39 districts in England and Wales during the period 1978 to 1982. In the other correlation study, Jacobsen *et al*<sup>29</sup> have analyzed the association between the occurrence of hip fractures among white females aged 65 years and over in the United States population by county of residence and the percentage of the population in each county receiving fluoridated water.

**Time-trend ecologic studies** - In an attempt to investigate the temporal relationship between hip fracture incidence and water fluoridation, Goggin *et al*<sup>30</sup> have studied the incidence rate in a population of women 60 years and older during the five years before (0.01 ppm - 0.02 ppm) and the five years after (1.0 ppm) fluoridation of public water supplies in Elmira, New York. Similarly, Jacobsen *et al*<sup>31</sup> have examined the incidence among men and women aged 50 years and older for the ten years prior to and the ten years following the fluoridation of the public water supply in Rochester, Minnesota. The city fluoridated its water supply in 1960 and has maintained fluoride concentration of 1.1 ppm during the study period.

In order to assess the quality of evidence from these studies, each of the papers was critically reviewed according to a set of following validity criteria: exposure measurement (level and length), determination of cases (case definition, case ascertainment, study follow-up), identification of population at risk, controlling for

potential confounding factors, sample size and method of statistical analysis.

Tables 1, 2 and 3 summarise information obtained according to these criteria. These tables show that the studies differ in many aspects of the research methods, which prevents the direct comparison of their findings. It is also obvious that they are the subject to many methodological (or reporting) flaws that compromise the quality of the evidence they provide.

**Exposure measurement** - *Exposure to fluoridated water* was measured in several ways: (a) fluoride concentration in public water supplies<sup>19,21-24,26,27,30</sup>, (b) fluoridation status of the community (presence/absence of water fluoridation)<sup>31</sup>, and (c) the proportion of the population served with fluoridated water<sup>20,25,29</sup> (Table 1).

The *length of exposure to fluoridated water*, when reported, varied significantly between studies, ranging from 5 years<sup>30</sup> to 25 years<sup>24</sup> (Table 2). Only a few researchers<sup>24,26</sup> made an effort to determine migration rates in the study populations, which might have had an effect on study results by affecting the length of exposure.

**Determination of cases** - *Case definition*, when provided, varied between studies. Different revisions of the International Classification of Diseases (mainly ICD-9-CM) and different disease codes (820.0 - 820.9) were used, rendering the finding less comparable (Table 2). In addition, while some studies excluded fractures due to high-energy accidents and those secondary to bone diseases (e.g. primary and metastatic carcinoma), in other studies these were also counted as cases. This represents a threat to the validity of the findings, especially when the sample size, i.e. number of cases is small.

*Case ascertainment* - All studies used hospital discharge data to identify cases. However, while some studies counted only persons where hip fracture was the primary discharge diagnosis, the others also included those for whom hip fracture was either a secondary or tertiary diagnosis as well as fracture revisions and second fractures. Only a few studies controlled for the transfer of cases.

*Follow-up periods* of the studies were also very different: three, four, five, seven and ten years (Table 2). This makes comparison of the results difficult. Also, the results of the studies of short duration could have been easily flawed by measurement error due to underestimate of the number of hip fracture cases.

**Population at risk** was determined by different means (Table 2), including Census information and population estimates for the midyear of the study period. Madans *et al*<sup>20</sup> determined the incidence of hip fractures among the participants of a health survey. Only two studies<sup>26,31</sup> used person-year analysis to estimate incidence rates, having population estimates for each year of the study period. This analysis should give more accurate results.

With the reference to the methods of identification of cases (numerator) and determination of population at risk (denominator) presented above, the calculation of hip fracture incidence rates in these studies might have been subject to measurement error. Differences in the methods could have also resulted in different findings in these studies.

The validity of the findings from some studies is further attenuated by the fact that hip fracture rates and levels of fluoride exposure were not determined for the

same but different time periods. Since fluoride concentration is not necessarily maintained at the same level over time, this may be a significant source of bias in these studies.

