BENEFITS AND RISKS OF WATER FLUORIDATION

An Update of the 1996 Federal-Provincial Sub-committee Report

Prepared under contract for:

Public Health Branch, Ontario Ministry of Health

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Submitted by:

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Authorship

This literature review was undertaken by three investigators from the Community Dental Health Services Research Unit, Faculty of Dentistry, University of Toronto.

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The remainder of the report was prepared by Dr David Locker, who retains responsibility for the critical appraisal and interpretation of the literature and all recommendations contained in the report.

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EXECUTIVE SUMMARY

This report provides an update of the 1996 Federal-Provincial Subcommittee Report concerning fluoride in the water supply. It consists of a review of the literature published between 1994 and 1999 concerning the benefits and health risks associated with drinking water that has been fluoridated to 'optimum levels'. The report is then limited by the relatively narrow scope of the review as requested by the Public Health Branch, Ontario Ministry of Health and the First Nations and Inuit Health Branch, Health Canada.

Mechanisms of action of fluoride in reducing dental caries

Although it was initially thought that the main mode of action of fluoride was through its incorporation into enamel, thereby reducing the solubility of the enamel, this pre-eruptive effect is likely to be minor. The evidence for a post-eruptive effect, particularly its role in inhibiting demineralization and promoting remineralization, is much stronger.

Reductions in dental caries

Although current studies of the effectiveness of water fluoridation have design weaknesses and methodological flaws, the balance of evidence suggests that rates of dental decay are lower in fluoridated than non-fluoridated communities. The magnitude of the effect is not large in absolute terms, is often not statistically significant and may not be of clinical significance. The effect tends to be more pronounced in the deciduous dentition. The effect tends to be maximized among children from the lower socioeconomic groups so that this section of the population may be the prime beneficiary. Canadian studies do not provide systematic evidence that water fluoridation is effective in reducing decay in contemporary child populations. The few studies of communities where fluoridation has been withdrawn do not suggest significant increases in dental caries as a result. More research is needed to document the benefits of fluoridation to adult and elderly populations in terms of reductions in coronal and root decay. Research is also needed to document improvements in the oral health-related quality of life that accrue to populations exposed to fluoridated water in order to enhance the credibility of this public health initiative.

Osteoporosis

Research on the contribution of fluoride to the treatment of osteoporosis in terms of reductions in osteoporotic fractures has produced inconsistent findings. This may be due to differences in the action of fluoride in different parts of the skeleton and/or to limitations in research designs.

Acute toxicity

Fluoride is a poison in large doses but toxic levels cannot be achieved by drinking fluoridated water. Fluoride products such as toothpaste should be kept out of the reach of children since toxic amounts could be ingested via these sources.

Dental fluorosis

Current studies support the view that dental fluorosis has increased in both fluoridated and non-fluoridated communities. North American studies suggest rates of 20 to 75% in the former and 12 to 45% in the latter. Although largely confined to the 'very mild' and 'mild' categories of the condition, they are of concern insofar as they are discernable to the lay population and may impact on those so affected. Although about half the fluorosis in contemporary child populations living in fluoridated communities can be attributed to fluoride from discretionary sources, efforts to reduce exposure to these sources may not be successful. Research is needed into the relative effects of dental decay and fluorosis on quality of life outcomes and community values regarding the balance between reductions in dental decay and increases in dental fluorosis associated with water fluoridation.

Bone health

Fluoride is incorporated into bone and may affect its biomechanical properties. Skeletal fluorosis is a crippling disease associated with chronic exposures of $\geq$ 10mg of fluoride per day for at least ten years. Studies of bone mineral density have not detected changes consistent with the clinical picture of skeletal fluorosis from water containing levels of fluoride optimal for the reduction of dental decay.

Bone fractures

Studies of the association between water fluoridation and bone fracture are largely ecological in design. Of 11 studies published prior to 1994, two showed a protective effect, five showed no association and four suggested an increase in hip fracture rates. In the latter, the strength of the association was weak, with relative risks ranging from 1.1 to 1.4. Of four studies published between 1994 and 1999, one showed a non-significant protective effect, two showed no association and one suggested an increased risk (RR=1.3-1.4). The public health significance of small increases in hip fracture rates in elderly populations means that more studies with better research designs are needed.

Cancer

The few studies published during the review period do not challenge earlier research showing that there is no reason to believe that exposure to fluoridated water increases the risk of cancer in bones or other body tissues. While an ecological study did suggest an association with uterine cancer, the limitations of this kind of study in terms of linking exposures and outcomes in individuals, mean that it does not contradict the evidence derived from more systematic and scientifically credible case-control studies.

Child development

Recent studies emanating from China have claimed that children exposed to high levels of fluoride have lower IQ's than children exposed to low levels. The two studies claiming such an effect are deeply flawed and provide no credible evidence that fluoride obtained from water or industrial pollution affects the intellectual development of children.

Recommended and actual intakes of fluoride in Canada

Given the lack of adequate contemporary data, recommendations regarding optimal daily intakes of fluoride were based on dose-response data published in the 1940's. Optimal intakes are those derived from water fluoridated at 0.8 to 1.2 ppm, assuming no other sources of fluoride except food. Maximum intakes were based on consumption of water at 1.6 ppm, the level before moderate fluorosis appears. Actual total daily intakes were derived from amounts present in water, food, breast milk, air, soil and toothpaste. In Canada, actual intakes are larger than recommended intakes for formula-fed infants and those living in fluoridated communities. Efforts are required to reduce intakes among the most vulnerable age group, children aged 7 months to 4 years. Children of this age who are consuming the maximum dose are at risk of moderate levels of dental fluorosis and are consuming amounts only 20% less than that at which skeletal fluorosis is possible if maintained over long periods.

Optimal levels of fluoride in the water supply

Standards regarding optimal levels of fluoride in the water supply were developed on the basis of epidemiological data collected more than fifty years ago. The optimal level of 1.0 ppm was chosen, largely on an arbitrary basis, to achieve the maximum reduction in dental caries and the minimum prevalence of fluorosis. Re-examination of the early dose response data suggests that levels as low as 0.6 ppm would have achieved approximately the same reduction in the prevalence of dental decay. There is a lack of contemporary data on dose-response relationships between fluoride concentrations in the water supply, dental caries and dental fluorosis. Nevertheless, it has been suggested that new and more flexible guidelines are needed which take into account the changing prevalence of dental

caries, access to other sources of fluoride and contemporary concerns with the cosmetic effects of fluorosis. Levels as low as 0.5 ppm may be optimal in some communities. Dental fluorosis has not been viewed as a public health problem in the past but may become so in the future.

Maximum allowable concentration

A maximum allowable concentration (MAC) for Canadian drinking water of 1.5 mg/L was established in 1978. The 1996 report recommended that this level be maintained. Since drinking water is not the only source of fluoride to which children are exposed, efforts to reduce exposure to other sources of fluoride are need in those communities in which fluoride in the drinking water approaches this concentration.

INTRODUCTION

This report forms part of a contract funded by the Public Health Branch (Ontario Ministry of Health) and First Nations and Inuit Health Branch (Health Canada) which has the following objectives:

1. Produce a technical report on water fluoridation;
2. The report would include a literature review to update the information contained in the Federal Provincial Subcommittee Report, August 1996, (edited February 1997) also known as the Patterson Report;
3. Substantiate or repudiate the recommendations contained in the Report mentioned in 2 above;
4. Substantiate or repudiate recent claims regarding the safety and need for water fluoridation;
5. Present the findings at a Public Health Branch-sponsored education day, to be held in Toronto, in mid to late November 1999.

The 1996 report contained two recommendations:

1. The maximum acceptable concentration (MAC) for fluoride in drinking water is 1.5mg/L.

This recommendation pertains to item 3 above. It was based on a tolerable daily intake (TDI) of fluoride of 122 micrograms/kg body weight for a child aged 22-26 months. This TDI value was taken from a 1994 report produced under contract to Health Canada. The age 22-26 months is the period of greatest risk for the development of fluorosis in the anterior permanent teeth. An intake of 122 micrograms/kg body weight was considered to be unlikely to result in moderate to severe fluorosis.

2. If it is desired that water supplies be fluoridated as a public health measure for the prevention of dental caries, an optimal concentration of 0.8-1.0 mg/L should be maintained.

The report did not address whether or not water fluoridation produces appreciable benefits in the modern context when caries rates in children are low and fluoride is obtained from many other sources. However, this issue has a bearing on item 4 above and is addressed in this report.

The contract called for a literature review to update the information contained in the 1996 report. Since the 1996 report included reference to very few papers published after 1993, the update undertaken in response to the contract included literature published between 1994 and 1999. For some sections of this report, papers published prior to 1994 were also obtained and reviewed in order to allow for a more comprehensive assessment of some of the issues involved in assessing the benefits and risks of water fluoridation.

Literature search

Studies concerning the benefits of and dental and non-dental risks associated with water fluoridation were identified by means of a search of the dental and medical literature covering the period January 1994 to November 1999. The electronic search covered the Medline and the CancerLit bibliographic databases. The Medical Index and the Index to Dental Literature were also searched. The Medline was searched under the following Medical Subject Headings (MeSH): fluoridation, fluorides, dental caries, dental fluorosis, cancer/neoplasm, bone mass/density/fracture, osteoporosis. These terms and their combinations were used in the key-word search. In an iterative fashion, the bibliographies from the papers retrieved by this search were screened and relevant references followed-up. Subsequently, the following journals with a high reference yield were hand-searched: Community Dentistry and Oral Epidemiology, Caries Research, Community Dental Health, Journal of Public Health Dentistry, European Journal of Oral Sciences, Journal of Dental Research, British Dental Journal, Advances in Dental Research and Paediatric Dentistry. Papers published before 1994 that have been included in the review were identified from the reference lists of the papers obtained. A complete bibliography of papers identified or utilized for this report is attached at the end of the document.

A number of reports from public bodies were accessed through the Internet and other sources and screened for references not identified by the electronic and hand search. These included:

Public Health Service Report on Fluoride Benefits and Risks. US Department of Health and Human Services, Public Health Service, 1991.

National Health Medical and Research Council. The Effectiveness of Water Fluoridation. Canberra: Australian Government Publishing Service, 1991.

Investigation of Inorganic Fluoride and its Effect on the Occurrence of Dental Caries and Dental Fluorosis in Canada. Final Report for contract no. 3726. Submitted to Health Canada, Health Protection Branch, 1994.

The Lord Mayor's Taskforce on Fluoridation – Final Report. Brisbane City Council, 1997.

City of Calgary, Expert Panel on Water Fluoridation Review, 1998

The search was limited to the English-language literature involving human subjects. Papers were required to be in English due to the necessity of a full text evaluation. (The non-English papers were recorded in order to estimate the literature search bias.) No attempt was made to identify unpublished studies. The literature search was carried out in August 1999. It was regularly updated until the first week of November 1999.

All papers retrieved in the literature were subjected to a preliminary evaluation. The following were excluded: animal studies, studies of the effects of drinking water containing levels of fluoride higher than those considered 'optimal' for caries prevention (0.7-1.2 ppm), reviews, case reports, abstracts, editorials and letters to the editor. The remaining papers were grouped according to topic and/or health effect and subsequently assigned to one of three reviewers. Each paper was assessed to determine the study research design and subjected to data extraction as necessary. Given the narrow time frame of the literature search and the exclusion criteria, the literature reviewed for this report addressed the following topics only:

- Mechanism of action of fluoride re: dental caries
- Benefits of water fluoridation
    - dental decay
    - osteoporosis

- Health risks of water fluoridation

    - acute toxicity
    - dental fluorosis
    - skeletal fluorosis
    - bone fractures
    - bone mineral density
    - cancer
    - child development

- Recommended and actual fluoride intakes in Canada
- Determining optimal levels for the water supply
- Maximum allowable concentration

Although research has been conducted on other potential health risks of water fluoridation, such as low birth rates, Down syndrome, hearing and immune function, these are not covered in this update since no papers were published between 1994 and 1999 that conformed to the inclusion criteria.

The main principle underlying this report is that dental public health interventions, particularly those aimed at total populations, must 1) make a demonstrable contribution to the oral health-related quality of life of the recipients of that intervention, and 2) avoid subjecting those recipients to risks which are not commensurable with the benefits obtained in terms of improved quality of life.

MECHANISM OF ACTION OF FLUORIDE: DENTAL CARIES

At one time, the National research Council in the US considered that fluoride was an essential nutrient. However, because it has not been possible to demonstrate that fluoride is essential for human growth it is now considered a beneficial element only (Burt and Eklund, 1999). The main benefit that stems from the consumption of fluoride is its positive impact on oral health through reductions in dental caries.

The pathogenesis and natural history of dental caries indicate that it results from the localized dissolution of tooth enamel caused by acids, produced by bacterial action on dietary fermentable carbohydrates, which if not stopped, can lead to considerable demineralization of tooth tissues. Initial studies of the role of fluoride as an anti-caries agent are related to the biochemical, pre-eruptive incorporation of fluoride ions directly into the developing enamel structure (fluoroapatite). This gives rise to a reduction in acid solubility attributed to improved crystallinity and the buffering action of fluoride released from enamel crystals during the earliest stages of acid attack (Aoba, 1997). However, recent reviews of clinical studies of water fluoridation and the effect of fluoride on mineralization point to fluoride's major cariostatic effect as post-eruptive or "topical", which works through the inhibition of demineralization and the enhancement of remineralization of early carious lesions (ten Cate, 1984; Arends and ten Bosch, 1986; Ekstrand et al., 1988; ten Cate, 1990; Limeback, 1999). Fluoride via its topical mechanism has also been shown to inhibit plaque bacterial acid production by interfering with essential enzyme (enolase) activity in the bacterium (for a review, see Featherstone, 1999) although a recent study did not find differences in plaque fluoride content either before, or after, discontinuation of fluoridation (Seppä et al., 1996). The effect of fluoride on enamel is also dose dependent, with evidence that excess fluoride ingestion results in protein retention and/or poor hydroxyapatite crystal formation during enamel maturation (for a review, see Limeback, 1994).

Laboratory studies have been successful in identifying possible mechanisms of fluoride action in the de- and re-mineralization processes of caries lesions. Specifically, intraoral models have shown that fluoride has an inhibiting effect on enamel caries development and progression *in vivo* (Øgaard, 1990; Wefel, 1990). Laboratory models and pH-cycling experiments have also shown that fluoride has an inhibiting effect on lesion progression in the dentine, although higher concentrations were needed in the dentine as compared with the enamel (Hoppenbrouwers et al., 1987).

