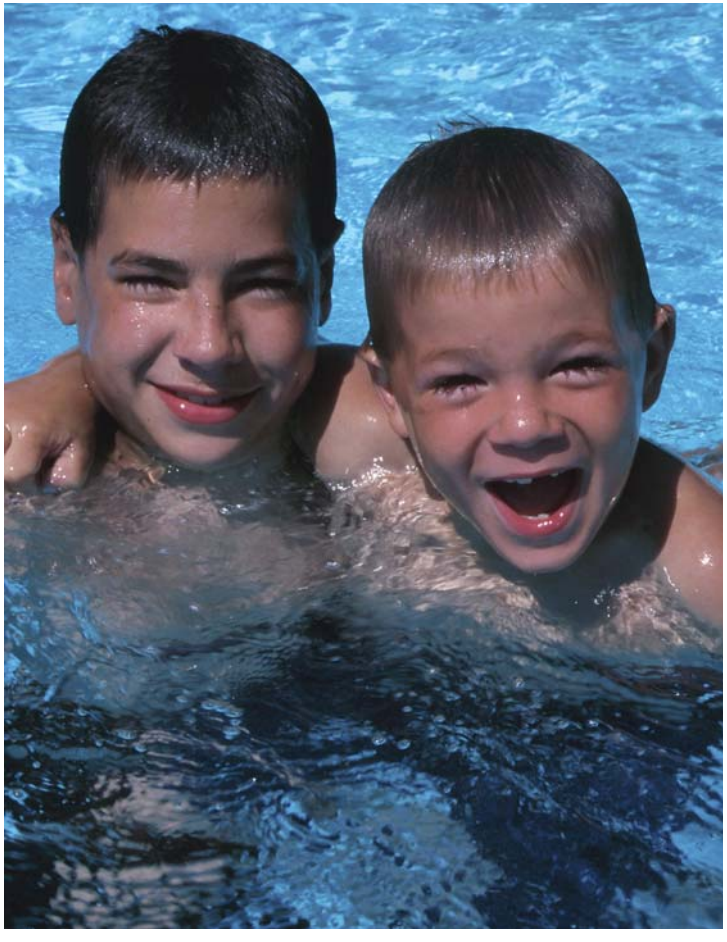
Fluoridation and general health

KEY POINTS

- **Oral health and general health are strongly linked. Poor oral health can impact adversely on general health and well-being.**
- **Epidemiological studies and independent reviews of the relevant medical and scientific literature have consistently failed to find evidence that fluoride in water at or around one part per million has any deleterious effect on general health.**
- **People have drunk naturally fluoridated water at or around the one part per million concentration for generations. There is no evidence that they have suffered harm to their general health from doing so. There is evidence, however, that naturally fluoridated water benefits dental health.**
- **Today, an estimated 50 million people around the world are drinking naturally fluoridated water. A further 370 million people in 27 countries are supplied with artificially fluoridated water.**



1. How oral health impacts on people's general health

Oral health and general health are strongly linked. Eating, speaking and most social activities are dependent to some extent on good oral health. Fluoridation improves a population's oral health and, as a consequence, contributes to its general health (1).

Tooth decay and its treatment are, at best, unpleasant for otherwise healthy individuals. However, for certain groups tooth decay or its treatment can present far more serious risks. For example, individuals suffering certain physical or mental disabilities are particularly vulnerable, and the cardiac status of children and adults with heart problems may be seriously affected by dental disease.

World Oral Health Report 2003

The extent to which oral health impacts on people's general health is discussed in the *World Oral Health Report 2003* published by the World Health Organisation: "The craniofacial complex allows us to speak, smile, kiss, touch, smell, taste, chew, swallow, and to cry out in pain. It provides protection against microbial infections and environmental threats. Oral diseases restrict activities in school, at work and at home, causing millions of school and work hours to be lost each year the world over. Moreover, the psychosocial impact of these diseases often significantly diminishes quality of life." (2)

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The interrelationship between oral and general health is proven by evidence.

More specifically, the report states: “The interrelationship between oral and general health is proven by evidence. Severe periodontal disease, for example, is associated with diabetes. The strong correlation between several oral diseases and non-communicable chronic diseases is primarily a result of the common risk factors. Many general disease conditions also have oral manifestations that increase the risk of oral disease which, in turn, is a risk factor for a number of general health conditions.”

Effects of poor oral health on the quality of life

The *World Oral Health Report 2003* further describes how poor oral health can have a profound effect on the quality of life: “The experience of pain, endurance of dental abscesses, problems with eating and chewing, embarrassment about the shape of teeth or about missing, discoloured or damaged teeth can adversely affect people’s daily lives and well-being. In recent years, much research has demonstrated the impact of oral health on quality of life.”

Attempts to reduce the population burden of dental caries may reasonably be expected to contribute to improvements in people’s general health.

It follows from this that attempts to reduce the population burden of dental caries may reasonably be expected to contribute towards improvements in people’s general health, especially among individuals ordinarily at the greatest risk of high levels of dental caries.

2. No evidence of harmful effects from naturally fluoridated water at the optimum level for dental health

The main purpose of fluoridation is to reduce tooth decay. The evidence on its effectiveness in achieving this aim is reviewed elsewhere in the Dental Benefits section of *One in a Million*. However, opponents of fluoridation claim that it causes, or may cause, serious problems for general health. It is important, therefore, for health agencies to examine and take full account of the available scientific evidence on the safety of fluoridation.

How nature showed the way through studies of people's teeth in the early part of the 20th century

Fluoride is naturally present at varying concentrations in all water supplies.

A starting point for reviewing the safety of fluoridation is to look at the health record of communities whose water supplies contain the same concentration of naturally occurring fluoride as other communities served by fluoridation schemes.

Fluoride is not a 'new' chemical in drinking water. It is naturally present at varying concentrations in all water supplies. In the United Kingdom, natural concentrations are typically lower than the 1 part per million (1ppm) which is recommended for dental health. However, some water supplies - for example, in Hartlepool in the North East of England and Uttoxeter in Staffordshire - have a natural fluoride concentration at about 1ppm, whilst supplies in parts of Essex used to contain even higher concentrations - up to nearly 6ppm - until the switch was

made to different water sources. Throughout the world, it is estimated that up to around 50 million people drink water with a natural fluoride level at about 1ppm.

In the early part of the 20th century, scientists were trying to find out why people living in certain places around the world had a particular type of mottling on tooth surfaces. By the early 1930s, a link was made between the mottling and very high concentrations of naturally occurring fluoride in people's drinking water (3). As a result, the term *dental fluorosis* was used to describe the phenomenon (See section on Dental Fluorosis in *One in a Million*).