**Sample size** - Little consideration was given to the *statistical power* of the study and the sample size varied significantly between the studies, ranging from 246<sup>24</sup> to 541,958<sup>25</sup> (Table 3). Some authors failed to provide information on sample size.

**Statistical analysis** - The studies also differ in many aspects of *statistical analysis*. While the majority provide age-specific rates by gender, one gives only crude rates for males and females<sup>20</sup>, which precludes comparison of the findings even within that given study. However, differences in the age breakdowns used in the studies prevent comparison of their age-specific rates. When rates were standardized, populations used as a standard were different (1980 US population, 1990 US population, population of fluoridated community), allowing comparison of the findings only within those studies.

**Confounding factors** - Potential confounders for the association between water fluoridation and the occurrence of hip fractures are numerous (Appendix 1). Of those that can be controlled for in ecologic studies only gender was taken into consideration in a few of the studies included in this review.

Population *gender and race composition* differed between studies. While some studies included both males and females, other studies were restricted to the population of white females only, rendering them less comparable. Comparability of the findings is also hampered by the differences in the *age composition* of the study

populations (Table 4), compounded by the failure to report the age-specific fracture rates. When standardized rates are given, standard populations are different, and, therefore, the results cannot be compared.

The findings from the comparison and time-trend studies are presented in Table 4 and Table 5, and from the correlation studies in Table 6.

The results of comparison and time-trend studies are conflicting, with five studies showing no association<sup>19,20,22,26,30</sup>, two studies showing a positive association<sup>24,25</sup>, and two showing a negative association<sup>21,31</sup> between the exposure to fluoride in drinking water, and the incidence of hip fracture. Positive associations were weak: risk ratios associated with fluoridation were 1.3 (95% CI = 1.41-1.81) for men, and 1.4 (95% CI = 1.08-1.46) for women in a study by Danielson *et al*<sup>24</sup>, while in a study by Jacobsen *et al*<sup>25</sup> these values were 1.2 (95% CI = 1.13-1.22) and 1.1 (95% CI = 1.06-1.10), respectively. Negative associations were stronger, with risk ratio of 0.4 (p<0.001) for men and 0.7 (P<0.05) for women in a study by Simonen *et al*<sup>21</sup>, and overall risk ratio of 0.6 (95% CI = 0.46-0.86) in a time-trend study by Jacobsen *et al*<sup>31</sup>. Risk ratios and corresponding confidence intervals are summarized in Table 5. The two correlation studies identified a positive association between water fluoride levels and the occurrence of hip fractures. In a study by Cooper *et al*<sup>27</sup>, the correlation between the concentration of fluoride and discharge rates for hip fracture was significant but moderate (r=0.41, P=0.009). Jacobsen *et al*<sup>29</sup> found a weak significant correlation (r=0.03, P=0.0009). However, the approach they used in the measurement of fluoride exposure (the percentage of population receiving fluoridated water) is more

susceptible to error than the method used by Cooper *et al*<sup>27</sup> (the water fluoride concentration in each community), and could have biased the findings in this study, i.e weakened the association. These results are presented in Table 6.

Because of the aforementioned methodological variations in the studies these results cannot be further compared and summarized.

## **DISCUSSION AND CONCLUSION**

This review shows that the evidence pertaining to the relationship between exposure to fluoridated water and the incidence of age-related hip fractures is very poor.

It is based solely on the findings from ecological studies, which represent a crude way of exploring the association between an environmental exposure and disease occurrence. Since the unit of the observation in these studies is not an individual but a group of individuals, exposure to the risk factor of interest is measured as a population average. However, it is not necessarily homogenous throughout the community and may fluctuate over the time. As a consequence, the association observed in an ecologic study is always tenuous. In some of the studies presented in this review, the association is further attenuated by not having a direct measure of fluoride exposure, i.e. fluoride water content, but a proxy measure in the form of the proportion of the population in a cathement area receiving water fluoridated or not to the level recommended for caries prevention. This is a likely source of error since the probability of exposure is a poor indicator of actual exposure

if within-area fluoridation levels are heterogeneous.

In addition, potential confounding factors cannot be controlled for in ecologic studies, which may introduce bias and compromise the validity of their findings. This inability may be considered the most critical flaw present in each of the studies included in this report.