A consistent presence of fluoride in the oral environment, particularly at low concentrations in saliva, plaque and gingival crevicular fluid, appears to have a greater effect in inhibiting the rate of enamel demineralization than a high concentration of fluoride incorporated into enamel during early tooth development (Fejerskov et al., 1981; Arends et al., 1984; Larsen and Jensen, 1985; Silverstone et al., 1988; ten Cate, 1997; Featherstone, 1999). The fluoride content of teeth exposed to drinking water with optimal and high fluoride levels is higher than that of teeth exposed to drinking water with low or no fluoride levels (Takeuchi et al., 1996; Mestriner Jr. et al., 1996; Cutress et al., 1996). However, *in vitro* studies have shown that the fluoride incorporated into the enamel mineral during tooth development does not always reflect the relative susceptibility of the enamel to acid attack (Kidd et al., 1980). Likewise, fluoride incorporated into the dentine is unlikely to play a major role in protecting it from acid attack (Samarawickrama and Speirs, 1993). These studies suggest that the cariostatic effect of fluoride in optimally fluoridated areas may well be a result of its "topical" rather than "systemic" effect. Moreover, when the impact of fluoride on lesion remineralization is considered, it

appears that high doses of fluoride administered over a short period of time yield surface layer precipitation which effectively slows the diffusion of calcium and phosphate into the deeper parts of the lesion (Featherstone and ten Cate, 1988). The precipitation of high doses of fluoride at the surface of the lesion could explain the large difference in surface porosities observed between "active" and "arrested" lesions (Thylstrup et al., 1983; Silverstone et al, 1988).

Chemical analysis of zones of demineralized enamel or "white spots" have revealed that they contain much higher amounts of fluoride than the surrounding sound enamel (Hallsworth et al., 1971; Weatherall et al., 1977). As a consequence of post-eruptive fluoride exposure, it is accepted that caries lesions may be arrested, but complete *in vivo* remineralization is unlikely because of the precipitation of fluoride on the enamel surface (Savage, 1983; Larsen and Fejerskov, 1989). In addition, areas of arrested caries exhibit a higher degree of resistance to further demineralization than sound enamel since the surface layer of fluoride has a tendency to protect the enamel from subsequent cariogenic challenges (Silverstone, 1977; Koulourides and Cameron, 1980; Weatherell et al., 1984).

In fluoridated areas, early caries lesions present a fluoride-rich surface layer covering the lesion body. It is believed that this layer acts as a substrate whereby fluoride ions are released from the surface layer pores to the liquid phase within the demineralized lesion body during episodes of cariogenic challenges (Arends et al., 1984). If this view can be substantiated then it supports the fact that fluoride should be present in the oral fluids during the years when the tooth is most susceptible to caries (Murray, 1991). The post-eruptive stage of tooth development is when the tooth is most susceptible to decay, since the enamel has not completely matured (Evans and Darvell, 1995). Following eruption of the tooth it takes approximately 2-3 years for the enamel to become more resistant to decay. This usually occurs between the ages of 12-15 years and often determines the individual's future dental treatment needs (Murray, 1987).

Consistent with this post-eruptive mechanism are observations of significantly lower incidence of decayed and filled tooth surfaces in young adults (ages 12 to 16) exposed to fluoridated drinking water as compared to those living in non-fluoridated areas (Lawrence et al., 1997). Significantly lower coronal and root caries incidences were also found for adults 65 years of age and older residing in fluoridated communities for at least 30-40 years compared with lifelong residents of non-fluoridated communities (Hunt et al., 1989; Brustman, 1986). However, a pre-eruptive mechanism cannot be ruled out in these studies since fluoride uptake by the cementum and root dentine of adult teeth in fluoridated areas is related to the fluoride content of the drinking water (Kato et al., 1997).

Further evidence for a post-eruptive caries-preventive effect of fluoride in drinking water comes from Groeneveld’s (1985) re-analysis of the data from the Tiel-Culemborg water fluoridation study which compared subjects born after the fluoridation program began in Tiel with those born in non-fluoridated Culemborg (Backer Dirks et al., 1961; Backer Dirk, 1961). The percentage reductions in caries incidence in Tiel were higher when enamel lesions were excluded than when they were included in the analysis. Since the

number of dentinal lesions in the non-fluoridated area was greater, it was concluded that progression was faster in the non-fluoridated area than in the fluoridated area. In other words, the pre-eruptive effect of water fluoridation could not be observed when the total numbers of lesions, including enamel lesions, were compared.

Based on our knowledge of the cariostatic mechanisms of fluoride, preventive programs should employ fluoride treatments which provide frequent low doses of free ionic fluoride to raise its local concentrations in saliva, plaque and gingival crevicular fluid so that fluoride ions can more readily diffuse into the lesion and precipitate in the form of fluoroapatite or fluorohydroxyapatite during times of acid attack (ten Cate and Arends, 1977). Water fluoridation does more to enhance the maintenance of salivary levels of fluoride which are compatible with the inhibition of demineralization and promotion of remineralization of enamel than other types of fluoride vehicles (Lewis et al, 1994). It is for this reason that many authorities contend that water fluoridation continues to be the fluoride technology of choice with respect to effectiveness, distribution, equity, compliance and costs.

Summary

Although it was initially thought that the main mode of action of fluoride was through its incorporation into enamel, thereby reducing the solubility of the enamel, this pre-eruptive effect is likely to be minor. The evidence for a post-eruptive effect, particularly its role in inhibiting demineralization and promoting remineralization, is much stronger.

BENEFITS OF WATER FLUORIDATION

DENTAL CARIES

The 1996 report did not contain a comprehensive assessment of the evidence concerning the current benefits of water fluoridation in terms of reductions in dental caries. Such an assessment is essential if the balance of the benefits and risks associated with the fluoridation of community water supplies is to be properly assessed.

There is a substantial literature comparing the prevalence and severity of dental caries among populations living in communities with differing levels of fluoride in the water supply. The initial research was conducted by McKay and subsequently, Dean, (Burt and Eklund, 1999) and culminated in the Twenty-One Cities Study. This showed that dental caries experience dropped sharply as fluoride levels rose to 1.0 ppm. This research was followed by a series of four community trials of water fluoridation begun in 1945 and 1946. Although these trials were relatively crude and subject to a number of methodological flaws (Burt and Eklund, 1999), they showed that after 13 to 15 years of fluoridation, rates of dental decay in children living in communities that were fluoridated to 1.0-1.2 ppm were 48% to 70% lower than in children living in control non-fluoridated communities. Since then, numerous studies have assessed the caries-protective effect of water fluoridation. These studies have been the subject of reviews by Murray and Rugg-Gunn, (1982), Newbrun (1989), Brunelle and Carlos (1990) and Lewis and Banting (1994).

Dental caries is a dynamic disease whose frequency and distribution in modern populations has changed dramatically and continues to change. Moreover, exposure to fluoride other than that found in, or added to, water supplies has increased substantially over the past two decades. The consensus of opinion is that secular declines in dental caries and increases in the vehicles and modalities through which fluoride is now delivered, mean that the effectiveness of water fluoridation, in terms of the relative difference in caries rates between optimally and negligibly fluoridated communities, has declined (Newbrun, 1989; Lewis and Banting, 1994). Murray and Rugg-Gunn (1982) examined 95 studies conducted between 1945 and 1978 and reported caries reductions of 40-50% for primary teeth and 50-60% for permanent teeth. Newbrun (1989) reviewed studies conducted between 1976 and 1987 and reported 30-60% reductions for deciduous teeth, 20-40% reductions for children with mixed dentitions and 15-35% reductions in the permanent teeth of adolescents. The 10 studies conducted between 1988 and 1992 reviewed by Lewis and Banting (1994) reported reductions ranging from 8 to 56%. Half reported reductions of less than 20%. Moreover, when the studies reviewed by Newbrun (1989) were re-examined there was also evidence of a reduction in the absolute differences between fluoridated and non-fluoridated communities over the period 1977 to 1991. As Lewis and Banting (1994) comment, the “small and in many cases non-significant differences in the more recent studies contrast sharply with the findings of the four North American community trials of fluoride where the differences were, on average, 5.0 DMFT (about 10 DMFS) for 14 to 15 year-olds”.

Consequently, the research conducted between 1940 and the late 1970's, while of historical interest, is no longer relevant to an assessment of the current benefits of water fluoridation. It is also likely that some of the research conducted in the 1980's is of little relevance, particularly research in communities which have seen increases in the proportion of children who have never experienced dental decay and/or a reduction in the severity of the disease in those still affected (Newbrun, 1989). It was for this reason that the review was largely confined to papers published between 1994 and 1999.

Papers published between 1994 and 1999

Among the papers published between 1994 and 1999, there was substantial variation in terms of the levels of exposure to water fluoridation. In general, papers were included in the review if they compared communities with, or populations exposed to, 'optimal' (0.7-1.2 ppm) and 'less than optimal' levels of fluoride (usually 0.3-0.5 ppm or less). Papers, or sections of papers, that examined communities with, or populations exposed to, 2 or 4 times the 'optimal' level were not included. While these studies are of scientific interest, they are not of relevance with respect to current policy concerns regarding water fluoridation. Using these inclusion/exclusion criteria, 29 papers were located. Sixteen provided data on reductions in dental caries in the deciduous dentition (dmft/dmfs/dfs) and 18 provided data on reductions in dental caries in the permanent dentition (DMFT/DMFS). These studies are difficult to compare for a number of reasons. There are differences in the way in which optimally and negligibly fluoridated communities are defined and differences in the ages of the populations examined. Some studies provide crude estimates of caries prevalence across broad age ranges, while others provide age or stratum-specific rates or rates adjusted for age and other factors such as socioeconomic status. The data from the 29 papers reviewed are summarized in Tables 1 and 2.

Although the review was intended to be confined to papers published between 1994 and 1999, papers published prior to that period were included if they described studies undertaken in Canada or studies of adult populations. The reason for this is that only one study using Canadian data and one pertaining to adults was published during the five-year review period. Nearly all of these additional studies were published subsequent to 1990.

The 29 papers reviewed described four types of studies. The majority were one-shot studies in which the caries experience of populations exposed to differing levels of fluoridated water was compared. Others were concerned with the differential effect of water fluoridation across high and low socio-economic groups. Some were trend studies in which differences in caries rates between fluoridated and non-fluoridated populations were examined at different points in time, and others were concerned with the effect on caries rates of a cessation of water fluoridation. Data from trend studies were abstracted for the last year in the series covered by the study.

Table 1: Differences in mean dmft/dmfs/dfs values : Fluoridated and non-fluoridated communities

Author/ Yr	Country	Design	Age	F Status	Prev >0	dmft	Absolute Diff	% Reduction	dmfs/ dfs	Absolute Diff	% Reduction
Evans et al 1995	UK	Two community	5	F NF	**39%** **55%**	**1.33** **2.41**	1.08	45%	**2.80** **5.77**	2.97	51%
Provart& Carmichael l995	UK	Ecologic	5	F* NF F** NF	**40%** **55%** 30% 34%	**1.2** **2.1** **0.8** **1.2**	0.9 0.4	43% 33%			
Thomas & Jones 1995	Wales	Two community	5	F*** NF		1.81 2.28	0.47	21%			
Thomas et al 1995	Wales	Two community	5	F**** NF		0.80 2.2.26	1.46	64%			
Evans et al 1996	UK	Two community	5	F* NF F** NF	31% 62% 23% 38%	**1.17** **2.74** **0.59** **1.46**	1.57 0.87	57% 59%	**1.17** **3.65** **0.85** **2.18**	2.48 1.33	68% 61%
Slade et al 1996a	Queensland Australia	Two community	5 8 10	F NF F NF F NF	38% 42% 49% 57% 42% 55%				1.35 2.98 2.61 4.99 2.03 3.97	1.63 2.38 1.94	55% 48% 49%

Author/ Yr	Country	Design	Age	F Status	Prev >0	dmft	Absolute Diff	% Reduction	dmfs	Absolute Diff	% Reduction
Slade et al 1995	South Australia	Cross-sectional	5 8 10	F NF F NF F NF					2.8^ 3.2 3.3^ 5.2 2.4^ 4.2	0.4 1.9 1.8	13% 37% 43%
Hawew et al 1996	Libya	Two community	6	F***** NF	39% 62%	**1.07** **2.32**	1.25	54%			
Cortes et al 1996	Brazil	Two community	6-12	F NF		**1.5** **2.1**	0.6	29%			
Jones et al 1997a	UK	Ecological	5	F* NF F** NF		1.46 2.78 0.80 1.41	1.32 0.61	48% 43%			
Heller et al 1997	US	Cross-sectional	5-10	F NF					**3.35** **4.49**	1.14	25%
Dini et al 1998a	Brazil	Two community	3-4 5-6	F# NF F# NF	**32%** **58%** **57%** **89%**	1.1 2.4 2.5 5.3	1.3 2.8	54% 53%			
Villa et al 1998a	Chile	Multiple community	7	F NF	**41%** **75%**	**1.56** **3.67**	2.11	57%			

Author/ Yr	Country	Design	Age	F Status	Prev >0	Dmft	Absolute Diff	% Reduction	dmfs	Absolute Diff	% Reduction
Jones & Worthington 1999	UK	Ecological	5	F NF		**1.41** **2.36**	1.02	43%			
Riley et al 1999	UK	Ecological	5	F NF		0.87 1.80	0.93	52%			
Adair et al 1999	US	Cross-sectional	Gds 3-5	F^^ NF					4.81 5.81	1.0	17%

Figures in bold indicate differences that are reported to be statistically significant

* High deprivation groups or lowest social class (IV&V)
** Low deprivation groups or highest social class (I&II)

*** F – children living in fluoridated area for 35% of lives; NF- children living in fluoridated area for less than 10% of lives
**** F – children living in area fluoridated for up to 35% of lives; NF - children living in non-fluoridated area

***** F=1.8mg/l; NF=0.8mg/l

F community fluoridated since 1963; NF community fluoridated one year prior to survey

^ Values estimated from graphs

Table 2: Differences in mean DMFT/DMFS values : Fluoridated and non-fluoridated communities