The scientists who had been investigating the possible cause of dental fluorosis also observed that people affected had remarkably low levels of tooth decay (4) (5). Soon, they were able to establish that, at one part per million, fluoride in water caused mottling of only minor cosmetic significance but brought with it the benefit of improved dental health (6). This pioneering public health investigation led to the suggestion that it might be possible to reproduce the benefits of nature by artificially adjusting the natural fluoride levels in drinking water to around 1ppm.

Replicating the dental health benefits associated with naturally occurring fluoride in water

Starting with the introduction of the world's first fluoridation scheme in Grand Rapids in Michigan in 1945, a series of studies were set up in the United States and Canada in the mid to late 1940s to explore the feasibility of replicating the dental benefits of naturally occurring fluoride in water at the 1ppm concentration. These studies provided the evidence. Surveys showed that children in the fluoridated communities had significantly less tooth decay than those from other communities whose water supplies did not have their natural fluoride level adjusted (7) (8) (9).

The key question to ask, of course, is whether fluoride at this level (at or around 1ppm) could or does cause harm to other parts of the body. The early research indicated that there was not a problem. There was no evidence to suggest that people in communities where naturally fluoridated water at or around a 1ppm concentration had been consumed for a generation or more were suffering from adverse health effects that could be attributed to the fluoride in their water.

No evidence to suggest health problems in naturally fluoridated communities at or around the 1ppm concentration.

Naturally occurring and added fluoride both present in water as ‘fluoride ions’

The laws of chemistry dictate that fluoride ions in solution in water are identical whether they occur naturally in the water or are added artificially. For this reason, it has long been believed that there is no difference in the way that people’s bodies absorb fluoride from naturally and artificially fluoridated water (10).

According to a report published in 2002 on a study conducted by the National Centre for Environmental Toxicology at the Water Research Centre (WRc): “…hexafluorosilicate added to fluoridate water is effectively 100% dissociated to form fluoride ion under water treatment conditions. In terms of chemistry and bioavailability there is absolutely no difference between the added and natural fluoride” (11).

The WRc report stresses that the fluoride present naturally in water is *not* calcium fluoride. It is present in water as ‘fluoride ions’. It means, therefore, that the fluoride consumed by residents of Birmingham in their water supply (a combination of naturally occurring and added fluoride ions) is chemically identical to the fluoride consumed at or around 1 ppm (approximately the same concentration as in Birmingham) by residents of Uttoxeter in Staffordshire, where all the fluoride ions in the water occur naturally.

To take this principle further, the fluoride that is present naturally in Birmingham’s water supply prior to fluoridation at the water treatment works is the same as the fluoride that has been added. If a sample of water from a Birmingham resident’s tap were taken to the laboratory for analysis, it would not be possible to differentiate between the fluoride ions in the water and to attribute a natural or artificial status to those ions.

No statistically significant difference between naturally and artificially fluoridated water in terms of comparative bioavailability.

In 2005, a research team from the University of Newcastle (Maguire et al) published a report on a study of the comparative bioavailability of fluoride in naturally fluoridated and artificially fluoridated water (12). The authors concluded: "This study provides the first data on fluoride pharmaco-kinetics and bioavailability of fluoride from naturally and artificially fluoridated tap drinking waters with different degrees of hardness. The results suggest that any differences between waters for these variables are small."

More recently, in 2008, a study by researchers in the United States and Brazil (Whitford et al) was reported in the scientific literature (13). Like the University of Newcastle study, it sought to compare the bioavailability of naturally and artificially fluoridated water. However, on this occasion the fluoride concentrations being compared ranged from 0.67ppm to 5.45ppm (the latter being over five times higher than the concentrations tested in the UK study). In their report, the authors of the US/Brazilian study said that their findings were in close agreement with those of the Newcastle study and provided support for the validity of that study's conclusions.

Whilst acknowledging that the size of their study resulted in a limited power to detect statistically significant differences, Whitford et al stress that at low concentrations such as those used in the Newcastle study and in their own study, the fluoride in the compounds studied is almost completely dissociated. They go on to argue that "…it is very likely that if there are true differences in the pharmacokinetics of fluoride related to the chemical compounds added to water, it appears that the differences would be small" and that "…if they exist, it is unlikely that the expected small differences in pharmacokinetic variables would have any clinical or toxicological significance".

The studies by WRc, the University of Newcastle team and the US/Brazilian researchers are important because, together, they suggest that evidence from populations such as Hartlepool, where water supplies have been naturally fluoridated at the right level for dental health (1 part of fluoride per million parts of water) for hundreds of years, and which have shown no increased risk of any adverse health effects, can reasonably be applied to populations receiving artificially fluoridated supplies.

Artificial fluoridation has been practised for 65 years in the United States. Today, an estimated 350 million people in around 30 countries around the world are supplied with water whose naturally occurring fluoride content has been increased through a fluoridation scheme. As a result, there have been opportunities – through routine public health monitoring, individually commissioned studies and reviews of the accumulating evidence – to study whether fluoridated water, in addition to reducing tooth decay, has any other effects on health.

3. No evidence of harmful health effects from artificially fluoridated water at the optimum level for reducing tooth decay

Many claims are made by opponents of fluoridation that it causes adverse health effects. They are not supported by authoritative, peer-reviewed evidence published in the scientific literature. Here, in this section of *One in a Million*, we summarise the available evidence on cancer, bone fractures and other adverse health effects that have been erroneously attributed to consumption of fluoridated water at or around the 1ppm concentration.

Bone health

Between 50% and 70% of the fluoride that people take in when drinking fluoridated water is rapidly excreted in the urine. Almost all of the fluoride retained by the body is deposited in the bones and teeth. It is plausible to speculate, therefore, that any adverse effects from fluoride intake *might* occur in bones and teeth, especially where naturally occurring levels of fluoride in water are exceptionally high. Research suggests, however, that apart from cosmetically significant dental fluorosis, only one condition – skeletal fluorosis – is known to result from long-term ingestion of such exceptionally high concentrations of fluoride in water in some developing countries.

Skeletal fluorosis

There are no reports of skeletal fluorosis in the UK or the US associated with fluoride concentrations at 1ppm in drinking water.

Skeletal fluorosis is a bone disease characterised by failure of the bone to mineralise properly. The bones tend to be weaker than normal bones and, typically, the bones of the legs become deformed because of the excessive weight bearing of the person affected. Calcification extends into tendons and ligaments, making them stiff and less mobile. The condition is very different from the forms of arthritis common in the UK. Indeed, there are no reports of skeletal fluorosis in the UK or the US associated with fluoride concentrations at 1ppm in drinking water. The condition is very rare in both countries, and only one indigenous case has ever been reported in the UK (14).

Skeletal fluorosis is a widespread problem in several developing countries such as India and Pakistan, and has also been reported sporadically in other parts of the world. These areas tend to have high fluoride exposures, mainly from high fluoride levels in drinking water (up to 18ppm in 15 states of India, for example) in hot climates, where people tend to consume higher quantities of water. In these developing countries, dietary deficiencies and a lack of safe water supplies also contribute to the much higher occurrence of crippling bone diseases than is seen in developed countries.