The potential confounders for the association between fluoridated water and quality of bone tissue are numerous. They are presented in Appendix 3, which includes also other potential sources of error when this relationship is examined using an ecologic study design.

The quality of evidence presented in this review is also hampered by the flaws in the design of some of the studies, as the analysis has shown. The non-standardized methodologies of the studies prevent any attempt to compare and summarize their findings.

In all, the conclusion to be drawn from this review is that the question whether water fluoridation at the levels conventionally used to prevent dental caries has protective, adverse or no effect on hip fracture rates among the elderly has not been answered by the studies conducted to date.

## **RESEARCH AND POLICY RECOMMENDATIONS**

It is not biologically plausible for fluorides to have the adverse effect on bone tissue at doses recommended for caries prevention. However, because of many unknowns that exist in the relationship between duration of fluoride exposure and

quality of bone tissue, this must not be dismissed as a possibility.

It is estimated that about 286 million people worldwide receive artificially fluoridated water presently<sup>32</sup>.

Hip fractures among the elderly are expected to reach epidemic proportions in Western countries during the early part of the next century, as their populations age.

Considering all this, it is essential that the effect of fluoride present in drinking water at the levels optimal for caries prevention on the occurrence of age-related hip fractures be completely understood.

Since the existing evidence concerning this association is equivocal and inconclusive, there is a clear need for further research. Ecological studies are not warranted because of their inability to establish cause-effect relationships. Instead, analytic epidemiologic studies, with precise measurement of fluoride exposure at the individual level and control for potential confounding factors, are necessary to obtain scientifically conclusive information needed to guide public policy about water fluoridation. However, while capable of identifying risk factors and causes, these studies are more difficult to conduct than the ecologic studies, since they require collecting detailed information from very large number of individuals. Using the formulae given by Elwood and Lemeshow<sup>33</sup>, it has been estimated that hip fracture case-control study comparing fluoridated and unfluoridated communities, in which the frequency of exposure to fluoridated water in the control group is 70%, would require 1629 cases to detect an odds ratio of 1.25. Another practical difficulty in conducting these studies is the need to measure fluoride exposure more precisely than



a simple estimate on the basis of fluoride concentration in the drinking water supply. This is because total fluoride exposure, i.e. exposure from the sources other than water is likely to have increased in both fluoridated and non-fluoridated communities in recent decades<sup>34</sup>.

In conclusion, until information from research at the individual level is obtained, there is no evidence that would indicate a need for a revision of the policy of water fluoridation for the prevention of tooth decay. The practice of adjusting fluoride concentration in community water supplies to the levels consistent with those recommended for caries prevention can still be considered to be safe, effective and cost-effective public health measure.

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Table 1

## MAIN CHARACTERISTICS OF THE STUDIES INCLUDED IN THE REVIEW

Author	Ecological study design	Fluoride exposure measure	Case definition	Case ascertainment	Follow-up (yrs)	Population at risk identification
Korns RF <sup>19</sup>	Comparison	Fluoride conc.	- <sup>5</sup>	Hospital discharge	3 (1964-66)	Census 1960
Madans J <sup>20</sup>	Comparison	% exposed	-	Hospital discharge	5 (1973-77)	Health survey respondents
Simonen O <sup>21</sup>	Comparison	Fluoride conc.	820.0, 820.9 ICD-?	Hospital discharge <sup>1,2</sup>	10 (1967-78)	-
Arnala I <sup>22,23</sup>	Comparison	Fluoride conc	- <sup>5</sup>	Hospital discharge	10 (1972-81)	Census 1980
Danielson <sup>24</sup>	Comparison	Fluoride conc	820.0-820.9 ICD-9 <sup>3,5</sup>	Hospital discharge	7 (1984-90)	Census 1980, 1987 estimate
Jacobsen <sup>25</sup>	Comparison	% exposed	820.0-820.9 ICD-9 <sup>4</sup>	Hospital discharge	4 (1984-87)	Census 1980, 1985 estimate
Almazor M <sup>26</sup>	Comparison	Fluoride conc	820.0-820.9 ICD-9 <sup>4</sup>	Hospital discharge <sup>1,2</sup>	7 (1981-87)	Census 1981 and 1986, midyear estimate
Cooper C <sup>27,28</sup>	Correlation	Fluoride conc	820.0 ICD-8	Hospital discharge <sup>1,2</sup>	5 (1978-82)	-
Jacobsen <sup>29</sup>	Correlation	% exposed	820.0-820.9 ICD-9 <sup>4</sup>	Hospital discharge	4 (1984-87)	Census 1980, 1985 estimate
Goggin JE <sup>30</sup>	Time trend	Fluoride conc	-	Hospital discharge	5	-
Jacobsen <sup>31</sup>	Time trend	Fluoride absent or present	-	Hospital discharge	10	-