Author/ Yr	Country	Design	Age	F Status	Prev >0	DMFT	Absolute Diff	% Reduction	DMFS	Absolute Diff	% Reduction
Treasure & Dever 1994	New Zealand	Multiple community	14	F PF NF	75% 82% 83%	**2.33** **3.36** **4.52**	 1.03 2.19	 31% 48%	**2.97** **4.42** **6.19**	 1.45 3.22	 30% 48%
Ellwood & O'Mullane 1995	Wales	Two Community	14	F NF	**66%** **77%**				**2.9*** **4.3**	1.4	33%
Jackson et al 1995	US	Two community	7-14 7-10 11-14	F NF F NF F NF	 	3.34 3.68 2.99 3.01 3.85 4.73	 0.34 0.02 0.88	 9% 1% 19%	**4.35** **5.34** 4.03 4.77 **4.81** **6.76**	 1.19 0.74 1.95	 22% 16% 28%
Clark et al 1995	Canada	Two community	6-14 10-14	F NF F NF	 				1.65 2.53 **2.03** **3.62**	0.88 1.61	35% 44%
Slade et al 1996a	Queensland Australia	Two community	6 9 12	N NF F NF F NF	4% 4% 24% 26% 36% 54%				0.04 0.10 0.41 0.51 0.94 1.80	0.06 0.10 0.86	60% 20% 40%

Author/ Yr	Country	Design	Age	F Status	Prev >0	DMFT	Absolute Diff	% Reduction	DMFS	Absolute Diff	% Reduction
Slade et al 1995	South Australia	Cross-sectional	12 15	F NF N NF					1.0^ 1.2 2.7^ 2.7	 0.2 0.0	 16% 0%
Hawew et al 1996	Libya	Two community	12	F** NF	34% 50%	0.87 1.17	0.30	26%			
Mestriner et al 1996	Brazil	Two community	7 10 12	F NF F NF F NF		0.40 1.19 1.60 3.68 2.80 5.98	0.79 2.08 3.18	66% 57% 53%			
Lawrence & Sheiham 1997 #	Brazil	Two community	12-16	F NF	89% 95%				**8.7** **15.4**	6.7	44%
Heller et al 1997	US	Cross-sectional	5-17	F NF	45% 47%				**2.53** **3.08**	0.55	18%
Dini et al 1998	Brazil	Two community	11-12	F NF****	69% 79%	2.3 2.8	0.5	18%			

Author/ Yr	Country	Design	Age	F Status	Prev >0	DMFT	Absolute Diff	% Reduction	DMFS	Absolute Diff	% Reduction
Grembowski et al 1997	US	Cross-sectional	20-34	F## NF					**18.0** **27.2**	9.2	34%
Seppa et al 1998	Finland	Two community	12 15	F NF F NF					1.88 2.99 4.00 5.62	1.11 1.62	37% 29%
Brett 1998	New Zealand	Two community	12-13	F NF F NF	54% 53% 50% 50%	1.04 1.60 1.24 1.39	0.56 0.15	35% 11%			
Kumar et al 1998	US	Two community	7-14	F(p) NF F(np) NF					1.28 1.55 1.35 0.80	0.27 - 0.55	17% -69%
Villa et al 1998a	Chile	Multiple community	12 15	F NF F NF	**58%** **77%** **68%** **85%**	**1.31** **3.10** **2.60** **5.06**	1.79 2.46	58% 49%			
Selwitz et al 1998	US	Multiple community (CS)	8-16	F NF NF	48% 60% 75%				**1.9** **2.6** **3.7**	0.7 1.8	17% 49%
Adair et al 1999	US	Cross-sectional	Gs 6-8	F***** NF					2.81 3.07	0.26	8%

Figures in bold indicate differences that are reported to be statistically significant

CS – convenience sampling

Status: F – fluoridated; PF – previously fluoridated; NF - non-fluoridated

* Adjusted for differences in social deprivation

** F=1.8mg/l; NF=0.8mg/l

*** Optimally fluoridated for 16 months only

**** F community fluoridated since 1963; NF community fluoridated one year prior to survey

***** F- fluoridated home supply; NF – non-fluoridated home supply. All schools attended by subjects had F water supply though at fluctuating levels.

^ Values estimated from graphs

Baseline data from prospective study of caries progression

F – life time exposure to fluoridated water of 50 to 100%; NF – no exposure to fluoridated water

(p) : poor children; (np) : non-poor children

Methodological issues in water fluoridation research

When addressing the effectiveness of water fluoridation there are three questions that need to be considered:

- Is there an effect?
- What is the magnitude of the effect?
- What is the significance of the effect?

Whether or not these questions can be answered with any degree of certainty depends predominantly on the methodological quality of the studies that have been conducted to date. Although the original community trials of water fluoridation had many methodological flaws (Burt and Eklund, 1999), they were conducted when the prevalence of dental caries in child populations was high. As a consequence, it is likely that the magnitude of the effect of fluoridation in reducing dental decay was large relative to the degree of bias induced by their methodological flaws. Given that caries rates are now low among the child populations included in water fluoridation research, and differences between exposed and not exposed subjects are small, bias induced by methodological flaws may be sufficiently large to create a difference where one does not exist or to mask or substantially reduce a difference that does exist. As Rozier (1995) commented, "Future studies focussing on effectiveness will require a high degree of methodologic sophistication to provide useful information about the impact of water fluoridation on dental caries". This means that all studies need to be carefully appraised in terms of their research design, measurement, data collection and analytic procedures (Lewis and Banting, 1994).

The question "Is there an effect?", involves issues of causality (i.e. does water fluoridation **cause** a reduction in the prevalence or severity of dental caries?). With respect to study design, randomized controlled trials, non-randomized trials and cohort studies provide the strongest evidence concerning cause and effect relationships. None of the papers included in this review used these designs. As the Tables 1 and 2 indicate, the study designs used to assess the effects of water fluoridation consist of the five types (Table 3).

The majority of the studies reviewed were geographically-based and measured exposure to water fluoridation at the aggregate level. Consequently, they were classified as ecological studies. This type of study provides the lowest quality of evidence as far as questions of causality are concerned (Hennekens and Buring, 1987; Lewis and Banting 1994). They are usually used to suggest plausible hypotheses for further study using analytical designs. Cross-sectional studies provide better evidence since exposure to water fluoridation is measured at the level of the individual. Moreover, retrospective cohort or case-control type analyses of the data from cross-sectional studies are possible. In the studies reviewed, only three approximated this design.

Table 3: Study designs in fluoridation effectiveness research 1994-99

Design	Number of studies	Description of design
Two-community comparison ecological studies	18	Dental caries rates are compared in one fluoridated and one non-fluoridated community
Multiple-community comparison ecological designs	3	Dental caries rates are compared in two to five communities with varying levels of water fluoridation
Correlational ecological studies	4	Studies using multiple groups with aggregate measurement of exposure and outcome
Simple cross-sectional studies	1	Cross-sectional study with no control for confounders
Complex cross-sectional studies	3	Cross-sectional studies which involve elements of case-control or cohort studies in their analytic approach and control for confounders

Other methodological problems encountered in some of the studies reviewed were as follows:

- Failure to control for residential histories of subjects
- Failure to control for access to other sources of fluoride
- Failure to control for other factors influencing caries rates i.e. socioeconomic status
- Non-standardization or calibration of examiners
- Lack of blinding of examiners to the exposure status of study subjects

Some of these problems will diminish the gap between fluoridated and non-fluoridated communities while others will widen it. For example, Treasure and Dever (1994) found a difference of 3.02 in mean DMFS scores between 14 year-old New Zealand children from fluoridated and non-fluoridated communities which widened to a difference of 3.22 when only continuous residents were included in the analysis. Kumar et al (1998) studied 7-14 year-old life-long residents of fluoridated Newburgh and non-fluoridated Kingston, New York. These communities were chosen in 1945 for one of the community trials of water fluoridation because of their similarities. Over time, however, the communities have become dissimilar, with the fluoridated community having a higher level of poverty, fewer persons with a college education, a lower percentage of Whites and more unemployment. These confounding factors may account for the fact that in 1995 age-standardized mean DMFS values were 1.7 in the fluoridated and 1.5 in the non-fluoridated community.

In addition, few of the studies used standard epidemiological measures of the strength of associations, such as odds ratios, and many failed to report on the statistical significance of the differences in means and proportions that they documented.

One problem affecting all studies of the effectiveness of water fluoridation is that of the halo effect. This is the spread of fluoride from fluoridated to non-fluoridated communities via the medium of foods and beverages manufactured in the former. Since this is impossible to control for, Lewis and Banting (1994) have suggested that the effectiveness of water fluoridation cannot now be determined. One way of avoiding or minimizing this problem is to study jurisdictions where only a small percentage of the population receives fluoridated water. This is the case in the study conducted in Queensland, Australia by Slade et al (1996a) where only 5% of the population consumed optimally fluoridated water. Studies in the UK are also less likely to be subject to the halo effect since only 10% of the population live in areas with optimally fluoridated water supplies.

The quality of the evidence provided by these recent studies of the effectiveness of water fluoridation is, in general, rather poor. Nevertheless, in spite of weak designs, methodological flaws and the publication of studies showing no significant differences in caries rates between fluoridated and non-fluoridated communities, the balance of the evidence does suggest that in many locations water fluoridation is associated with a reduction in rates of dental decay. This conclusion is strengthened by the findings of the few studies that are more robust in methodological terms. However, questions concerning the strength of the association and the magnitude of the effect need to be considered.

Magnitude of the effect

The magnitude of the difference in dental decay experience between populations exposed and not exposed to fluoridated water can be measured in four ways:

1) **differences in the prevalence of dental caries** (ie. differences in the percentage of persons with a dmft/s or DMFT/S greater than 0)
2) **percent reductions** (ie. the difference between mean dmft/s or DMFT/S values for exposed and non-exposed groups divided by the mean for the non-exposed, expressed as a percentage),
3) **absolute differences in mean values**, and
4) **differences in distributions**.

Since dental caries is a multi-site disease, differences in prevalence estimates can be misleading. For example, Treasure and Dever (1994) found no differences in the prevalence of caries in fluoridated, previously fluoridated and non-fluoridated communities but significant differences in mean DMFT and DMFS scores. Since means can be misleading in populations where a substantial proportion is caries free, measures based on means are also less than ideal (Burt and Eklund, 1999). This is particularly the case with respect to the use of percent reductions. These are especially misleading if not related to a base. For example, a 50% reduction would be worthy of note if it meant a

decline in mean DMFS values from 12 to 6. However, a decline from a mean of 0.5 to a mean of 0.25 would be of questionable clinical value. Unfortunately, percent reductions have historically been the main, if not the only, way in which the magnitude of the effect of water fluoridation has been assessed. The most appropriate method of assessment of effectiveness is to compare distributions. However, such a method is only rarely used in the current literature. Consequently, absolute differences provide the most useful indicator in spite of their derivation from mean values.

As the data in Tables 1 and 2 indicate, summarizing the effectiveness of water fluoridation is complicated by the fact that effectiveness can vary substantially between and within countries according to whether the deciduous or permanent dentition is assessed, the age of subjects and their socio-economic status. To make perusal of the data easier, Tables 4 and 5 below provide a further summary of data according to the countries in which studies were undertaken. The ranges of absolute differences and percent reductions in mean dmft/s and mean DMFT/S are presented for each country. Even so, these summaries need to be treated cautiously. For example, the 11 estimates of absolute differences in mean dmft values between UK populations exposed and not exposed to water fluoridation range from 0.4 to 1.57. However, 6 of the differences were less than 1 and a further two were only marginally greater than 1 (1.02 and 1.08).

Table 4 indicates that absolute differences in mean dmft values ranged from 0.4 to 2.8 while absolute differences in mean dmfs values ranged from 0.4 to 2.97. Table 5 indicates that absolute differences in mean DMFT and DMFS values ranged from 0.10 to 3.18 and -0.55 to 6.7. The higher values, that is, differences of three or more, come from studies conducted in New Zealand and South America. It should be emphasized that many of the differences reported by these studies were not statistically significant or were not subject to significance tests (see Tables 1 and 2) so that their statistical significance is unknown.

Table 4: Ranges of absolute differences in means and percent reduction by country for the deciduous dentition.

	dmft			**dmfs**		
Country:	No.	Range of absolute differences	Range of percent reductions	No.	Range of absolute differences	Range of percent reductions
UK	11	0.4-1.57	17%-64%	3	1.33-2.97	51-68%
US				2	1.0-1.14	17-25%
Australia				6	0.4-2.38	13-55%
Libya	1	1.25	54%			
Brazil/Chile	4	0.6-2.8	29-53%			

Table 5: Ranges of absolute differences in means and percent reduction by country for the permanent dentition.

	DMFT			DMFS		
Country:	No.	Range of absolute differences	Range of percent reductions	No.	Range of absolute differences	Range of percent reductions
UK				1	1.4	33%
US	1	0.34	9%	8	-0.55-1.19	-69-49%
Canada				2	0.88-1.61	35-44%
New Zealand	4	0.15-2.19	11-48%	2	1.45-3.22	30-48%
Australia				5	0-0.86	0-40%
Libya	1	0.30	26%			
Brazil/Chile	6	0.5-3.18	18-58%	1	6.7	44%

The table excludes the study of adults aged 20 to 34 years by Grembowski et al (1997) which is listed in Table 2

Two studies worth examining in some detail are those by Slade et al (1995) and Heller et al (1997). Slade et al (1995) examined South Australian children aged 5-15 years and Queensland children aged 5 to 12 years and recorded dmfs and DMFS data. The children were randomly sampled from one fluoridated and one non-fluoridated site in each state. A parental questionnaire obtained detailed information about residential history that was used to calculate a continuous exposure variable: children's lifetime exposure to optimally fluoridated water. This ranged from 0% to 100% of lifetime. A multivariate model containing age and the fluoride exposure variable showed that both were significant predictors of dmfs scores in 5 to 10 year-olds in each state. Parameter estimates suggested that, in South Australia, children with no exposure to fluoridated water had an average of 1.8 more dmfs than children with 100% lifetime exposure. In Queensland they had an average of 2.3 more dmfs. Model R-square statistics were small and indicated that these two variables explained 3.4% and 2.5% respectively of the variation in dmfs experience at age 5 to 10 years.

Models examining the association between DMFS scores and exposure to water fluoridation in 6 to 12/15 year-old children controlled for the confounding effects of age, parental income and education and use of fluoride supplements. Parameter estimates suggested that in South Australia children with no exposure had on average 0.12 more DMFS than children with lifetime exposure, while in Queensland children with no exposure had an average of 0.30 more DMFS compared to their exposed counterparts. R-square statistics remained low at 0.169 and 0.102, respectively.