Bone fractures

There is a large body of evidence from populations drinking *naturally fluoridated* water that it has no adverse effect on our bones (15, 16, 17). However, as hip fracture is the most important of the potential effects of fluoride on bone in developed countries, a number of studies have investigated fluoride exposure and hip fracture risk. Results vary: some studies have shown a slight protective effect, others have shown a slight increase in fracture rates, while still others have found no effect.

Systematic review by the Centre for Reviews and Dissemination at the University of York (2000)

The analysis found a more or less equal number of cases where hip fracture rates increased or decreased slightly in fluoridated areas, with some studies showing no measurable effect either way.

In its systematic review published in 2000, the Centre for Reviews and Dissemination (CRD) at the University of York conducted a meta-analysis (analysing the pooled results) of 18 studies designed to identify possible increases in hip fractures associated with the consumption of fluoridated water (18). The CRD analysis found a more or less equal number of cases where hip fracture rates increased or decreased slightly in fluoridated areas, with some studies showing no measurable effect either way. A similar pattern emerged when data from studies on other types of bone fracture (i.e., not hip fractures) was analysed.

The CRD report states: “A forest plot of all the bone studies showing the measures of effect and their 95% confidence intervals was produced for all studies that provided sufficient data to calculate a relative risk, odds-ratio or standardised rate-ratio and its 95% confidence interval. The majority of the measures and their confidence intervals were distributed around 1, the line of no effect for related measures (suggesting no association), with no obvious outliers noted.”

Systematic review by the Australian National Health and Medical Research Council (2007)

Bone health studies were also considered in a later systematic review of fluoride-related evidence undertaken by the Australian National Health and Medical Research Council (NHMRC) (19). Its report, published in 2007, cites three previously conducted systematic reviews of the evidence on fluoride levels in water and the incidence of bone fracture:

- Jones et al (1999), who concluded that water fluoridation levels aimed at preventing dental caries, and possibly at somewhat higher naturally occurring levels, appear to have little effect on fracture risk (20).
- Demos et al (2001), who concluded that the addition of fluoride to water at approximately 1 ppm does not increase the incidence of fracture and that the body of epidemiological evidence suggests either no association or a slight beneficial effect on bone strength, bone density and fracture risk (21).
- the York CRD review reported by McDonagh et al (2000), who found five studies with a statistically significant reduction in fractures in fluoridated areas, four with an increase and 21 with no effect either way (18).

Study of communities in China with varying levels of naturally occurring fluoride in water

The Australian NHMRC looked also at three post-York studies of bone fractures in areas with different levels of naturally occurring fluoride in water. Of particular interest is a study conducted by Li et al (2001) in China, where the researchers compared bone fracture rates in communities with naturally fluoridated water at concentrations ranging from 0.25 ppm to 7.97 ppm. The lowest fracture rates were found in the communities with a natural fluoride level in water that equated to the 1 ppm used in fluoridation schemes in the UK (22).

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According to the NHMRC, the Li study "supports the conclusion of the previous systematic reviews that intentional water fluoridation has no negative effect on fracture risk." The NHMRC report also points to the results of the Chinese study providing some suggestion of U-shaped relationship, whereby bone fracture rates in areas with fluoridated water at around 1 ppm are lower than in areas with both higher and lower fluoride concentrations. However, because of the many potentially confounding factors involved, the report says this relationship should be interpreted with caution.

US study of around 10,000 women aged 65 and over

One of the largest studies conducted on bone fractures and fluoride, reported in the British *Medical Journal* in 2000, was undertaken in the United States to determine whether, on an individual level, older women with long term exposure to fluoridated water had different bone mass and rates of fracture compared with women with no exposure (23). Nearly 10,000 white women aged 65 and over were recruited into the study in four different US States between 1986 and 1988.

In addition to having their bone density measured, they were interviewed about their level of physical activity, diet, smoking habits, coffee and alcohol consumption, medical history, and the number and types of bone fractures they had previously experienced. To establish the degree to which they had or had not been exposed to fluoridated water, they were also asked to give their addresses and sources of water supply between 1950 and 1994.

Following their initial recruitment and examination, the women were contacted every four months to ascertain whether they had since suffered a fracture. All fractures up to December 1995 were recorded and taken into account in the subsequent analysis. In reporting the outcome of their study, the authors wrote: "We found that exposure to fluoridation was associated with an increase in bone mass at the lumbar spine and proximal femur and a slight decrease in the risk of hip and vertebral fractures."

The study found that exposure to fluoridation was associated with an increase in bone mass at the lumbar spine and proximal femur and a slight decrease in the risk of hip or vertebral fractures,

They concluded: “Our results show that long term exposure to fluoridation may reduce the risk of fractures of the hip and vertebrae in older white women. Because the burden of osteoporosis is largely due to fractures of the hip, this finding may have enormous importance for public health. If fluoridation does reduce the risk of hip fracture it may be one of the most cost effective methods for reducing the incidence of fractures related to osteoporosis….In addition, our results support the safety of fluoridation as a public health measure for the control of dental caries.”

UK Medical Research Council Epidemiology Unit study of men and women aged 50 and over

Also of interest is a case control study of men and women aged 50 and over that was conducted by researchers at the Medical Research Council’s Epidemiology Unit at the University of Southampton and reported in *The Lancet* in 2000 (24). They examined two groups of men and women aged 50 and over from the north east of England. The first group comprised nearly 1,000 people who had experienced hip fractures over a 17-month period at one of three hospitals. The second group comprised individuals randomly selected from the same age group in the general population.

No difference was found in the risk of hip fractures between those who had been drinking water with a fluoride level of 0.9ppm or less and those who had been drinking water with a fluoride level of more than 0.9ppm.

In addition to information about the subjects’ level of physical activity, diet, alcohol consumption and smoking habits, the researchers ascertained a residential history that enabled them to determine whether individuals had lived in areas supplied with water whose natural fluoride content was at, above or below 0.9 ppm. No difference was found in the risk of hip fractures between those who had been drinking water with a fluoride level of 0.9 ppm or less and those who had been drinking water with a fluoride level of more than 0.9 ppm. The MRC team concluded: “There is a low risk of hip fracture for people ingesting fluoride in drinking water at concentrations of about 1 ppm. This low risk should not be a reason for withholding fluoridation of water supplies.”

Cancer

There have been many epidemiological studies examining whether or not there could be any link between fluoride in water and cancer. Probably the earliest, published over fifty years ago, was conducted in the UK (25). It was a simple comparison of death rates, for 1930-39, in South Shields (fluoride naturally present in water at l.4ppm) and Tynemouth (fluoride less than 0.25ppm). The author concluded that the death rates from 'malignant disease' in the two communities were 'approximately the same'.