<sup>1</sup> Controlled for transfer of cases<sup>2</sup> Controlled for readmission of cases<sup>3</sup> Primary discharge diagnosis only<sup>4</sup> Primary, secondary or tertiary diagnosis<sup>5</sup> Fractures secondary to bone diseases other than osteoporosis excluded

Table 2

**THE LENGTH OF EXPOSURE TO FLUORIDATED WATER  
IN COMPARISON AND TIME-TREND STUDIES INCLUDED IN THE  
REVIEW**

Study	Length of exposure (yrs)
Korns RF <sup>19</sup>	20-22
Simonen O <sup>21</sup>	7-17
Madans J <sup>20</sup>	Not reported
Arnala I <sup>22</sup>	13-23
Danielson C <sup>24</sup>	19-25
Suarez-Almazor M <sup>26</sup>	14-20
Cooper C <sup>27</sup>	Not reported
Goggin JE <sup>30</sup>	5
Jacobsen S <sup>31</sup>	10

**Table 3****SAMPLE SIZE IN THE STUDIES INCLUDED IN THE REVIEW**

<b>Study</b>	<b>Sample size</b>
Korns RF <sup>19</sup>	4,379
Madans J <sup>20</sup>	-
Simonen O <sup>21</sup>	395
Arnala I <sup>22</sup>	461
Danielson C <sup>24</sup>	246
Jacobsen S <sup>25</sup>	541,985
Suarez-Almazor M <sup>26</sup>	5,267
Jacobsen S <sup>31</sup>	751
Goggin JE <sup>30</sup>	98,706
Cooper C <sup>27</sup>	20,393
Jacobsen S <sup>29</sup>	218,751

**Table 4 HIP FRACTURE INCIDENCE RATES  
Comparison and Time-Trend Studies**

		Water fluoridation														
		Yes					No									
Author	Age group	Hip fracture rate per 1,000														
		Age specific		Age adjusted		Crude		Age specific		Age adjusted		Crude				
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female			
Korns RF <sup>19</sup>	55-64	0.7	2.5													
	65+	6.1	12.7													
Madans J <sup>20</sup>	45+					1.1	2.2								1.0	2.4
Simonen O <sup>21</sup>	50-59	0.1*	0.4*													
	60-69	0.3	0.8													
	70-79	1.3	2.7													
	80+	3.2	7.6													
Arnala I <sup>22,23</sup>	50-59	0.2	0.2													
	60-69	0.5	0.9													
	70-79	0.8	2.0													
	80+	5.6	10.6													
Danielson C <sup>24</sup>	65-69	1.1	1.2													
	70-74	2.8	5.8													
	75-79	8.3	13.3													
	80-84	13.9	9.6													
	85+	40.0	30.8													
Jacobsen S <sup>25</sup>	65+					4.7***	8.6***							4.0	7.9	
Almazor M <sup>26</sup>	45-64	0.6	0.6													
	65+	5.1	9.5													



Table 3 (Continued)

Jacobsen S <sup>31</sup>																			
Goggin JE <sup>30</sup>	60-64					2.2										1.2		7.3	
	65-69																		
	70-74																		
	75-84																		
	85+																		