Heller et al (1997) used data from the 1986/87 National Survey of US Schoolchildren to examine the association between water fluoridation and dfs and DMFS scores. Fluoride levels of school water were used as an indicator of water fluoride exposure. Only children

with a single continuous residence were included. Regression models controlling for age and exposure to other sources of fluoride indicated that on average dfs scores declined by 1.08 for every 1 ppm increase in water fluoride level. In the model for DMFS, the comparable figure was 0.59. Model R-square statistics were 0.110 and 0.258, respectively. This was the only study to provide data on the distributions of dfs and DMFS scores. These data reveal only small differences between children with life-long exposure to <0.3 ppm and 0.7-1.2 ppm. For example, 15% of the former had a mean dfs score of 11 or over compared with 13.2% of the latter. The figures for DMFS scores were 7.5 and 5.8% respectively.

These two studies provide some of the better evidence that water fluoridation is beneficial in terms of reductions in dental caries. However, they indicate that the effect is more pronounced in the deciduous than the permanent dentition, that declines in caries are relatively small in absolute terms, particularly in permanent teeth, and that water fluoridation explains very little of the variation in caries experience in either the deciduous or permanent dentition.

Canadian studies

During the period of the review only one Canadian study of the effectiveness of water fluoridation was published (Clark et al, 1995). This examined dental caries rates among 6-14 year old children who were lifelong residents of a fluoridated community (1.2 ppm F) and a non-fluoridated community (0.1 ppm F). DMFS scores were 1.65 for the former and 2.53 for the latter. Although this difference of 0.88 tooth surfaces saved represented a reduction of 35%, it was not statistically significant. When only children aged 10-14 years old were considered, the mean values were 2.03 and 3.62, a difference which was statistically significant. However, a multiple regression analysis showed that age and parental education were significant predictors of DMFS scores while the fluoridation status of the community was not.

These results are best seen in the context of previous studies of Canadian populations published prior to our 1994-1999 time frame. A study in the late 1980's compared children with a mean age of 12 years living in a fluoridated (1.08 ppm F) and a non-fluoridated (0.23 ppm F) community in western Canada (Clovis et al, 1988). No statistically significant differences in DMFT or DMFS values were found when all children were compared or when children with a 5-year minimum residency in their respective communities were compared. Ismail et al (1993) also found no significant differences in DMFS scores between fluoridated and non-fluoridated children in Grades 5 and 6 in Nova Scotia. A regression analysis controlling for use of fluoridated toothpaste in early life and parental education showed that exposure to water fluoridation did not contribute to differences in caries prevalence. A study in Quebec (Ismail et al, 1990) found significant differences in mean DMFS scores of public school students aged 15-17 years of age living in fluoridated Trois-Rivieres (9.76) and non-fluoridated Sherbrooke (12.77). No differences were found for children aged 11 to 14 or for students attending private schools. Unadjusted odds ratios suggested that type of school attended, fluoride tablet use, age and gender had more influence on caries rates than community water

fluoridation. Taken together, these studies provide little systematic evidence that water fluoridation is of substantial benefit to Canadian children in terms of reductions in caries experience.

Differential effects according to socioeconomic status

One issue that is a subject of ongoing discussion is the relative effect of water fluoridation on children from high and low socioeconomic groups. Some studies have reported that fluoridation has a greater effect on low compared to high social groups, while other have shown no differential effect. The debate is not resolved by the nine studies reviewed that examined this issue. One problem is that studies do not clearly distinguish between multiplicative and additive interactions (Slade et al, 1996b). Another is that the ability to detect multiplicative interactions appears to be related to study design. Four correlational ecologic studies report significant interactions between socioeconomic status and fluoridation status (Provart and Carmichael, 1995; Jones et al, 1997a; Jones and Worthington, 1999; Riley et al, 1999) and only one did not (Ellwood and O'Mullane, 1995). Studies using other designs did not find evidence of a multiplicative effect (Treasure and Dever, 1994; Evans et al, 1996; Slade et al, 1996b). However, these studies reported that caries rates are highest of all in children from low socioeconomic groups living in non-fluoridated communities. Moreover, the absolute difference in dmft/s or DMFT/S scores between populations living in fluoridated and non-fluoridated communities is consistently larger in lower SES children than in higher SES children (Table 6).

Table 6. Absolute differences in mean dmft/s or DMFT/S scores between children in fluoridated and non-fluoridated communities by SES

Author/yr	Country	Index	SES group	Absolute difference
Treasure and Dever 1994	New Zealand	DMFT	Highest Lowest	1.20 3.07
		DMFS	Highest Lowest	1.04 5.40
Provart & Carmichael 1995	UK	dmft	Highest Lowest	0.33 0.90
Evans et al 1996	UK	dmft	Highest Lowest	0.87 1.57
		dmfs	Highest Lowest	1.33 2.48
Slade et al, 1996b	Queensland	dmfs	Highest Lowest	2.18 3.50
		DMFS	Highest Lowest	0.29 0.35

Table 6 contd

Kumar et al 1998	US	DMFS	Highest Lowest	0.55 0.27

Expressed another way, the difference in caries rates between children from the upper and lower SES groups is narrower in fluoridated than non-fluoridated communities. This points to an additive interaction between water fluoridation and SES (Slade et al, 1996b). However, the magnitude of this effect is more pronounced in the deciduous dentition and is generally small.

Discontinuation of water fluoridation

Three papers examined caries rates in the deciduous or permanent dentition following the cessation of water fluoridation. These studies are based on repeated cross-sectional surveys so that sampling variation may account for part of the differences observed. Moreover, all three studies were simple geographic comparisons with no attempt to control for potential confounding factors.

Only one of the three studies reported an increase in caries rates following the cessation of water fluoridation (Table 7). Mean dmft values among five year-olds in Angelsey increased from 0.8 in 1987, the last year of fluoridation, to 2.01 in 1993 (Thomas et al, 1995). However, increases were also observed among children living in mainland Wales who had not been subject to water fluoridation. The full extent of the increase in this population cannot be determined since data were not available for the final year of observation.

A study of two towns in Germany with variable fluoridation histories found that caries rates in adolescents declined between 1987 and 1995 in Cheminitz, fluoridated until 1987, and Plauen, where fluoridation ceased in 1984 (Kunzel and Fischer, 1997). Similarly, caries rates in adolescents declined in Kuopio between 1992, the last year of fluoridation, and 1995 (Seppa et al, 1998). Sharper declines also occurred in non-fluoridated Jyvaskyla, so that the relative advantage of the Kuopio in terms of caries rates had been eliminated by 1995.

Table 7: Data from fluoride discontinuation studies.

Mean dmft values at age 5 years: Angelsey and mainland Wales: Thomas et al, 1995

	Angelsey **Fluoridated to 1987**	**Mainland** **Not fluoridated**
1987/88	0.80	2.26
1989/90	1.26	2.27
1992/92	1.44	2.41
1993	2.01	-

Mean DMFT at 12 and 15 years: Cheminitz and Plauen: Kunzel & Fischer, 1997

	Age group:	**1987** **F**	**1991** **NF**	**1995** **NF**
Cheminitz	12	2.55	2.48	1.87
	15	4.87	4.44	3.78
		NF	**NF**	**NF**
Plauen	12	2.42	2.54	1.98
	15	5.64	4.47	3.47

Mean DMFS at 12 and 15 years: Kuopio and Jyvaskyla: Seppa et al, 1998

	Age group:	**Kuopio** **Fluoridated to 1992**	**Jyvaskyla** **Non-fluoridated**
1992	12	1.88	2.99
	15	4.00	5.62
1995	12	1.62	1.63
	15	3.19	3.91

Studies of adults

Water fluoridation is a total population strategy for reducing rates of dental decay. However, the effectiveness of this strategy has been assessed in studies that have focussed almost exclusively on children. Only one study of adults was published during the review period and only four others have been published since 1971 comparing caries rates among adults exposed to optimally and negligibly fluoridated water

The absence of adults from water fluoridation studies is difficult to explain; it may have arisen because of the view that the effect of fluoride was largely systemic or concerns about the validity of fluoride exposure histories provided by adults and the elderly. It may simply reflect dentistry's traditional concern with the oral health of children. Whatever the reason, it must be regarded as a major limitation in the research effort to date. First, the aging of modern populations means that children make up only a small percentage of those populations. Second, while rates of dental decay have also declined in adult populations (Grembowski et al, 1992), the incidence of coronal and root decay is substantial, particularly among older adults. Third, since dental decay is cumulative across the life-span, the magnitude of the difference between individuals living in fluoridated and non-fluoridated communities should increase with aging. Fourth, given that fluoride's effects are largely topical, adults are likely to benefit as much as if not more than children in terms of reductions in the incidence of disease.

Only one study of adults was published between 1994 and 1999 (Grembowski et al, 1997). This study is one of the few that estimated exposure to fluoridated water through

individual residential histories. An earlier paper, which contained a more extensive analysis of the data, showed that adults aged 20 to 34 years with no exposure to fluoridated water had a mean coronal DFS of 27.9 (Grembowski et al, 1992). This was significantly higher than the mean of 15.7 for subjects exposed for the majority of their lives. After controlling for an extensive array of variables related to caries experience in adults, each year of fluoridation exposure reduced DFS scores by 0.29 surfaces and DMFS scores by 0.35 surfaces

This confirmed the results of previous uncontrolled ecological studies of adults by Stamm et al (1990), in which the coronal and root decay experience of life-long residents of a naturally fluoridated community was lower than that of life-long residents of a non-fluoridated community, and Wiktorsson et al (1992), in which coronal DFS scores of life-long residents of an optimally fluoridated community were lower than that of life-long residents of a community with negligible levels of fluoride in the water. A rare prospective study (Hunt et al, 1989) of coronal and root caries incidence provides the strongest evidence of the protective effect of water fluoridation among adults aged 65 years and over. When compared with life-long residents of fluoridated communities, the relative risk of developing new coronal caries over an 18-month observation period was 0.80 or less for subjects who had lived in fluoridated communities for 30 years or more. The risk of root caries was 0.73 or less.

The significance of the effect

Few of the papers considered the “clinical” or economic significance of the reductions in caries rates that they detected. Nor do they consider what would constitute a clinically significant difference in caries experience at the level of the individual or community.

When considering individuals, the term ‘clinical’ significance refers to issues such as longevity (either of teeth or people), functioning and quality of life. Burt (1995) has claimed that the greatest gains in oral health have been in areas not captured by disease-based indices: namely, “whole generations of young people have never suffered toothache and broad toothy smiles enhance self-esteem and self-confidence”. To date, there is no evidence to support this claim. Consequently, studies need to consider what improvement in oral health-related quality of life accrues to a population of five year-olds by a reduction of 1 in mean dmft values or to 12 year-olds by a reduction of 1 in mean DMFS values. Such improvements need to be balanced by decrements that may result from increases in dental fluorosis.

A study of five year-olds in the UK (Evans et al, 1996) attempted to address this issue by examining differences between fluoridated and non-fluoridated communities in the percentage who had experienced toothache, visited a dentist for treatment or had a general anaesthetic for tooth extractions. The only significant difference was for having experienced a general anaesthetic. The rates were 3.5% for the fluoridated and 9.4% for the non-fluoridated community. However, since this outcome was also related to socioeconomic status, factors other than water fluoridation have an influence on these rates. Locker and Slade (1994) found a significant, though relatively weak correlation

(r=0.31) between DMFS scores in adults aged 50 and over and scores from the Oral Health Impact Profile, a measure of oral health-related quality of life. However, other data from the study suggested that this relationship was the product of the missing component of the DMFS score. Moreover, the concept of the shortened dental arch is now generally accepted and entails the view that the loss of 8 to 12 teeth in an older adult does not necessarily compromise oral function.

Spencer et al (1996) suggested that even small differences in mean dmfs/DMFS scores between groups living in fluoridated and non-fluoridated areas can be of public health significance when translated into population needs for and costs of dental care. Arguably, savings in treatment costs are only relevant in countries where dental care is publicly funded. Where dental care is provided under private-fee-for-service arrangements, neither governments nor public health authorities have a legitimate interest in the way in which private dollars are spent across different sectors of the economy.

To date, discussion of the benefits and risks of water fluoridation has been conducted from within a disease frame of reference. Contemporary thinking requires that the health outcomes of exposure to water fluoridation in functional and psychosocial terms is documented and incorporated into the benefit-risk equation. This means that research is needed which addresses the oral health-related quality of life of children and adults with differing levels of caries experience in terms of pain, ability to chew and self-esteem.

Summary

Given the weaknesses in design and the methodological flaws to which many of the studies were subject, the data from these more recent studies must be treated with some caution. While the balance of evidence overall suggests that water fluoridation does reduce caries experience, the magnitude of the effect is subject to a degree of uncertainty but is unlikely to be large in absolute terms. While there is some evidence to suggest that children from lower socioeconomic groups benefit more, such children constitute only a small proportion of the child population overall. The few studies that have assessed rates of dental decay in communities where fluoridation has been discontinued do not suggest that dental decay increases to any significant degree.

Caries rates are now so low in most child populations that future research should focus more on adults and the elderly in order to more fully document the benefits to this section of the population in terms of reductions in the incidence of coronal and root decay. In addition, studies need to go beyond disease-based indices and document improvements in the quality of life that accrue to those exposed to optimal levels of fluoride. In the absence of such data, a comprehensive assessment of the benefits of water fluoridation cannot be undertaken. In the long term, this undermines the credibility of water fluoridation as a public health initiative.

OSTEOPOROSIS

Because excessive amounts of fluoride produce denser bones, it has been suggested that a lifetime of exposure to high levels of fluoride may be of benefit to individuals with osteoporosis.

It has been firmly established in controlled and uncontrolled clinical trials that fluoride at a dose of ≥11-14 mg/day is efficacious in increasing trabecular bone mass in the spinal column. While some studies have reported a reduction in vertebral fracture rates following fluoride therapy (Pak et al, 1994), its efficacy in with respect to vertebral fracture rates is controversial since research results have been inconsistent. Any benefits to the bone comprising the vertebral column do not appear to apply to other parts of the skeleton which is mostly cortical bone. One study did report an increase in fracture rates in cortical bone following treatment with high doses of fluoride (Riggs et al, 1994). However, the effect of fluoride on cortical bone mass and non-vertebral fracture rates has not been clearly established (Kleerekoper, 1998; Lau, 1998; Reginster, 1998; Seeman, 1997, Kleerekoper, 1994).

Several explanations (Kleerekoper, 1998; Balena, 1998; Reginster, 1998; Seeman, 1997) have been proposed for the inconsistent results emerging out of this body of research:

1. new appositional bone is biomechanically impaired due to inadequate (defective and/or insufficient) mineralization of the substantial osteoid
2. the failure of fluoride therapy to restore the microarchitecture of the cancellous bone in advanced osteoporosis
3. variations in fluoride dose, formulation and regimen
4. differences in treated populations including the severity of osteoporosis
5. unmet study design requirements (e.g. sample size, follow-up period) needed to identify antifracture efficacy.