However, Weaver's analysis did not take into account other relevant differences between the communities, such as the proportions of males and females and the proportions of people in different age groups. These factors have important effects on cancer rates and have been accounted for in many subsequent investigations of the possibility of any link with fluoridation that have been carried out over the years.

The Knox report (1985)

An expert Working Party convened by the UK Department of Health and Social Security and led by Professor George Knox reported in 1985 on its evaluation of analyses of cancer data available at that time (26). Members of the Working Party included some of the country's leading cancer epidemiology experts from the Institute of Cancer Research, supported by colleagues from the Medical Research Council, the University of Birmingham Cancer Epidemiology Research Unit and the Water Research Centre. They reviewed around 110 published papers and commissioned re-analyses of some of the most important data and results.

In their report, they concluded : "We have found nothing in any of the major classes of epidemiological evidence which could lead us to conclude that either fluoride occurring naturally in water, or fluoride added to water supplies, is capable of inducing cancer, or of increasing the mortality from cancer. This statement applies both to cancer as a whole and to cancer at a large number of specific sites. In this we concur with the great majority of scientific investigators and commentators in this field. The only contrary conclusions are in our view attributable to errors in data, errors in analytical technique, and errors in scientific logic.

"We have found nothing which could lead us to conclude that either fluoride occurring naturally in water, or fluoride addes to water supplies, is capable of inducing cancer or increasing mortality from cancer."

"The routine monitoring of public health has been an important feature of many fluoridation programmes and has contributed to the confidence with which we can assert the safety of fluoridation with respect to cancer."

"The evidence permits us to comment positively on the safety of fluoridated water in this respect. The absence of demonstrable effects on cancer rates in the face of long-term exposures to naturally elevated levels of fluoride in water; the absence of any demonstrable effect on cancer rates following the artificial fluoridation of water supplies; the large human populations observed; the consistency of the findings from many different sources of data in many different countries; lead us to conclude that in this respect the fluoridation of drinking water is safe.

"The routine monitoring of public health has been an important feature of many fluoridation programmes, and has contributed to the confidence with which we can assert the safety of fluoridation with respect to cancer. We recommend that such monitoring should continue."

Hoover et al study in the United States (1991)

Up to 35 years of fluoridation did not increase the risk of death from cancer for either men or women.

An important study by Hoover et al for the US National Cancer Institute was published in 1991 (27). It examined a total of 2.3 million cancer deaths to try to establish whether the introduction of fluoridated water in US communities had affected mortality rates.

Figures 1 and 2 show the pattern of cancers deaths in 1.2 million men and 1.1 million women for a period 35 years before and 35 years after fluoridation compared with cancer deaths in similar, but non-fluoridated, populations. The horizontal line at 1.0 is the theoretical line of no difference. As can be seen from this analysis, up to 35 years of fluoridation did not increase the risk of death from cancer for either men or women compared with the risk before fluoridation, or compared with non-fluoridated populations.

Figure 1 NCI study, Hoover et al 1991

Mortality ratios, all cancers in men before and after fluoridation. Mortality relative to non-fluoridated counties, adjusted for age, calendar-time, and geographic region. (1.2 m deaths) (Adapted from Hoover et al 1991)