\* Mean annual age-specific rates

\*\* Fluoridated community population used as a standard population

\*\*\* 1980 US population used as standard population

\*\*\*\* 1990 US population used as standard population

(a) p<0.001

(b) p<0.05

Table 5

**HIP FRACTURE RELATIVE RISKS STANDARDIZED BY AGE  
AND P-VALUES / CONFIDENCE INTERVALS**

**Comparison and Time-Trend Studies**

<b>Study</b>	<b>Relative Risk*</b>	<b>P-value or 95% Confidence Interval</b>
Korns RF <sup>19</sup>	No association	
Madans J <sup>20</sup>	No association	
Simonen O <sup>21</sup>	Male: 0.4 Female: 0.7	Male: <0.001 Female:<0.05
Arnala I <sup>22</sup>	No association	
Danielson C <sup>24</sup>	Male: 1.3 Female: 1.4	Male: 1.41-1.81 Female: 1.08-1.46
Jacobsen S <sup>25</sup>	Male: 1.2 Female: 1.1	Male: 1.13-1.22 Female: 1.06-1.10
Suarez-Almazor M <sup>26</sup>	No association	
Jacobsen S <sup>31</sup>	Male: 0.8 Female: 0.6	Male: 0.37-1.66 Female: 0.46-0.48
Goggin JE <sup>30</sup>	No association	

\* Non-fluoridated community is the referent category

**Table 6****RESULTS FROM THE CORRELATION STUDIES**

<b>Study</b>	<b>Correlation Coefficient</b>	<b>P-value</b>
Cooper C <sup>27</sup>	0.41	0.009
Jacobsen S <sup>29</sup>	0.03	0.0009

## Appendix 1

### RISK FACTORS FOR OSTEOPOROSIS

1. age
2. gender
3. race
4. reproductive history (parity, length of lactation, age at first live birth)
5. menstrual history (age at menarche, menstrual cycle variations)
6. menopause history (age at menopause, natural or surgical menopause, ovary disease)
7. dietary factors (consumption of calcium, phosphorus, vitamin D and its metabolites)
8. medical conditions:
  - a) endocrine diseases (diabetes mellitus, hyperthyroidism, ovary diseases)
  - b) renal diseases and failure
  - c) cardio-vascular diseases
  - d) gallbladder diseases
9. medicaments use (oral contraceptives, diuretics)
10. anthropometric measures (body built, body mass index: weight-kg / height-m)
11. smoking
12. alcohol consumption
13. physical activity
14. residence history (number of sunny days, i.e. length of sun exposure)

**Appendix 2****ECOLOGICAL RESEARCH DESIGN  
OF THE STUDIES INCLUDED IN THE REVIEW****Comparison or exploratory  
ecologic studies**

Compare the incidence of hip fracture in a community with drinking water fluoridated to the level optimal for dental caries prevention (0.7 ppm - 1.2 ppm) and in a community with traces of fluoride in drinking water (<0.3 ppm)

**Multiple group comparison or  
correlation ecologic studies**

Examine the correlation between the level of fluoride in drinking water and the incidence of hip fracture in communities with water fluoridated at different levels. The fluoride exposure does not exceed the optimal for dental caries prevention

**Time-trend ecologic studies**

Compare the incidence of hip fractures in a community before and after introduction of water fluoridation

### Appendix 3

#### POTENTIAL BIASES IN THE STUDIES INCLUDED IN THE REVIEW

1. risk factors for osteoporosis (Appendix 1)
2. exposure to alternative fluoride sources (toothpaste, mouth rinses, foods, drinks, dietary supplements containing fluoride, professionally applied fluoride)
3. inaccuracy of numerator data
  - diagnostic miscoding
  - readmission of cases
  - transfer of cases
  - bone diseases other than osteoporosis (e.g. primary and metastatic carcinoma)
  - fractures due to high energy injuries
  - access to health care services (treatment within/outside community of residence; frequency of estrogen replacement therapy)
4. inaccuracy of denominator data
5. discrepancies between county boundaries, hospital admission boundaries and boundaries of public water system
6. insufficient length of fluoride exposure, i.e residency in communities
8. insufficient follow-up period
9. number of nursing homes in a geographic unit (cluster of frail elderly)