Therefore, it may be that uncertainties regarding the efficacy of fluoride in reducing osteoporotic fractures is more of a problem of the design, execution and interpretation of the studies. It also seems likely fluoride may be efficacious when osteoporosis is mild or moderate. This is because osteoporosis is characterized not only by decreased bone mass but also by disruption of the microarchitecture of the remaining trabeculae and because fluoride is expected to work as anabolic agent without restoring the integrity of cancellous bone (Balena,1998; Reginster, 1998; Kleerekoper, 1994). However, this has yet to be proven.

Summary

Research on the contribution of fluoride to the treatment of osteoporosis has produced inconsistent findings. This may be due to differences in the action of fluoride in different parts of the skeleton and/or to limitations in research designs.

HEALTH RISKS OF FLUORIDE

ACUTE TOXICITY

Like many other nutrients and substances, fluoride is beneficial in small amounts but toxic in large amounts. Ingestion of a single dose of 5 to 10 grams of sodium fluoride by an adult male would be rapidly fatal. The equivalent dose for a child of 10 kg would be 320 mg, although 50 mg may constitute a toxic dose. A small number of case reports have documented toxic levels of intake of fluoride (Burt and Eklund, 1999). Such levels cannot be reached by drinking fluoridated water.

A recent paper analyzed reports to the American Association of Poison Control Centres (Shulman et al, 1997) of suspected over-ingestion of fluoride from home-use dental products. Children under the age of 6 years accounted for 80% of the reports. Although the outcomes were not serious, many required medical treatment. Fluoridated toothpastes and mouthrinses can result in levels of ingestion that may be toxic. For example, 50 g of 1,000 ppm of toothpaste could result in toxicity in a child of 10 kg body weight. Consequently, products containing fluoride should be kept out of reach of children to prevent these potentially serious levels of ingestion.

Summary

Fluoride is a poison in large doses but toxic levels cannot be achieved by drinking fluoridated water. Fluoride products such as toothpastes should be kept out of the reach of children since toxic amounts could be ingested via these sources.

DENTAL FLUOROSIS

Dental fluorosis refers to a set of defects of enamel associated with hypoplasia or hypomineralization of dental enamel and dentine as a result of excessive ingestion of fluoride during the critical period of tooth formation. It ranges from barely perceptible striations in the enamel to severe pitting and subsequent staining. Consequently, its cosmetic significance depends upon its severity. Fluorosis is, however, only one cause of a wide range of defects of tooth enamel. A number of indexes have been developed to describe the extent and severity of fluorosis (see below). Only one index, the Developmental Defects of Enamel Index (FDI, 1992) attempts to describe the full range of defects that can affect enamel. The use of different indices complicates comparisons across studies in terms of the prevalence of moderate to severe fluorosis.

Recent reviews have suggested that the prevalence and severity of dental fluorosis has increased in both fluoridated and non-fluoridated communities with the latter exhibiting the largest increase of all (Lewis and Banting, 1994; Clark, 1994). A review by Clark

(1994) of North American studies published prior to 1994 indicated that prevalence ranged from 35 to 60% in fluoridated communities and from 20 to 45% in non-fluoridated communities. These increases have been attributed to the consumption of fluoride from sources other than community water supplies (Lewis and Banting, 1994). Although they are largely confined to the so called 'very mild' and 'mild' categories of dental fluorosis the increases are a cause for concern. The rationale underlying this concern is that fluorosis at this level is discernable by children aged 10 years and over and can lead to embarrassment, self-consciousness and a decrease in satisfaction with the appearance of the teeth (Spencer et al, 1996). This work confirms and expands previous surveys which have shown that lay people can detect fluorosis and both professionals and lay people view the more severe forms as having negative consequences for children (Riordan, 1993; Clark, 1993; Hawley et al, 1996). If the descriptions of the 'very mild' and 'mild' categories of Dean's Fluorosis Index are reviewed (Table 8), it is by no means certain that they are insignificant to the individuals affected. These terms were coined in the 1930s when concerns with and awareness of appearance were less marked than at the present time. Consequently, these professionally-based judgements may need to be modified in the light of contemporary patient concerns. Certainly, the assumption that 'very mild' and 'mild' forms of fluorosis are acceptable, which underlies much current thinking about fluoridation, may need to be reconsidered

Table 8: Criteria for Dean's Fluorosis Index

Category:	Criterion:
Very mild	Small, opaque, paper white area scattered irregularly over the tooth but not involving as much as approximately 25% of the tooth surface. Frequently included in this classification are teeth showing no more than about 1 to 2 mm of white opacity at the tip of the summit of the cusps of the bicuspids or second molars
Mild	The opaque areas in the enamel of the teeth are more extensive but do not involve as much as 50% of the tooth surface

The most recent estimates of the prevalence of fluorosis in both fluoridated and non-fluoridated communities are to be found in Tables 9-11. These studies suffer from the same design and methodological limitations as the studies of the effectiveness of water fluoridation discussed earlier. The studies are grouped according to which of three indexes were used to measure fluorosis; the Community Fluorosis Index, the Tooth Surface Index of Fluorosis and the Thylstrup and Fejerskov Index. A comprehensive review of these indices is to be found in Rozier (1994).

North American studies, which confined their estimates to children who were life-long residents of fluoridated and non-fluoridated communities respectively, reported prevalence rates of 20 to 75% for the former and 12 to 45% for the latter. European studies reported ranges of 54 to 79% and 14 to 36%, respectively. Studies from Mexico and Brazil reported rates of 61 to 64% and 31 to 50%, respectively.

Two U.S. studies using repeated cross-sectional designs were undertaken by the same investigators and provide the best recent estimates of trends in fluorosis. Jackson et al (1999) studied 7 to 14 year old children who were life-long residents of a fluoridated and a non-fluoridated city. In the fluoridated city the proportion of children who had a TSIF score of 1 or more increased from 45% in 1992 to 65% in 1994 (NS). In the non-fluoridated city there was a significant increase from 18 to 33%. Kumar and Swango (1999) also compared 7 to 14 year old children who were life-long residents of a fluoridated community, Newburgh, and a non-fluoridated community, Kingston. Dean's CFI indicated a significant increase in both communities between 1986 and 1995; from 7.9 to 18.6% in the former and from 7.4 to 11.7% in the latter. The difference in rates between the studies is probably due to the fact that Dean's CFI has a "questionable" category which is categorized as 'normal' for the purpose of calculating prevalence estimates.

Table 9: Prevalence of fluorosis in fluoridated and non-fluoridated communities (Community Fluorosis Index)

Author/Yr	**Country**	**Age**	**LTR**	**F Status**	**% Fluorosis***	**% Moderate /severe****
Jackson et al 1995	US	7-14	Yes	F NF	38.8% 14.5%	0% 0%
Grimaldo et al 1995	Mexico	11-13	Yes	F NF	64.2% 50.0%	27.0% 25.0%
Heller et al, 1997	US	7-17	Yes	F NF	29.9% 13.5%	1.3% 0.5%
Karthikeyan et al 1996	India	8-15	Not reported	F NF	30.1% 0.0%	
Kumar et al 1998	US	7-14	Yes	F NF	19.6% 11.7%	0.7% 0.3%
Villa et al 1998a	Chile	12	NR	F NF	**51.3%** **3.0%**	
Adair et al 1999	US	G3-5 G6-8	NR	F NF F NF	45.9% 21.4% 56.8% 52.6%	

* Score of 1 or above; ** CFI index score of 3/4; LTR – study confined to lifetime residents

Table 10: Prevalence of fluorosis in fluoridated and non-fluoridated communities (Tooth Surface Index of Fluorosis)

Author/Yr	Country	Age	LTR	F Status	% Fluorosis*	% Moderate /severe**
Clark et al 1994	Canada	6-14	Yes	F NF	**76.0%** **45.0%**	11.0% 1.0%
Brothwell & Limeback 1999	Canada	Grade 2	No	F NF	31.3% 22.5%	**18.8%** **4.8%**
Jackson et al 1999	US	7-14	Yes	F NF	65.0% 32.0%	17.0% 6.0%

* Score of 1 or above; ** Score of 2 or above; LTR – study confined to lifetime residents

Table 11: Prevalence of fluorosis in fluoridated and non-fluoridated communities (Thylstrup and Fejerskov Index)

Author/Yr	Country	Age	LTR	F Status	% Fluorosis*	% Moderate /severe**
Wiktorsson et al 1994	Sweden	31-43	Yes	F NF	8.8% 0.0%	
Elwood & O'Mullane 1995	UK and Ireland	14	Yes	F NF	62.0% 36.0%	3.0% 0.0%
Ellwood & O'Mullane 1996	UK	14	Yes	F NF	54.0% 36.0%	3.0% 0.0%
Heintze et al 1998	Brazil	5-24	Not reported	F NF	13.3% 1.7%	
Sampaio et al 1999	Brazil	6-11	Yes	F NF	61.1% 30.5%	0.0% 3.0%
Bardsen et al 1999	Norway	5-18	Yes	F NF	79.0% 14.0%	8.0% 0.0%

* Score of 1 or more; ** Score of 4 or more; LTR – study confined to lifetime residents

The conventional way of estimating the contribution of water fluoridation to dental fluorosis is by the use of relative risks and attributable risk percents (Lewis and Banting, 1994). Relative risks in North American and European studies varied from 1.5 to 2.7,

except for one Norwegian study that had a relative risk of 5.4. Attributable risk percents measure the proportion of the fluorosis in those exposed to water fluoridation which can be attributed to that exposure rather than other sources of fluoride. In the North American studies this varied from 40 to 63% and in the European studies from 33 to 82%. These studies suggest that approximately half of the fluorosis affecting contemporary child populations is the result of water fluoridation and half is the result of exposure to other, discretionary, sources of fluoride. However, in some jurisdictions the halo effect could potentially affect these somewhat crude estimates (Lewis and Banting, 1994). While these estimates of the contribution of water fluoridation are somewhat larger than those based on studies published prior to 1994, comparisons across time should be viewed cautiously.

Two Canadian studies are worth highlighting here. Clark et al (1994) used the TSIF to compare life-long residents of a fluoridated and a non-fluoridated community in British Columbia. Among samples of children aged 6 to 14 years, the prevalence of fluorosis (TSIF $\geq$ 1) was 75% in the former and 45% in the latter (relative risk=1.7; attributable risk percent=41%). Brothwell and Limeback (1999) examined Grade 2 students living in a non-fluoridated rural area in Ontario, approximately 10% of whom lived in homes where the water was naturally fluoridated to 0.70 mg/L or more. There were no significant differences in the prevalence of fluorosis among students from fluoridated and non-fluoridated homes when judged by a TSIF score of 1 (31% vs 25%). However, there was a significant difference among the proportions with TSIF scores of 2 or more (18.8% vs 4.8% respectively; relative risk=3.9; attributable risk percent=77%). This latter study suggests that water fluoridation may play a more prominent role in moderate to severe fluorosis than in fluorosis overall. It was not possible to explore this hypothesis using data from any of the other studies reviewed.

The risks associated with the discretionary use of fluorides in both fluoridated and non-fluoridated communities have been addressed in a number of recent studies (Table 12). Of thirteen papers published during 1994-1999, six described case-control and seven described cross-sectional studies. The majority were conducted either in fluoridated or non-fluoridated communities so that the relative effect of water fluoridation versus other sources of fluoride cannot be discerned. In addition, two reviews, one of the role of fluoridated toothpaste in the genesis of fluorosis (Warren and Levy, 1999) and the other a meta-analysis of the use of fluoride supplements in non-fluoridated areas, have been published (Ismail and Bandekar, 1999).

The main risk factors to emerge from the case-control and cross-sectional studies were the use of infant formula, use of fluoride supplements and brushing with fluoridated toothpaste early in life. The two reviews confirm the etiological role of fluoridated toothpaste and fluoride supplements with respect to fluorosis. The strength of the independent effects of these three exposures, judged by means of adjusted odds ratios, varied across the studies. The magnitude of the effect also varied according to whether the study was conducted in a fluoridated or non-fluoridated community. However, differences in the ways in which exposures to these discretionary sources of fluoride were defined and measured preclude direct comparisons across studies.

Table 12: Summary of studies of risk factors for dental fluorosis

Author/ year	Country	Design	Age	F status	Index	Risk Factors	OR
Pendrys et al 1994	US	C-C (Pop)	12-16	F	FRI Class I	Fed milk–based formula 10-24 months Fed soy-based formula 10-24 months Frequent brushing birth to 8 years Fluoride supplements 1-4 years Fluoride supplements 1-6 years	**3.34** **7.16** **2.80** **11.47** **23.74**
					FRI Class II	Fed milk–based formula 10-24 months Fed soy-based formula 10-24 months Frequent brushing birth to 8 years Fluoride supplements 1-4 years Fluoride supplements 1-6 years	- - **2.63** **19.28** **9.86**
Clark et al 1994	Canada	Cross-sectional	6-14	Mixed	TSIF	Continuous residence in F community F supplement use during first year of life Fluoride supplement use between 4-5 years Parental education	**0.9** **0.6** **1.9** **1.2**
Skotowski et al 1995	US	C-C (Clin)	8-17	Mixed	TSIF	Five or more years exposure to F water Amount of F toothpaste used up to age 8	4.0 2.7
Lalumandier & Rozier	US	C-C (Clin)	5-19	F NF	TSIF	Brushing with F toothpaste before age 2 Brushing with F toothpaste before age 2 Daily F supplement use	**3.1** **3.0** **6.5**

Author/ year	Country	Design	Age	F status	Index	Risk Factors	OR
Pendrys et al 1996	US	C-C (Pop)	10-13	NF	FRI Class I	F supplements age 2 to 8 Brush before 2 yr, >1/day Breast feeding Caucasian	**2.25** **2.56** **1.62** **3.31**
					FRI Class II	F supplements age 2 to 8 Brush before 2 yr, >1/day Breast feeding Caucasian	**7.97** **4.23** **1.86** **4.28**
Clark & Berkovitz 1997	Canada	Cross-sectional	Grade 2-9	Mixed	Esthetic problem	Residence in F community in 3rd year of life Used F dentifrice in 3rd year of life F supplement use in 3rd year of life	**3.9-13.1** **7.2-7.7** **2.7-4.0**
Wang et al 1997	Norway	Cross-sectional	8	NF	TFI	Use of F toothpaste before 14 months Additional year of F supplement use	**2.44** **1.84**
Pendrys et al 1998	US	C-C (Pop)	10-14	F	FRI Class I	Used powdered formula 10-12 months Early tooth paste use, >pea sized, > once/day Supplements year 1-2	 **6.35** **5.95**
					FRI Class II	Used powdered formula 10-12 months Early tooth paste use, >pea sized, > once/day Supplements year 1-2	**10.77** **8.37** **10.83**
Villa et al 1998b	Chile	C-C (Pop)		F	CFI	Unborn before start of community water F Age 16-24 months at start Exclusively breast fed	**20.44** **4.15** **0.86**
Mascarenhas & Burt 1998	India	Cross-sectional	12	NF	TFI	Use of F toothpaste before age 6 Gender (males)	**1.81** **1.51**
Brothwell & Limeback 1999	Canada	Cross-sectional	7-8	NF	TSIF	Home water F conc Duration of breast feeding Use of F supplements Use of fluoridated mouthwash	**2.91** **0.71** **1.93** **2.73**

Author/ year	Country	Design	Age	F status	Index	Risk Factors	OR
Kumar & Swango 1999	US	Cross-sectional	7-14	Mixed	CFI	Fluoridation alone Fluoridation+ early brushing or tablet Fluoride tablet+early brushing Early brushing Fluoride tablet	2.5 3.3 4.0 2.0 2.9

OR in bold – multivariate adjusted estimates

C-C: Case-control study. (Pop): population-based. (Clin): clinic-based

FRI: Fluorosis Risk Index; CFI: Dean's Community Fluorosis Index; TSIF: Tooth Surface Index of Fluorosis; TFI: Thylstrup and Fejerskov Index.