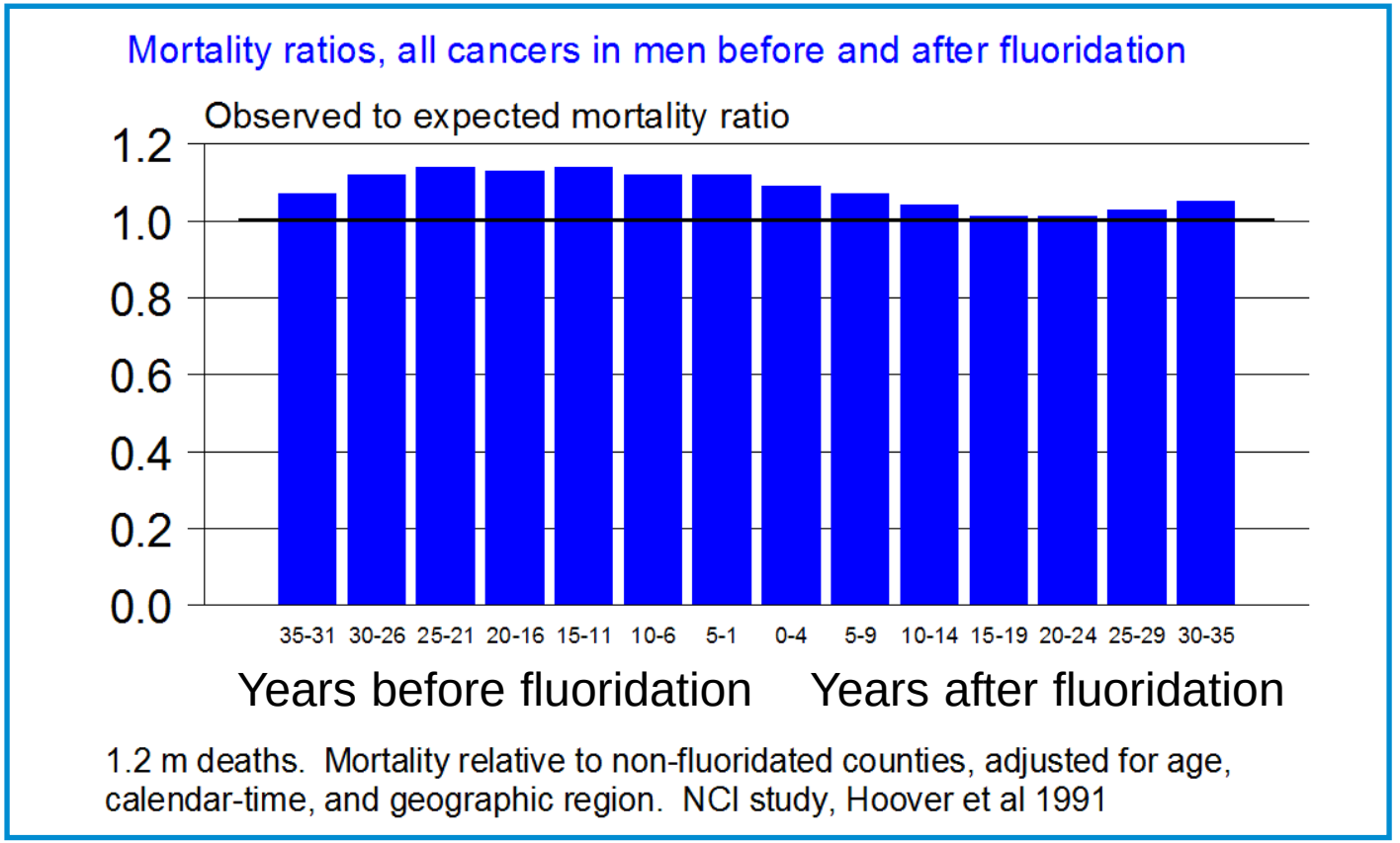
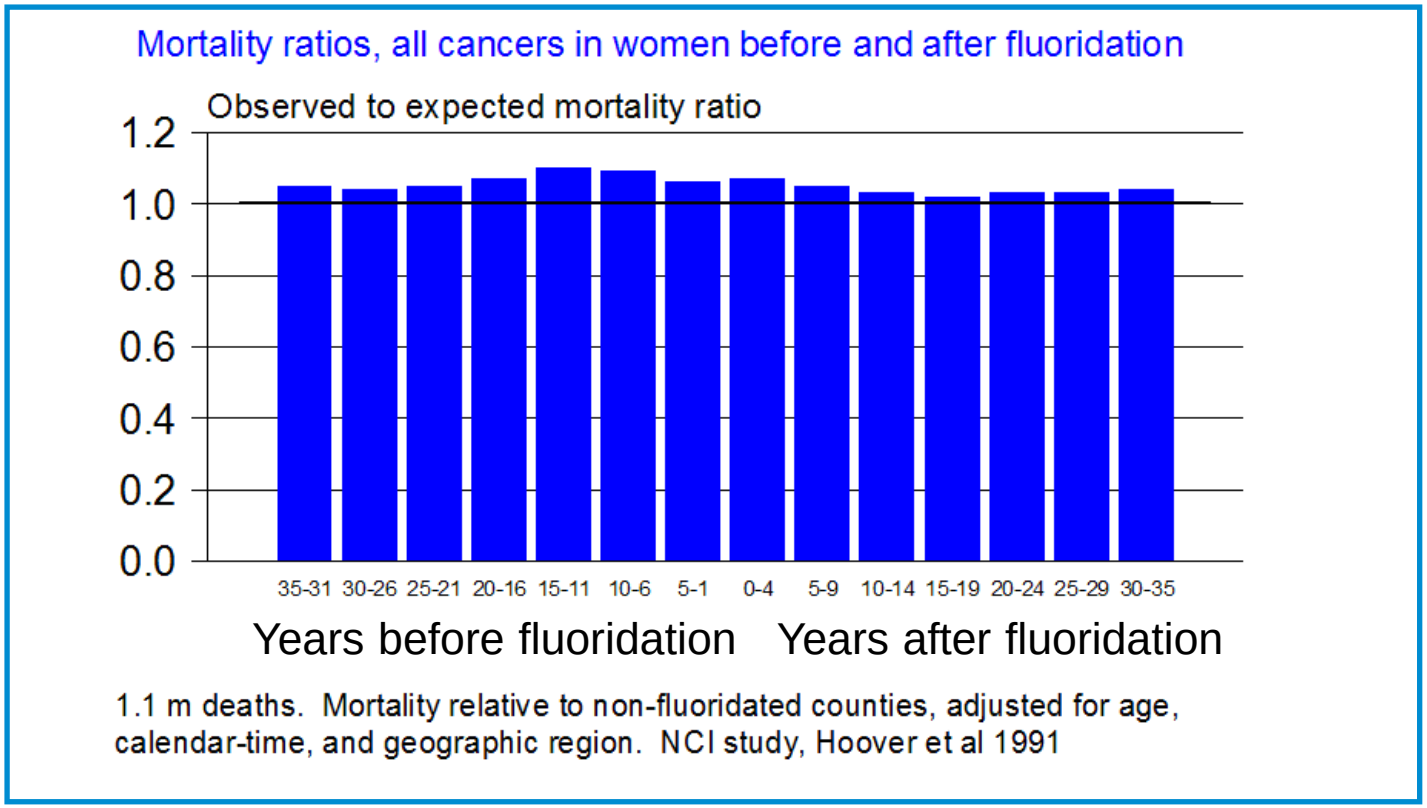


Figure 2 NCI study, Hoover et al 1991

Mortality ratios, all cancers in women before and after fluoridation. Mortality relative to non-fluoridated counties, adjusted for age, calendar-time, and geographic region. (1.1 m deaths) (Adapted from Hoover et al 1991)

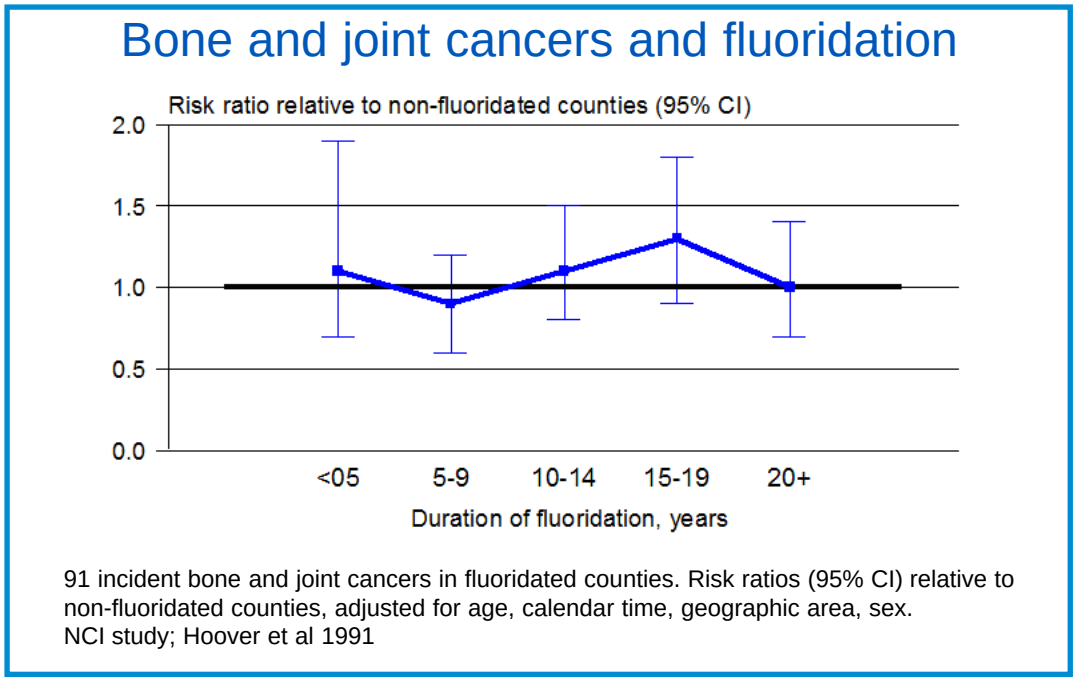


Hoover et al analysis of specific data on bone and joint cancers

The Hoover study singled out bone and joint cancers for detailed analysis and found no relationship with fluoridation. Figure 3 shows the relative risk of in fluoridated compared with non-fluoridated US counties. The horizontal line at 1.0 is the theoretical line of identical risk. As can be seen, the actual risk over a 20+ year period hovers above and below the line of identical risk. The bar lines indicate that, statistically, the risk of osteosarcoma is no different in fluoridated counties compared with non-fluoridated counties for any of the 5-year periods.