While water fluoridation, infant formula, fluoride supplements and fluoridated toothpastes are risk factors for dental fluorosis, efforts to reduce children's exposure to fluorides during the years of enamel formation have focussed on discretionary sources. Reducing fluoride levels in infant formulas, changing practices of preparing formula to avoid the use of fluoridated water, reducing the use of fluoride supplements, ensuring the availability of low fluoride toothpastes and increasing compliance with appropriate toothbrushing practices in early childhood have been recommended by a number of authorities (Spencer et al, 1996). Since these involve altering the practices and behaviours of commercial organizations and individuals, their likelihood of success is at best questionable. It has often been claimed that one of the advantages of community water fluoridation, and a major factor in terms of its effectiveness, is that it does not rely on organizational or individual compliance with health recommendations.

Clearly, the simplest way of reducing the prevalence of fluorosis in child populations is to cease to fluoridate community water supplies. Whether or not this is an acceptable option depends on the balance of benefits and risks with respect to dental caries and fluorosis. This balance is difficult to assess when the discussion takes place at the level of disease. The ultimate concern here should be to maximize quality of life outcomes. However, data on the effects on health and well-being of the relatively small decreases in caries rates in children and adolescents currently achieved by water fluoridation is non-existent. Similarly, data on the negative health consequences of current levels of fluorosis in child and adolescent populations is scant. Such data are urgently needed in order to facilitate decisions about the benefits and risks for dental health of changing exposures to various sources of fluoride. Without such data the 'value' to individuals and communities of decreases in the prevalence and severity of dental decay and increases in the prevalence and severity of fluorosis cannot be determined. Research is needed which

measures the oral health-related quality of life of children, adolescents and adults who are affected by dental decay and dental fluorosis to varying degrees.

Summary

Current studies support the view that dental fluorosis has increased in both fluoridated and non-fluoridated communities. North American studies suggest rates of 20 to 75% in the former and 12 to 45% in the latter. Although largely confined to the 'very mild' and 'mild' categories of the condition, they are of concern insofar as they are discernable to the lay population and may impact on those so affected. Although about half the fluorosis in contemporary child populations living in fluoridated communities can be attributed to fluoride from discretionary sources, efforts to reduce exposure to these sources may not be successful. Research is needed into the relative effects of dental decay and fluorosis on quality of life outcomes and community values regarding the balance between reductions in dental decay and increases in dental fluorosis associated with water fluoridation.

BONE HEALTH

Fluoride affects the skeleton in three ways. *First*, it incorporates into bone tissue by replacing the hydroxyl group of hydroxylapatite to form fluorapatite (Kleerekoper, 1998). The latter is more resistant to osteoclastic resorption, which may result in an altered bone remodeling cycle. 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. *Second*, in higher serum concentrations, fluoride is anabolic to bone in that it increases cancellous bone mass (Kleerekoper, 1998; Lau, 1998, Kleerekoper, 1994). It appears that the threshold dose is between 11 and 14 mg/day for fluoride to exert its osteoanabolic effect. This effect is linear with time for at least six and possibly ten years or more. *Third*, in dose-dependant manner fluoride may cause impairment in mineralization of the newly synthetized osteoid and consequently affect biomechanical properties of the bone (Kleerekoper, 1998; Fejerskov , 1996).

Skeletal fluorosis

The intake of fluoride at high levels for protracted periods results in a systemic osteosclerosis known as skeletal fluorosis or osteofluorosis. This condition is characterized by: 1. a thickened cortical and cancellous bone with signs of hypomineralization and mineralization defects; 2. spur bony formations at tendon insertions; and 3. ossification of interosseous membranes and ligaments. These changes are more pronounced in the central skeleton and to a lesser degree in the skull and the peripheral bones (Fejerskov, 1996). Clinically they range from asymptomatic radiographic bone mass increase to crippling skeletal fluorosis involving spine and joint deformities and dysfunctions, muscle wasting and neurological problems due to spinal cord compression (Whitford, 1996; Kleerekoper, 1996). Additional clinical manifestations that may indicate toxic effects of chronic fluoride exposure have been observed in skeletal fluorosis. They include: 1. gastrointestinal symptoms, the most common being abdominal pain associated with chronic atrophic gastritis (Dasarathy, 1996); 2. a decreased level of serum testosterone, suggesting the possibility of an adverse effect on spermatogenesis (Susheela, 1996); and 3. An increase in the levels of markers of inflammatory reactions (haptoglobin and C-reactive protein) (Susheela, 1994).

Most estimates indicate that crippling fluorosis is associated with chronic fluoride exposures of ≥ 10 mg/day for at least ten years. These exposures occur as either endemic (exposure to the naturally fluoridated drinking water) or industrial (e.g. exposure to the cryolite dust) (Fejerskov, 1996; Whitford, 1996). Beside the dose and duration of fluoride exposure, the development of skeletal fluorosis is influenced by various other factors. The most common are age, physical activity, kinetics of bone remodeling, nutritional status and renal insufficiency (Kleerekoper, 1996). Epidemiological studies of bone mineral density have not detected changes consistent with skeletal fluorosis resulting

from the consumption of drinking water containing fluoride at the concentrations considered optimal for caries prevention.

Effects of water fluoridation on bone fractures and bone mineral density (BMD)

Knowledge about the modes of action of fluoride on bone tissue and about the effects of long-term exposure to high levels of fluoride in drinking water and air, i.e. skeletal fluorosis as well as the uncertainty regarding antifracture efficacy of fluoride treatment of osteoporosis, raise concerns about the relationship between exposure to water fluoridated for caries prevention and bone health. Does it influence peak bone mass and density? Does it alter biomechanical properties of the skeletal system? Does it affect bone fracture risk? Do elderly citizens in communities with water fluoridation programs accumulate a toxic burden of fluoride? What is its effect on the prevalence of osteoporosis? What is its outcome on existing osteoporosis?

These are important questions due to the fact that in western society large numbers of people are exposed to water fluoridation programs and that persons over age 65 years (those at greatest risk for osteoporosis) are increasing in number. For example, it has been estimated that in the United States over 144 million people are exposed to public water systems and the lifetime risk for hip fractures for white women living to the age of 80 years has been estimated to be 15 % (Jacqmin-Gadda, 1998). In Australia a person aged 60 years with average life expectancy has a residual lifetime osteoporotic fracture risk of 56% for females and 29% for males (Jones, 1999). Therefore, any intervention with even a small effect on bone fracture risk is important because at a population level it may lead to marked changes in the number of bone fractures.

At concentrations aimed at caries prevention, water fluoridation provides an average fluoride dose of about 1.8 mg/day (Jones, 1999; Phipps, 1998). This is a small fraction of the minimal dose of fluoride that has been shown to have an anabolic effect on cancellous bone, and such exposure for 30 years would be one order of magnitude lower than that used in clinical osteoporosis trials (Allolio, 1999). It has been estimated that consumption of 250 ml of this water induces a peak fluoride concentration of 8.75 ng/ml which is below the suggested threshold value of 95 ng/ml for the stimulation of osteoblast activity. Even consumption of 1000 ml would not reach osteoanabolic levels (Allolio, 1999).

It does not seem plausible then that water fluoridation programs represent a risk for bone health. However, there are factors other than intermittent and total exposure that may influence the bone effects of long-term or lifetime exposure to such levels of fluoride: 1. progressive accumulation in the skeletal system in the form of fluorapatite that is less resorptive than hydroxilapatite and therefore alters the remodeling cycle that in turn may result in impaired biomechanical properties, 2. exposure extended to more than 30 years, 3. substantial individual variations in the resorption from the stomach, and 4. renal insufficiency (the risk of which increases with the age) that may result in increased fluoride retention in bone. Therefore, while serum fluoride levels induced by drinking water treated for caries prevention may not reach an osteoanabolic threshold, a long-term

(>30 years) fluoride accumulation in bone has the potential to lead to a fluoride content which may adversely affect bone strength.

This issue of the relationship between the exposure to fluoride added to drinking water for the prevention of dental caries (0.7-1.2 mg/l) and bone health has been studied ever since the introduction of water fluoridation programs. The studies addressing this issue, that have been retained following the preliminary assessment of the papers retrieved in the literature search, are summarized in Tables 13-15. The earlier studies were ecological in design, while some of the studies published during the last five years have elements of an ecologic design (measurement of fluoride exposure) hybridized with individual measures of BMD/fracture and known confounding variables in cross-sectional or prospective/retrospective designs. Of the two indicators of bone health, mineral density and fracture incidence, the latter has been studied more frequently

The bone fracture studies vary in their research design, the methods used to measure exposure to fluoridated water (level and duration), determination of the population at risk and methods of identifying fracture cases (case definition and ascertainment, follow-up period). Bone fracture sites assessed also differ, with hip fractures being the most commonly studied (Table 13).

The studies published prior to 1994 reported conflicting results, with two showing a protective effect, 5 showing no significant association, and 4 showing that exposure to fluoridated drinking water increased the risk for hip fracture. The last four reported relative risks in the range of 1.1 - 1.4 for women and 1.2 - 1.3 for men. When a protective effect was found, relative risks were between 0.6 to 0.7 for women and 0.4 to 0.8 for men. Of the studies published after 1994, one reported a protective effect with a relative risk of 0.44, one reported that exposure to fluoridated drinking water increased the risk of hip fracture, with a relative risk of 1.3 for males and 1.4 for females and two found no dose response relationship. For example, Jacqmin-Gadda H (1998) reported no dose-effect relation between self-reported non-hip fractures in a random sample of people aged 65 years and over and fluoride concentrations in drinking water in areas of ranging from 0.05 to 1.83 mg/l. Similarly, there was no dose-response relationship between fluoride concentrations in well water and hospital discharge data for hip fractures in a Finnish rural population aged 50 years and over (Kurttio P, 1999). Fluoride concentrations were estimated on the basis of a nationwide database. They ranged between 0.05 and 2.4 mg/l, with 99% of the estimates being below 0.63 mg/l .

Five studies published between 1994 and 1999 were concerned with exposure to fluoridated water and bone mineral density (BMD). The main characteristics of these studies and their findings are presented in Tables 14 and 15.

Kröger (1994) studied axial BMD in a random sample of perimenopausal women aged 47-59, using dual X-ray absorptiometry (DXA). The effects of exposure to drinking water with fluoride content of 1-1.2 mg/l for over 10 years and to drinking water with either <0.3 mg/l or 1-1.2 mg/l for less than 10 years were compared. BMD of the spine was significantly higher in the fluoride than in the non-fluoride group, while femoral neck

BMD did not differ between the groups. When controlled for potential confounders, including age, weight, calcium intake, alcohol consumption, estrogen use, menopausal status and physical activity class, the differences increased and reached statistical significance for the femoral neck. These results suggest that the long-term exposure to fluoride in concentration of 1-1.2 mg/l of drinking water has a slight effect on BMD. However, this is no more than speculation considering that the fluoride group was urban and the non-fluoride group was predominantly rural so that the differences may reflect unknown confounding factors. As the authors suggest, the effect of increased mineral density on the risk for fractures can only be determined in a follow-up study.

Table 13: Studies of bone fracture and exposure to fluoridated drinking water

Author	Study design	Population at risk identification	Case ascertainment	Exposure duration (yrs)	Association	p-value or 95% CI
Korns RF 1969	Comparison Ecological	Census	Hospital discharge	2—22	NA	
Madans J 1983	Comparison Ecological	Health survey respondents	Hospital discharge	-	NA	
Simonen O 1985	Comparison ecological	-	Hospital discharge	7-17	RR(m)=0.4 RR(f)=0.6	<0.001 <0.05
Arnala I 1986	Comparison ecological	Census	Hospital discharge	13-23	NA	
Danielson C 1992	Comparison ecological	Census	Hospital discharge	19-25	RR(m)=1.3 RR(f)=1.4	1.41-1.81 1.08-1.46
Jacobsen S 1992	Comparison ecological	Census	Hospital discharge	-	RR(m)=0.8 RR(f)=0.6	0.37-1.66 0.46-0.48
Suarez-Almazor M 1993	Comparison ecological	Census	Hospital discharge	14-20	NA	
Cooper C 1990&1991	Correlation	-	Hospital discharge	-	r=0.41	p=0.009
Jacobsen S 1990	Correlation	Census	Hospital discharge	10	r=0.03	p=0.0009
Goggin JE 1965	Time-trend	-	Hospital discharge	5	NA	
Jacobsen S 1993	Time-trend	-	Hospital discharge	10	RR(m)=1.2 RR(f)=1.1	1.13-1.22 1.06-1.10

Table 13 cont'd

Cauley JA 1995	Prospective cohort with ecological fluoride measurement	Convenience sample (community residents)	Self-report & X-ray	3	RR(m)=1.3 RR(f)=1.4	<0.0001 <0.0001
Lehman R 1998	Comparison ecological	-	Hospital discharge	-	RR=0.40	0.10-1.86
Jacqmin-Gadda H 1998	Prospective cohort with ecological fluoride measurement	Random sample (community residents)	Self-report	5	NA	
Kurttio P 1999	Retrospective cohort with ecological fluoride measurement	Census	Hospital discharge	15	NA	

NA: No association

Cauley (1995) measured BMD in a convenience sample of US white women aged 65 years and older according to length of exposure to drinking optimally fluoridated water. BMD was measured at the distal and proximal radius and the calcaneus using single-photon absorptiometry and at the lumbar spine and the proximal femur using dual X-ray absorptiometry. Fluoride exposure duration was estimated for each individual by means of residential histories. BMD was similar across fluoride exposure strata. Since the uptake of fluoride is greater during the period of bone formation than thereafter, the no difference found in this study may be explained by the fact that most of the study subjects were exposed to fluoridated water after achieving peak skeletal mass since they were on average 34 years of age when the fluoridation was instituted.

In a comparison ecological study, Lehmann R (1998) did not find a significant difference in age-adjusted BMDs of the spine (L2-L4) and the femoral neck between volunteers who have been the residents for at least 10 years in two German communities with water fluoridated to 0.77-1.20 mg/l and 0.08-0.36 mg/L. Since the majority of the subjects had been exposed for >30 years, including the bone modeling period, these findings may indicate that water fluoridation does not have an influence on peak bone density. The study groups were similar with respect to known bone-affecting confounders except that calcium intake was significantly higher in the non-fluoridated group and could have biased the findings towards no association. The age-adjusted annual incidence rates of low-energy trauma hip fractures, determined from hospital discharge data for patients aged 60 years and over, were significantly lower in the fluoridated community. For women the relative risk was 0.79 and for men 0.81.

Table 14: Characteristics of studies of the effects of water fluoridation on bone mineral density

Author	Study design	Sample	Fluoride content (mg/l)		Bone site	Exposure duration (yrs)
			Fluoridated	Non-fluoridated		
Kröger H 1994	Cross-sectional with ecological fluoride exposure measurement	Random • community residents • female • 47-49 yrs	1-1.2	0.03	Spine: L_{2-4} Femoral neck	>10 (25.9±6.4)
Cauley JA 1995	Cross-sectional with ecological fluoride exposure measurement	Convenience • community residents • female • 65+ yrs	1.01±0.21	0.15±0.10	Lumbar spine Femoral neck Radius	13 (mean)
Lehman R 1998	Cross-sectional with ecological fluoride exposure measurement	Convenience • hospital employees • 20-69 yrs	0.77-1.20	0.08-0.36	Spine: L_{2-4} Femoral neck	>10 (25.2±7.3)
Arnold CM 1997	Cross-sectional with ecological fluoride exposure measurement	Convenience • university students • female • 18-25 yrs	0.9-1.25	0.12-1.15	Spine Proximal femur	Lifetime (21.3±1.6)
Phipps KR 1998	Cross-sectional with ecological fluoride exposure measurement	Convenience • community residents • 60+ yrs	0.7	.03	Lumbar spine Proximal femur Forearm	20

Table 15: Bone mineral density (G/cm^2) by fluoride exposure status

Author	Bone site	Fluoridation status		P-value
		Yes	No	
Kröger H	Spine (L2-4):	(n=2253)	(n=969)	
	Unadjusted	1.123	1.138	0.026
	Adjusted*	1.121	1.151	0.001
	Femoral neck:			
	Unadjusted	0.927	0.928	ns
	Adjusted*	0.930	0.940	0.004
Cauley JA		Exposure 0 yrs (n=1243)	Exposure>20 yrs (n=192)	
	Lumbar spine	0.842**	0.849**	ns
	Femoral neck	0.640**	0.658**	ns
Lehman R	Spine (L2-4)	Male: 1.045±0.171* (n=41)	Male: 0.997±0.129* (n=98)	0.08
		Female: 1.046±0.117* (n=201)	Female: 1.055±0.112* (n=215)	0.47
	Femoral neck	Male: 0.876±0.120*	Male: 0.820±0.101*	0.008
		Female: 0.809±0.102*	Female: 0.814±0.100*	0.65
Arnold CM	Spine (total anterior – posterior)	1.028±0.12	0.986±0.7	<0.05
	Proximal femur	0.951±0.14	0.936±0.09	ns
Phipps KR	Lumbar spine	Male (n=112) 1.070*	Male (n=112) 1.057*	?
		Female (n=137) 0.892*	Female (n=112) 0.894*	?
	Proximal femur	Male 0.924*	Male 0.913*	?
		Female 0.747*	Female 0.747*	?

* Adjusted for bone-affecting confounders; ** Age-adjusted

Arnold (1997) found significantly higher mean BMD of the total anterior-posterior lumbar spine and no difference in mean BMD of proximal femur between female University students aged 18-25 years who were lifetime residents of Saskatoon (1.0 - 1.25 mg F/l) and Regina (0.12 - 0.15 mgF/l). Since the two groups did not differ in self-reported lifestyle, medical history and dietary habits that could explain differences in BMD, these finding may indicate that fluoride has an effect on peak bone density. However, this is only a speculation since water fluoride intake was not determined and the "halo" effect was not assessed. After controlling for variables known to influence bone tissue, Phipps (1998) found that the long-term exposure (≥ 20 yrs) to water with fluoride at levels considered optimal for caries prevention did not have an impact on BMD of lumbar spine, proximal femur and forearm of adults aged 60 and over. Whether the study subjects were exposed to such water during bone formation was not indicated in this study.

Summary

The conclusions reached by each of these studies are limited since they used an ecologic measure of fluoride exposure. The associations found in studies using aggregate level data may differ from the associations measured with individual level data are collected. Even when the residential history is determined for each subject, the measurement of the fluoride exposure may be biased since fluoridation of the public water supplies does not necessary mean that all residents are equally exposed and individual variations in water intake can be such that residents of different communities have similar fluoride intakes. In addition, ecological studies do not allow for the control of potential confounders and effect modifers. In the studies with a hybrid design this has been overcome to some degree by collecting data on variables known to be cofounders on the individual level. Therefore, the association observed in an ecological study is always tenuous. Nevertheless consistency of evidence across studies should enhance the overall credibility of risks or benefits suggested by ecological data. Since the results of the ecologic studies on water fluoridation and hip fracture have been far from consistent, the possibility of a cause-effect relationship cannot be established. Consequently, the studies conducted to date do not provide systematic and compelling evidence of an adverse effect on bone.

However, considering the public health implications of a potentially adverse impact, further research is necessary using more appropriate study designs. Prospective cohort studies with a detailed ascertainment of fluoride exposure (level and duration), measurement of the total skeletal burden of fluoride and assessment of potential confounders need to be undertaken.

CANCER

Numerous studies have been undertaken to determine if water fluoridation is linked to increases in the risk of cancer. Many studies claiming that such a risk exists have been re-analyzed and found to provide no evidence of a link. Moreover, many used the correlational ecologic design which has significant limitations in terms of establishing cause and effect relationships.

A recently published ecological study (Tohyama, 1996) did find a significant correlation between fluoride concentration in drinking water and uterine cancer mortality in 20 municipalities in Okinawa, Japan. This association remained significant after adjusting for a number of confounders such as population ratio, income gap, stillbirth rate and divorce rate. However, the study did not control for more relevant confounders such as smoking and sexual activity.

A 1990 animal study showing a possible link between fluoride and osteosarcoma stimulated a number of more rigorous studies using case-control designs which were published between 1994 and 1999. Three case-control studies from the U.S. found no association between exposure to fluoridated drinking water and osteosarcoma (Moss et al, 1995; McGuire et al, 1995; Gelberg et al, 1995). For example, a multi-centre study involving 147 patients and 248 controls found no differences between the proportions exposed to optimally fluoridated water or the average yearly exposure (McGuire et al, 1995). The study by Gelberg et al (1995) found no association between fluoride exposure and osteosarcoma in a study of 130 cases aged 24 years or less and 130 age and sex matched controls. The finding of no association held whether fluoride exposure was based on data provided by patients or their parents. The study also suggested that there may be a protective effect for males.

Studies of other cancer sites, one an ecologic study from South Africa (Bourner and Aggett, 1994) and a case-control study of bladder, colon and rectal cancer in Ontario (Marrett and King, 1995) showed no association between water fluoridation and increased risk of cancer. Two recent reviews of the literature also concluded that there is no evidence that fluoride in the water supply is linked with an elevated risk of cancer at any body site (Cook-Mozaffari, 1996; Cantor, 1997).

Summary

The few studies published during the review period do not challenge earlier research showing that there is no reason to believe that exposure to fluoridated water increases rates of cancer either of bone or other body tissues. While an ecological study did suggest an association with uterine cancer, the limitations of this kind of study in terms of linking exposures and outcomes in individuals, mean that it does not contradict the evidence derived from more systematic and scientifically credible case-control studies.

CHILD DEVELOPMENT

Early studies of child development in fluoridated and non-fluoridated communities focussed on physical health. No differences were documented with respect to body processes, blood chemistry, vision, hearing or any other general health parameter.

More recent studies have focussed on intellectual development. Two conducted in China claimed to have found differences in IQ between children exposed to differing levels of fluoride. Although both fell outside the inclusion criteria they were reviewed to illustrate the flaws in this research. The first (Zhao et al, 1996) compared the IQ of children in one village where the water supply contained 4 ppm fluoride and one village where the concentration of fluoride was 0.9 ppm. The mean IQ of random samples of children was 105 in the former and 98 in the latter, a statistically significant difference. In both villages, children of parents with a higher education had a higher IQ. However, analysis of mean IQ scores adjusting for the confounding effect of parental education was not undertaken. Nor was the effect of other potential confounders taken into account. The second study compared the IQ scores of children from four areas with differing levels of dental fluorosis. The source of fluoride was not water but soot due to coal burning. The Dental Fluorosis Index scores varied from 0.4 to 3.0. The latter is seen in areas fluoridated to approximately 8 ppm. Significant differences were observed in the IQ scores of children living in non-fluorosis and severe fluorosis areas (90 vs 80, respectively). It is not clear if the children examined in each area were randomly sampled. Nor was any attempt made to control for potential confounders or the effects of other pollutants present in soot from coal.

IMMUNE FUNCTION

No studies of the effect of water fluoridation on immune function were published between 1994 and 1999. However, a review paper (Challacombe, 1996) examined studies of fluoride and immune response published prior to 1992 and found no support for the suggestion that fluoride affects immunity.

FLUORIDE INTAKE IN CANADA: RECOMMENDED AND ACTUAL

The most recent discussions of fluoride intake in Canada come from two federal reports completed in 1993 and 1994. They were prepared by officials of Environment Canada, Health Canada, and by a group of dental specialists contracted by Health Canada to examine the use of inorganic fluoride in the promotion of oral health. Their findings have been published in two papers (Lewis et al, 1994; Lewis and Limeback, 1996). One paper (Lewis et al, 1994) made recommendations regarding total daily intake of fluoride for Canadians, while the second (Lewis and Limeback, 1996) compared these recommended intakes with actual intakes of Canadians.

The first endeavor sought to develop recommendations for total daily intakes of fluoride at different ages that would minimize the prevalence of dental decay and, at the same time, minimize the prevalence of fluorosis. The recommendations regarding optimum and maximum fluoride intake were based on the original dose-response data published by Dean in the early 1940's and the dose-response data of Eklund and Striffler published in 1980. Dean provided data on mean DMFT values among 12 to 14 year old lifelong residents of 21 cities with differing levels of fluoride in the water supply and the work of Eklund and Striffler extended this to 41 communities. In the 1940's when Dean undertook his work, fluoride intake was a product of the amount of water consumed and its natural fluoride concentration, with a small additional amount consumed through food. Because more recent dose-response studies were not appropriate for determining optimal fluoride intakes, these older data sets were used to estimate and recommend optimal and maximum daily intakes of fluoride. Optimal intakes were based on consumption of water fluoridated at a level of 0.8 to 1.2 ppm and maximum intakes based on consumption of water fluoridated to a level of 1.6 ppm. The former was chosen since it maximized the reduction in dental caries while minimizing dental fluorosis. The latter was chosen since it was the maximum level before moderate dental fluorosis appeared.

The recommended and maximum intakes were derived from the selected standards using fairly simple mathematical calculations. They involved the use of estimated mean body weights and estimated daily fluid intakes for five age groups. For example, the lower value of the range for children aged 12 to 14 years in Dean's time was calculated to be 0.88 mg from the consumption of an average of 1.1 liters of water per day at 0.8 ppm plus an estimated 0.2 mg daily from food for a total of 1.08 mg daily. This was divided by the mean body weight for a child of that age (44 kg) to give 25 micrograms per kilogram body weight. The range of values in micrograms/kg body weight for the five age groups are given in the middle column of Table 16.

Table 16 also gives the actual total daily fluoride intake (ATDFI) for Canadians at the same five ages also assuming average body weights. The following fluoride sources were considered: drinking water, food, breast milk (in the case of infants up to 6 months of age), air, soil and toothpaste. The estimates were based on a review of the literature and some survey data. Since there was variation among studies in the average amount of intake reported for these different sources of fluoride, high and low estimates were

calculated The proportions of the ATDFI that came from drinking water in fluoridated communities were estimated to be: 35 to 65% at 7 months to 4 years; 49-53% at 5 to 11 years; 52 to 64% at 12 to 19 years, and 34 to 47% at 20 or more years. In these age groups 7 months to 4 years and 5 to 11 years, 38% and 62%, respectively, of the upper range of values were attributed to the swallowing of toothpaste.

A comparison of the data in the two right hand columns of Table 16 indicates that for breast fed infants and those living in non-fluoridated communities, estimates of actual intake are mostly lower than the recommended intake. The only exception is the 7 month to 4 year age group. However, when formula-fed infants and those living in fluoridated communities are considered, the estimates of actual intake are substantially larger than the recommended levels. For the age groups 7 months to 4 years and 5 to 11 years the ATDFI for those living in fluoridated communities exceed the levels recommended in order to avoid moderate fluorosis.

It is also the case that the maximum daily mean fluoride intake of children aged seven months to 4 years (160 micrograms/kg body weight) is only 20 percent lower than the lowest intake (200 microgram /kg body weight) at which skeletal fluorosis can occur. Presumably, this maximum intake falls as the child ages so that a level of intake approaching that necessary for skeletal fluorosis is not sustained over a long period of time. Nevertheless, fluoride intake should be monitored closely to ensure that the gap between recommended and actual intakes does not widen over time.