Figure 3 NCI study, Hoover et al 1991

Bone and joint cancers and fluoridation. Risk ratios relative to non-fluoridated counties, adjusted for age, calendar time, geographic area, and sex. (Adapted from Hoover et al 1991)



Overall, no association was detected between water fluoridation and mortality from any cancer, or from bone or thyroid cancers specifically.

Systematic review of cancer studies by the Centre for Reviews and Dissemination at the University of York (2000)

In 2000, the Centre for Reviews and Dissemination at the University of York published the findings of a systematic review of 26 previously conducted studies exploring whether there was an association between consumption of fluoridated water and a range of health problems, including cancer (18).

The CRD reviewers classified the studies as being of 'moderate to low' quality against particular criteria they had agreed at the start of their review. On the basis of their analysis they concluded: "The findings of cancer studies were mixed, with small variations on either side of no effect. Individual cancers examined were bone cancers and thyroid cancer, where once again no clear pattern of association was seen. Overall, from the research evidence presented, no association was detected between water fluoridation and mortality from any cancer, or from bone or thyroid cancers specifically."

Medical Research Council report (2002)

In 2002, the Medical Research Council considered the findings of the York systematic review with a view to identifying future research priorities regarding fluoridation and general health (28). With regard to any possible link between fluoridated water and cancer, the MRC report said: "Several studies have analysed data sets from ten fluoridated and ten non-fluoridated cities in the USA. With the exception of the analysis by Yiamouyiannis and Burk, which did not adjust appropriately for sex, age and ethnic group, none of these analyses has suggested that overall cancer mortality rates were positively associated with fluoridation. Similar analyses in other areas in the US, and in the UK and elsewhere, have not shown any differences in total cancer rates between fluoridated and non-fluoridated populations, or between populations with water supplies naturally high or low in fluoride. Some ecological studies have looked specifically at bone cancer or at osteosarcoma, and have not observed any associations with water fluoridation."

Overall, the current evidence does not support the hypothesis that exposure to artificially fluoridated water causes an increase in the risk for cancer in humans.

The MRC report also commented on the large study by Hoover et al in the United States which, it believed, should have been included in the analysis of cancer data undertaken by the Centre for Reviews and Dissemination at York. Despite meeting the CRD's criteria for inclusion in the systematic review, the Hoover study had been excluded. This, the CRD team explained in the York report, was on the grounds that Hoover et al had grouped together cancer deaths from non-fluoridated and fluoridated areas for the most recent 5-year period out of the 70 years of data they were examining. However, as the MRC report points out, it is very unlikely that cancer incidence or mortality would increase enough within five years of fluoridation to affect the results. It adds: "We also consider that the results of this study are very important for the evaluation of the effects of fluoridation, because the large number of cancers studied produces high power to detect small effects."

The MRC report concluded: "Overall, the current evidence does not support the hypothesis that exposure to artificially fluoridated water causes an increase in the risk for cancer in humans. It is too early to see whether there might be an effect after very long exposure, but the results available rule out more than a very small effect of artificial fluoridation on cancer risk for up to about 35 years of exposure. Furthermore, studies of cancer rates in relation to variations in naturally occurring fluoride levels provide information on lifetime exposure and the absence of any detectable adverse effects of fluoride in these studies provides a high level of reassurance concerning safety."

Systematic review of cancer studies by the Australian National Health and Medical Research Council (2007)

The Australian NHMRC has also systematically reviewed available evidence on whether fluoridated water has any effect on cancer risk (19). In analysing the data, the Australian reviewers took full account of the York report published seven years earlier (see above). They point out that the York review had included studies comparing communities with differing levels of natural fluoridation and that, in many cases, the communities concerned had fluoridation levels "many times the optimal level for intentional water fluoridation".

The Australian NHMRC report, published in 2007, concurs with the York report's conclusion that "…there is no clear association between water fluoridation and overall cancer incidence or mortality (for 'all cause' cancer, and specifically for bone cancer and osteosarcoma)." It explains that the York review included 11 studies that found fewer cancers in fluoridated areas, nine studies that found more cancers and two studies that found no difference.

The Australian reviewers also highlight the fact that of all the cancer studies included in the York review, the one that was accorded the highest validity score by the York team was a study by Smith et al (1980) that showed a reduction of 4.4% in the incidence of cancer in fluoridated areas compared with non-fluoridated areas (29).

Post-York cancer studies reviewed by the Australian NHMRC

A number of post-York cancer studies were reviewed by the NHMRC. They include:

- Takahashi et al (2001), who made no adjustment for confounding factors and did not consider the specific level of fluoridation (30). Readers are warned to exercise extreme caution in interpreting the finding of increased cancer incidence in 23 out of 36 bodily sites investigated, decreased incidence in four sites and no significant association in the nine others.
- Yang et al (2000), who compared ten non-fluoridated municipalities with ten that had natural fluoride at less than 0.28 ppm, found no association for cancer mortality rates except for bladder cancer in females (31). The Australian report stresses that the authors of the Yang study suggest that this is a chance finding.
- Steiner et al (2002), who presented international, age-standardised cancer incidence relative to each country's fluoridation, latitude and temperature and concluded that fluoride concentration in water is inversely correlated with cancer incidence (i.e., the lower the fluoride level, the higher the cancer incidence) (32). Again, the NHMRC advises extreme caution in interpreting these results because of what it calls "an overly simplistic analysis".
- Bassin et al (2006), whose results indicated a possible increase in osteosarcoma rates in young males living in fluoridated areas but could not be replicated in a larger study being carried out by her colleagues at Harvard University (33). The NHMRC points out that Bassin and her co-authors acknowledged the shortcomings of their original study. A letter from Professor Chester Douglass at the Harvard School of Dental Medicine and Kaumudi Joshipura at the Medical Sciences Campus of the University of Puerto Rico (34) appeared in the same publication as the Bassin study, stressing that it presented only a partial view of an ongoing study. Alluding to the larger study of which it was a part, they wrote: "Our findings, currently being prepared for publication, do not suggest an overall association between fluoride and osteosarcoma."

Cancer studies with data for fluoride exposure in individuals

There are few cancer studies where data on fluoride exposure were estimated for individuals rather than populations. However, three small case control studies of osteosarcoma have been reviewed by the Australian National Health and Medical Research Council (34, 35, 36). None of these studies found any evidence of fluoride increasing the risk of cancer.

Osteosarcoma (primary bone cancer)

Because fluoride accumulates in bone and has an effect on bone formation, particular attention has been given to bone cancer - especially osteosarcoma (primary bone cancer), which is very rare (most bone cancers are 'secondaries' from cancer in other organs). There are only about 125 new cases of osteosarcoma per year in England and Wales (28).

In 1990, the independent Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC) - which assesses and gives advice to the government on carcinogenic risk to humans - concluded that there was no evidence that fluoride causes bone cancer in humans, even in people in whom long term exposure to excessive levels of fluoride had caused skeletal fluorosis.

In 2000, the York review could find no clear association between osteosarcoma and fluoridation, and in 2002 the Medical Research Council agreed with York that, overall, the evidence does not suggest that artificially fluoridated water increases the risk of cancer. However, because osteosarcoma is a difficult cancer to study, and because its causes are poorly understood, the Medical Research Council suggested that if new studies are undertaken, exposure to fluoride should be included along with the other possible risk factors.

The Medical Research Council report commented: "Further data are expected from an extension of the preliminary report of McGuire et al (osteosarcoma case control study)". (37). Professor Chester Douglass of Harvard University presented preliminary results,from that and a separate National Cancer Institute study by Hoover et al at a symposium held at the Royal College of Physicians, London, in November 2002. These two large case-control studies showed no association between fluoride exposure and osteosarcoma.

Review by West Midlands Cancer Intelligence Unit

No evidence of an elevated incidence of osteosarcoma in fluoridated areas, whether in the general population or in young people.

In 2008 the West Midlands Cancer Intelligence Unit (WMCIU) completed an analysis of primary tumours of the bone, joints and articular cartilage in all age groups in the region between 1989 and 2005 (38). Comparisons were made of the 5-year rolling, age-standardised incidence of tumours in fluoridated and non-fluoridated areas. There was no evidence of an elevated incidence of osteosarcoma in fluoridated areas, whether in the general population or in young people.

Review by joint team of researchers at the Universities of Leeds, Newcastle and Oxford

No statistically significant difference in osteosarcoma rates between areas with very low fluoride concentrations and those with a 1mg/L concentration.

In 2010 a team of researchers from the Universities of Leeds, Newcastle and Oxford completed an analysis of osteosarcoma cases occurring in the whole of the UK between 1980 and 2005 in people up to the age of 50 (39). They found no statistically significant difference in osteosarcoma rates between areas with very low fluoride concentrations in water and those with a 1mg/L concentration. The results were the subject of a poster presentation at a scientific conference in Birmingham in June 2010 and were due to be presented at a conference in Boston, Massachusetts in October 2010.

Results of Irish study on osteosarcoma

In April 2011 the results of an Irish study of osteosarcoma and fluoridation were published (40). Data relating to cases of osteosarcoma between 1994 and 2006 in the mainly fluoridated Irish Republic and entirely non-fluoridated Northern Ireland were used to calculate age-specific incidence rates. No significant differences were observed between fluoridated and non-fluoridated areas in either age-specific or age-standardised incidence rates of osteosarcoma. The study authors concluded: "The results of this study do not support the hypothesis that osteosarcoma incidence in the island of Ireland is significantly related to public water fluoridation."

Results of US study on bone fluoride and osteosarcoma

In July 2011 a team of US researchers published the results of a study they had carried out to determine whether bone fluoride levels are higher in individuals with osteosarcoma (41). Segments of bone taken from patients with osteosarcoma were compared for their fluoride content with segments of bone taken from other patients with types of tumours that had never previously been linked in the scientific literature with exposure to fluoride.

The researchers said that If chronic fluoride intake was a risk factor for osteosarcoma, it would be reasonable to expect that cases would have significantly higher bone fluoride concentrations than individuals not affected by osteosarcoma. However, the study found no association between the disease and fluoride levels in bone.

The weight of evidence shows that fluoride is unlikely to produce hypersensitivity or other immunological effects.

Allergy and immunological effects

Claims that fluoridated water may cause allergic reactions in some people have been investigated and found not to be supported by the evidence. In its 2002 report on Fluoride and Health, the Medical Research Council said: “Reviews by the US National Research Council (1993), the Australian National Health and Medical Research Council (1991), and Challacombe (1996) all concluded that the studies undertaken do not support claims that fluoride is allergenic. (42) (43) (44). They considered the weight of evidence to show that fluoride is unlikely to produce hypersensitivity or other immunological effects…Further work in this area would be useful, but in the absence of obvious toxic mechanisms for such an effect is considered to be of low priority.”

The plausibility of fluoride affecting the reproductive capacity of humans at the intakes experienced from fluoridated drinking water is low.

Effects on reproduction

On the question of whether fluoridation affects reproduction, the Medical Research Council’s 2002 review said: “Adverse effects of fluoride intake on reproductive performance, such as reduced lactation, have been demonstrated in many species. However, these studies have used dietary concentrations very much higher than those in the fluoridated drinking water of humans (National Research Council, 1993).” (28) (42)

It added: “Fluoride has also been implicated in a number of adverse outcomes relating to fertility and pregnancy, but there is insufficient evidence to establish a link between decreased fertility and fluoride exposure (Australian National Health and Medical Research Council, 1999) (45). The York Review found no evidence of reproductive toxicity in humans (McDonagh et al, 2000) …The plausibility of fluoride affecting the reproductive capacity of humans at the intakes experienced from fluoridated drinking water is low.” (18)

Birth defects

Human and experimental animal data suggest that drinking even high levels of fluoride in water does not cause birth defects.

Fluoride reaches the unborn baby and is incorporated into the developing tissues. For this reason, it is theoretically plausible that it might cause birth defects. However, studies in areas of India and Africa that have high levels of naturally fluoridated water have not shown an increase in birth defects (16). Whilst in 1957 an investigator linked an excess of Down’s Syndrome to fluoridation, later studies by other investigators provided evidence against this suggestion (16) (18).

On this question, the Medical Research Council’s 2002 review concluded: “Human and experimental animal data suggest that drinking even high levels of fluoride in water does not cause birth defects…. Further work on this aspect is not considered to be of high priority (28).”

One recent study has concluded that there is no evidence that fluoridation has had any influence on the rate of congenital abnormalities or stillbirths in the North East of England (46). Another study, which looked at all pregnancies that were recognised to be affected by Down’s Syndrome in England and Wales over a 5-year period, found no convincing evidence of an association between water fluoridation and Down’s Syndrome (47).

Renal effects

Several large community-based studies have found no increase in kidney disease associated with long-term exposure to drinking water with fluoride concentrations of up to eight times the optimal for dental health.

The kidney is exposed to relatively high fluoride concentrations. The potential for it to be harmed by fluoride therefore exists. However, several large community-based studies have found no increase in kidney disease associated with long-term exposure to drinking water with fluoride concentrations of up to eight times the optimal for dental health (16) (42). The Medical Research Council’s 2002 review concluded that further research on this question was not a high priority.

Gastrointestinal tract

High concentrations of fluoride can be irritating to the stomach. However, at optimal drinking water fluoride concentrations (1 part per million) this is not a problem (16) (42). Again, the Medical Research Council's 2002 review concluded that further research on this question was not a high priority.