Table 16: Recommended and actual fluoride intake estimates (Lewis and Limeback, 1996)

Age group:	**Recommended F intake (microgram/kg bw/day)**	**Actual F intake (microgram/kg bw/day)**
Up to 6 months	3-71 (99)	14-93 (formula-fed) 0.5-2.6 (breast-fed)
7 months to 4 years	56-81 (105)	87-160* 45-96**
5 to 11 years	32-45 (58)	49-79* 26-44**
12 to 19 years	24-33	33-45* 17-21**
20 years and over	32-41	47-58* 32-36**

( ): Upper value to prevent moderate fluorosis
* Estimate of actual intake based on consumption of fluoridated water
** Estimate of actual intake based on consumption of non-fluoridated water

As noted earlier, the reduction of fluoride intake in fluoridated communities may be achieved by lowering the fluoride content of the water supply (including the cessation of water fluoridation altogether) or by attempting to reduce the consumption of fluoride from discretionary sources. Since those aged 7 months to four years are most at risk, reducing the ingestion of fluoride toothpaste and the use of inappropriate fluoride supplements during this age period are prime targets in terms of promoting the proper use of fluorides (Pendrys and Morse, 1995). This approach is generally advocated by those who have argued that water fluoridation still has a major role to play in reducing dental decay.

Which of the strategies for reducing fluoride intake represents the best option is likely to be determined 1) by the prevalence of dental caries in the fluoridated communities in question, 2) the magnitude and significance of the reduction in caries as a result of fluoridated water, and 3) the relative value attached to dental decay and fluorosis as disease entities. As we have argued earlier, data on the oral health-related quality of life of those affected by these diseases/disorders are needed to inform policy decisions regarding water fluoridation programs.

Summary

Given the lack of adequate contemporary data, recommendations regarding optimal daily intakes of fluoride were based on dose-response data published in the 1940's. Optimal intakes are those derived from water fluoridated at 0.8 to 1.2 ppm, assuming no other sources of fluoride except food. Maximum intakes were based on consumption of water at 1.6 ppm, the level before moderate fluorosis appears. Actual total daily intakes were derived from amounts present in water, food, breast milk, air, soil and toothpaste. In Canada, actual intakes are larger than recommended intakes for formula-fed infants and those living in fluoridated communities. Efforts are required to reduce intakes among the most vulnerable age group, children aged 7 months to 4 years. Children of this age who are consuming the maximum dose are at risk of moderate levels of dental fluorosis.

WHAT IS THE OPTIMAL LEVEL OF WATER FLUORIDATION? THE NEED FOR NEW GUIDELINES

Questions concerning the so-called optimal level of water fluoridation cannot be addressed without data on dose response relationships; that is, reductions in caries and increases in fluorosis at differing concentrations of fluoride. As noted in the previous section, most contemporary discussions of optimal levels have been based on the original work of Dean in the 1930s and 1940s which included 21 communities, and the subsequent work by Eklund and Striffler in 1980 which extended the study to 41 communities (Ismail, 1997). As Ismail (1997) notes, Dean's data is limited by the fact that there were only three observation points between 0.5 ppm and 0.9 ppm and no observation points between 0.9 and 1.2 ppm which severely restricts the utility of this data set. The data of Eklund and Striffler, which has 15 data points over the critical range, suggest that caries rates decline only marginally between 0.6 and 1.2 ppm. Ismail (1977) fitted a regression line to these 15 data points and found that while the DMFT scores declined as fluoride concentration increased, the slope of the line was not significant.

It should be noted that the use of Dean's data and the cut-off point of 0.8 to 1.2 ppm fluoride in determining optimal levels and intakes is based on a number of key assumptions. First, it assumes that the dose-response relationship between dental caries prevalence and levels of fluoride in the water supply still holds. Second, it assumes that Dean's designation of 'very mild' and 'mild' degrees of fluorosis as acceptable is appropriate for contemporary populations. Further, the selection of the level on which to base calculations makes an arbitrary trade off between reductions in dental caries and increases in fluorosis. Table 17 uses data provided by Dean and graphed by Ismail (1997) to illustrate the trade-offs between mean DMFT values at age 12 to 14 years and the prevalence of fluorosis at different fluoride concentrations. A fluoride concentration of 1.2 ppm is associated with a mean DMFT of approximately 2.8 and a prevalence of fluorosis of 30%. At a level of 0.6 ppm the DMFT value is 4.2 (50% higher than at 1.2 ppm and 30% higher than at 0.8 ppm) but the prevalence of 'very mild' and 'mild' fluorosis is less than 10%.

Table 17: Mean DMFT at 12 to 14 years and percent with fluorosis at different fluoride levels (Values estimated from graph in Ismail, 1997)

F level in ppm:	**0.6**	**0.8**	**1.2**
Mean DMFT	4.2	3.2	2.8
Prevalence of fluorosis	8.0%	25.0%	30.0%

More recent dose-response data are extremely limited. Heller et al (1997) explored the relationship between fluoride levels in the water supply, dental caries and fluorosis among child participants in the 1986-87 National Survey of Caries in United States schoolchildren (Table 18).

Table 18: Mean DMFS and percent with fluorosis at different concentrations of water F (Heller et al, 1997). Values estimated from graphs.

Fluoride concentration (ppm)	Mean dfs	Mean DMFS	Percent with fluorosis
0.0	3.9	3.2	13
0.1	4.8	3.0	13
0.2	5.5	2.8	11
0.3	4.6	3.0	21
0.4	4.8	2.4	13
0.5	3.9	3.1	10
0.6	3.1	2.2	28
0.7	3.0	2.3	27
0.8	3.2	2.7	25
0.9	3.5	2.3	38
1.0	3.3	2.9	31
1.1	3.2	2.3	20
1.2	3.9	2.3	29
1.3	2.5	1.6	39
1.4	2.2	2.7	47
1.5	3.0	1.3	56
1.6+	2.9	3.4	55

When graphed, neither data series show the characteristic curve evident in data from Dean's 21 cities study. There is not, for example, a steep decline in caries rates over the range 0.1 to 0.5 ppm. Moreover, the relationship is not very pronounced. The mean dfs values of children exposed to 0.5 to 1.2 ppm fluoride all fall in the range 3.0 to 3.9, while the mean DMFT values in children exposed to 0.1 to 1.2 ppm all fall between the very narrow range 2.3 to 3.1. The shifting of these water fluoridation-caries curves to the left probably reflects the influence of exposure to fluoride other than in the water supply. When fitted with regression lines, these dose response data suggest only minor increases in mean dfs and DMFT values of the order of 0.5 and 0.25 as fluoride concentrations decline from 1 to 0.5 ppm. However, the same data suggest a marked increase in the prevalence of fluorosis at 0.6 ppm and above. Heller et al (1997) concluded that an appropriate trade off between dental caries and dental fluorosis occurs at around 0.7 ppm. How this standard was determined is not explained. Nevertheless, the study does suggest that standards formulated thirty or forty years ago need to be revisited in the light of current data and exposure to other sources of fluoride.

Given that over half the population of the US is receiving fluoridated water (Burt and Eklund, 1999) the does-response data of Heller et al (1997) may be compromised by the halo effect. Further studies of dose response relationships are needed from jurisdictions where only small proportions of the population are receiving fluoridated water in order to minimize the potential influence of the halo effect. Villa et al (1998) examined children from five cities in Chile where the fluoride concentration in the water supply ranged from

0.07 ppm to 1.10 ppm. All were located within a temperate climatic zone. The data, though limited, suggested that 0.5-0.6 ppm was optimal in terms of reductions in DMFT values and the prevalence of fluorosis. However, these data may not be generalizable to other populations.

In 1991, the National Health and Medical Research Council of Australia used historical data to estimate that caries rates would increase by 10 to 15% overall if water fluoride concentrations were reduced from 1.00 ppm to 0.5 ppm. However, along with the studies on the discontinuation of water fluoridation, the studies by Heller et al (1997) and Villa et al (1998) suggest that reducing levels of fluoride in the water would not necessarily result in marked increases in caries rates in child populations. Since total fluoride intake is higher than in the 1940s when the first standards regarding optimal fluoride concentrations were first specified (Ismail, 1997), further research regarding the effectiveness of reduced levels of fluoride in the water supply is needed.

The original recommendation of 1 ppm was an arbitrary standard developed by Dean in the mid-1930's based on his judgement that the degree of fluorosis associated with fluoride concentrations below this level was of no public health significance. This was subsequently expanded to the range 0.7 to 1.2 ppm according to the mean annual temperature of the community in question and variations in water consumption patterns that were observed as a consequence of climatic differences. The standard 1.0 to 1.2 ppm for temperate climates is in place today (Burt and Eklund, 1999).

Ismail (1997) has suggested that there is a need for new guidelines regarding levels of fluoride in the water supply. The amount recommended for each community should be based on the prevalence of caries and fluorosis in each community, exposure to other sources of fluoride and the prospects for reducing exposure to discretionary sources. The values of the community in terms of the trade-off between reductions in caries and increases in fluorosis also need to be considered. Relatively high levels of fluorosis might have been acceptable forty years ago when reductions in caries of 10 or more tooth surfaces were being achieved, but may not be acceptable in an era in which reductions in decay of only 1 tooth surface can be expected. Burt and Eklund (1999) suggest that fluorosis may well emerge as a public health problem as technologies for treating cosmetic defects are developed and marketed by the dental profession.

The limited information that is currently available suggests that there is no longer one fixed concentration that can be considered effective. Ismail (1997) suggests that a range from 0.5 to 1.2 ppm is more appropriate since it can be adapted in the light of local needs. However, it is increasingly unlikely, given access to other sources of fluorides, that concentrations at the upper end of this range would be necessary in contemporary North American populations. Ismail (1994) has also suggested that since fluoride is available from a number of sources, the absence of water fluoridation does not mean that the population is not exposed to levels of fluoride effective in terms of reducing dental decay. Rather, water fluoridation should be targeted to areas where the prevalence of decay is unacceptably high. This conforms to the recent observation by Rozier (1994) that an emerging body of professional opinion is claiming that not all communities need to be

fluoridated. Moreover, since even mild forms of dental fluorosis may well emerge as a public health problem, fluoride intake during the period of susceptibility should be kept as low as possible. Concentrations of 0.5-0.6 ppm may well be sufficient to bring about meaningful reductions in dental decay while avoiding the development of fluorosis in many individuals. The aim of public health interventions such as water fluoridation should not be to reduce dental decay but to maximize the oral health-related quality of life of the population as a whole. This involves making trade-offs between dental decay and fluorosis and also further consideration of the so-called social equity aspect of fluoridation programs. A careful balancing of the interests of majority and minority populations is necessary if a community wide intervention such as water fluoridation is to be ethically and politically acceptable.

Summary

Standards regarding optimal levels of fluoride in the water supply were developed on the basis of epidemiological data collected more than fifty years ago. The optimal level of 1.0 ppm was chosen, largely on an arbitrary basis, to achieve the maximum reduction in dental caries and the minimum prevalence of fluorosis. Re-examination of the early dose response data suggests that levels as low as 0.6 ppm would have achieved approximately the same reduction in the prevalence of dental decay. There is a lack of contemporary data on dose-response relationships between fluoride concentrations in the water supply, dental caries and dental fluorosis. Nevertheless, it has been suggested that new and more flexible guidelines are needed which take into account the changing prevalence of dental caries, access to other sources of fluoride and contemporary concerns with the cosmetic effects of fluorosis. Levels as low as 0.5 ppm may be optimal in some communities. Dental fluorosis has not been viewed as a public health problem in the past but may become so in the future.

MAXIMUM ACCEPTABLE CONCENTRATION FOR FLUORIDE

A MAC for fluoride in the water supply was established in 1978 and set at 1.5 mg/L.

A MAC for fluoride was calculated in the 1996 report based on a tolerable daily intake (TDI) of fluoride of 122 micrograms/kg body weight for a child aged 22-26 months. This TDI value was taken from a 1994 report produced under contract to Health Canada. The age 22-26 months is the period of greatest risk for the development of fluorosis in the anterior permanent teeth. An intake of 122 micrograms/kg body weight was considered to be unlikely to result in moderate to severe fluorosis.

Using this TDI in a formula to calculate the MAC produced a value of 1.0 mg/L. A reduction in the MAC from 1.5 to 1.0 mg/L was not considered to significantly decrease the risk of negative health effects since the total daily intake of fluoride of communities with 1.5 mg/L in the water supply is below the estimated 200 micrograms/kg body weight associated with skeletal fluorosis. The value is also below the level of 1.7 ppm at which moderate fluorosis begins to appear. Consequently, the MAC was maintained at

1.5 mg/L in order to avoid the excessive costs associated with meeting the lower guideline of 1.0 mg/L.

However, the water supply is not the only source of fluoride to which children are exposed. Consequently, in communities where the level is 1.5 mg/L, children in the vulnerable age range are at increased risk of exceeding the maximum recommended daily intake. If the 1978 guideline is to be maintained, then efforts to reduce exposure to discretionary sources of fluoride need to be undertaken in those communities where fluoride levels exceed the 1.0 mg/L calculated on the basis of the 1994 TDI.

RECOMMENDATIONS

While the evidence suggests that water fluoridation continues to be beneficial in terms of reducing the prevalence of dental decay, the magnitude of the difference between fluoridated and non-fluoridated communities is small in absolute terms, particularly in communities where the prevalence of dental caries is low. In such communities a careful assessment of the balance between reductions in dental decay and increases in dental fluorosis should be undertaken.

Data on dose-response relationships between water fluoridation and dental caries rates are sparse. However, there is a suggestion in the evidence available that fluoridating water to 0.5-0.6 ppm may be adequate in terms of achieving reductions in dental caries while minimizing dental fluorosis. Guidelines should be flexible to accommodate communities with different prevalences of dental decay and different values concerning the balance of dental benefits and risks.

If the maximum acceptable concentration of fluoride is to be maintained at 1.5mg/L, efforts need to be taken in communities at the upper end of the range to reduce exposure to other sources of fluoride.

The main limitations of current research on the effectiveness of water fluoridation are its exclusion of adults and elderly and failure to consider quality of life outcomes. Since water fluoridation is a total population strategy, its benefits to the population as a whole need to be documented. Those benefits should encompass reductions in disease and contributions to oral health-related quality of life.

Research also needs to be undertaken to determine when and what level of dental fluorosis has a negative effect on those with the condition and the trade-offs the lay population is willing to make with respect to reductions in dental decay and increases in dental fluorosis.

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