Intelligence

Some opponents of water fluoridation have claimed that it may be responsible for reducing average intelligence. They appear to base these claims on studies conducted primarily in remote, rural areas of China. A much smaller number of studies have been reported in India, Mexico and Iran. None of these four countries practises artificial water fluoridation.

Consequently, none of the studies involved communities with fluoridation schemes, whilst many of them had water supplies with much higher levels of naturally occurring fluoride (between 2ppm and 9ppm) than are found in artificially fluoridated supplies in the UK or elsewhere.

People in the communities included in the IQ studies were often also exposed to high levels of fluoride from sources other than water, including high-fluoride coals used for heating and drying grain. Their water sources are much less likely to be subject to the stringent regulatory controls that exist the UK, with more reliance on non-public, and therefore unregulated, water sources (e.g., wells). Water supplies could therefore be contaminated with other chemicals such as arsenic, which may affect IQ. Whatever results may have been obtained from the IQ studies conducted in China, India, Mexico and Iran are not applicable to environmental and social conditions prevailing in fluoridated communities in the UK.

During the public consultation which took place during 2008 on proposals to fluoridate water supplies in Southampton and neighbouring areas of south west Hampshire, opponents of fluoridation cited Chinese studies – and a systematic review of those studies by Tang et al – as evidence that IQ could be impaired as a result of drinking fluoridated water (48). To address these concerns, the director of public health of South Central Strategic Health Authority commissioned an independent analysis of both the Tang review and the individual studies on

which it was based (49). Key conclusions from that analysis were that:

- the authors of the individual IQ studies had not consistently adjusted their findings to take account of potentially confounding factors between the communities being compared, such as environmental arsenic and iodine in water, parental education, and socio-economic factors;
- the authors of the Tang et al systematic review had combined the results of the studies into summary measures by meta analysis in a way that is not statistically appropriate or valid;
- the findings are unlikely to be directly applicable to the population of Southampton because the level of fluoride found in the high fluoride areas in this research was generally higher than that intended for use in water fluoridation schemes (1ppm), or was confounded by varying levels of other chemicals in drinking water that are not a problem in the UK (iodine or arsenic);
- sources of fluoride exposure exist in these settings that do not exist in the UK setting - for example, burning high fluoride coal and eating contaminated grain – which can substantially contribute to fluoride exposure.

Thyroid disease

In 2000, the Centre for Reviews and Dissemination at York reported on two studies which had found no significant association between water fluoride level and goitre (50, 51), and an unpublished study that appeared to have found an association between combined high fluoride/low iodine levels and goitre (52). However, the Medical Research Council's 2002 review urged that the results should be treated with caution. It also concluded that further investigation of this aspect of fluoridation and general health was of low priority.

Miscellaneous effects

The Medical Research Council's 2002 review concluded that further targeted research on several other possible health outcomes, such as effects on the pineal gland, dementia, and Sudden Infant Death Syndrome, was of low priority "unless and until critical literature reviews are undertaken that demonstrate specific research needs".

US National Research Council report (2006)

In 2006 the US National Research Council (NRC) published the findings of its review of the US Environmental Protection Agency (ERA) guidelines for naturally occurring fluoride levels in water (53).

It should be stressed that this was not a review of the efficacy or safety of artificially fluoridated water. Rather, the NRC was commissioned to establish where the ERA's maximum of 4 ppm of naturally occurring fluoride in water would protect consumers against any potential harms associated with very high levels of fluoride in water, including bone fractures, skeletal fluorosis and severe mottling of tooth enamel.

The NRC also investigated whether the ERA's recommended secondary limit of 2 ppm of fluoride in water was adequate to prevent the occurrence of fluorosis of cosmetic concern. Both the 4 ppm and 2 ppm limits had been set by the EPA in 1985/86 and were retained following an NRC review in 1993.

These limits are important in the United States because an estimated 1.4 million people drink water with a naturally occurring fluoride level of between 2 and 3.9 ppm, and an estimated 200,000 people drink water with a naturally occurring fluoride at 4 ppm or above. They are not relevant to the UK, where the maximum legal limit for fluoride in water is 1.5 ppm and where the target level in fluoridation schemes is 1 ppm.

As a result of the most recent review, the NRC recommended the ERA to reduce the maximum 4 ppm limit on naturally occurring fluoride in water but made no recommendations relating to the 2 ppm level, where the primary concern is the possibility of dental fluorosis of cosmetic concern. Specifically, on this issue, the NRC report said: "The prevalence of severe enamel fluorosis is very low (near zero) at fluoride concentrations below 2 mg/litre. However, from a cosmetic standpoint, the 2 mg/litre level does not completely prevent the occurrence of moderate enamel fluorosis." The NRC calculated that, at the 2 ppm concentration (twice the concentration for UK fluoridation schemes), between 0% and 15% of children drinking the water could experience this cosmetic effect.

The prevalence of severe enamel fluorosis is very low (near zero) at fluoride concentrations below 2mg/litre.

European Commission's Scientific Committee on Health and Environmental Risks (SCHER) report (2011)

In May 2011 the EU Commission's Scientific Committee on Health and Environmental Risks (SCHER) published a report on the health effects of fluoride and fluoridating agents of drinking water (54). In summarising its overall conclusions on health effects, SCHER said that:

- Fluoride, either naturally present or intentionally added to water, food and consumer products, e.g., toothpaste, is generally considered beneficial to prevent dental caries.
- The occurrence of endemic skeletal fluorosis has not been reported in the general EU population.
- There is not sufficient evidence linking fluoride in drinking water to the development of osteosarcoma.
- Fluoride intake from drinking water at the level occurring in the EU does not appear to hamper children's neurodevelopment and IQ levels.
- Human studies do not suggest adverse thyroid effects at realistic human exposures to fluoride.
- There is no new evidence from human studies to indicate that fluoride in drinking water influences male and female reproductive capacity.

Conclusion

Water fluoridation has been practised for more than 65 years. In addition, people have drunk naturally fluoridated water for generations. Worldwide, over 400 million people consume fluoridated water, including the residents of 47 of the 50 largest US cities.

Given the number of research reports reviewed by the Centre for Reviews and Dissemination at York, the Medical Research Council, the Australian National Health and Medical Research Council, and other expert panels, it seems inconceivable that any adverse health effects would not by now have been uncovered.

As previously mentioned, a study by researchers at University of Newcastle suggests that there is no significant difference in the absorption of fluoride from naturally and artificially fluoridated water. It is supported by further evidence from a similar study conducted by US and Brazilian researchers. Together, these investigations lend weight to the view that as there is no evidence of harm to people in communities that have been supplied with naturally fluoridated water at 1 ppm for generations, there is no reason to believe that artificially fluoridated water at the same concentration should cause problems.

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