Fluoridation of water: a literature review of risks or benefits for the population in Ireland exposed to the current levels – including a European policy examination of water fluoridation practices

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Contents

Aims of the review

The overall aim of this review has been to carefully examine the evidence available on the positive and negative effects of population wide drinking water fluoridation.

Objectives:

Objective 1: Does water fluoridation have positive health effects?

Objective 2: Does water fluoridation have negative health effects?

This literature review has been commissioned by the Irish Water Board Institute to carry out an up to date expert literature review of fluoridation of water and the benefits and risks to the population of Ireland at current levels. The literature review was conducted in June 2014. The search was limited to English and included all study designs. Articles published from 1985 to date were included. Studies were also identified by screening the reference lists of the selected articles.

Inclusion criteria

The following inclusion criteria were developed:

a) Papers should be published between 1985 and the present day

b) Papers should be published in English in peer-reviewed journals

c) Papers should refer to the health effects of fluoridation of water on populations

Searching databases

Searches were conducted on the following databases; selected on the basis that they hold a range of references across the social and medical and health sciences.

ASSIA: Applied Social Sciences Index and Abstracts covers topics relevant to this review including health, social services, psychology, sociology, and education

Cinahl Plus provides indexing from the fields of nursing and allied health

OVID Medline covers the international literature on biomedicine, including the allied health fields and the biological and physical sciences, humanities, and information science as they relate to medicine and health care. Information is indexed from approximately 5,400 journals published world-wide

PubMed Provides authoritative medical information on medicine, nursing, dentistry, veterinary medicine, the health care system, pre-clinical sciences, and much more.

Embase is the most comprehensive database in biomedicine and pharmacology with access to the most up-to-date information about medical and drug-related subjects with over 11 million records. The EMBASE journal collection is international with over 4,500 biomedical journals from 70 countries.

Search Strategy
A search strategy was developed as outlined below:

1. drinking water and fluoridation
2. drinking water and fluoridation or fluoride
3. drinking water and fluoridation and benefits
4. drinking water and fluoridation and risks
5. fluoridation or fluoride and benefits and risks
6. fluoridation of water AND benefits
7. fluoridation of water AND risks

This strategy produced a good range of relevant results.

A first screen of results from searches of databases was undertaken by carefully reading the titles of all the papers returned for the searches of databases. A limiter was applied to return only review articles. Those that were clearly not relevant were deleted at this stage, whilst those that appeared

broadly or specifically relevant with online text were saved to '*Qiqqa*' – a reference management software.

References, which survived the first screen, were stored within *Qiqqa* for the second screening procedure, which was the next stage of the project. This process is completed through a careful reading of the reviews for each paper. Papers at this stage are again judged against the inclusion criteria and are included if they meet this criteria. Reference lists of included papers are also screened to identify any further relevant publications, which have not been found through searching databases.

Database	Search results	1st screen
Assia	11	0
Ovid	795	55
Embase	1148	92
Cinahl	77	0
PubMed	854	58

Total online reviews available   14

Executive Summary

This report provides a wide ranging review for the Irish Water Board concerning fluoride in the water supply. It investigates the positive and negative effects of water fluoridation at optimum levels on health and provides a European wide policy examination of water fluoridation practices. Current fluoridation levels within Ireland fall between 0.6 and 0.8 mg/L below the level of 1.5 mg/L recommended by the World Health Organization.

Water fluoridation practices were introduced in Grand Rapids, Michigan in the 1940s to assess its effectiveness at reducing dental caries. To date epidemiological studies suggest water fluoridation is effective in lowering dental caries through inhibiting demineralization and promoting re-mineralization making teeth stronger and more resistant to decay. As a community wide public health measure fluoridation is accessible to all regardless of socio-economic status, educational attainment or other social variables. For several decades, opposition to water fluoridation practices has been ongoing with proponents citing 'social medication' to 'violation of human rights'. To date, dental, medical and scientific communities continue to investigate the effects of fluoridation of water on health.

Cancer
Animal studies conducted on the cancer-causing effect of fluoridated water make suggestions of association, however, upon further investigation it appears there are limitations and an inability to link such outcomes to humans. More effective studies in the majority, show little evidence to suggest an increase in cancer occurrence in fluoridated areas.

Bone health
Fluoride may be associated with skeletal fluorosis, however, studies with such findings are limited to naturally occurring areas where fluoride levels are extremely high and combined with indoor burning of fluoride rich coal. There are suggestions of lower overall risk of bone fracture in areas where fluoride is below 1.1 mg/L with little or no fracture risk or decrease in bone mass density. Possibilities exist of an association with bone fracture at levels >4 mg/L and a slight protective effect of fluoridated water versus non-fluoridated water.

Neurotoxicity
From available studies on fluoride and neurotoxicity, it is clear that they do not support impairment of IQ, impaired thyroid function and deterioration of the central nervous system at permitted EU

levels. Extremely high levels of fluoride, the inclusion of burning coals and poor methodological design suggest it is not possible to establish any firm conclusions.

Reproductive and developmental effects

The effects of fluoride exposure on the reproductive system are mostly animal studies dealing with male mice or rats**.** Overall, fluoride doses used in these studies were high making observed effects irelevant for the European situation. No evidence to suggest fluoride effects on human reproductive hormones or fertility were discovered.

Dental caries/fluorosis

Majority of studies concluded that areas with water fluoridation showed an increase in children without dental caries and a reduction in children with dental caries. Approximately 12.5% of children exposed to levels of 1ppm experience aesthetically related fluorosis.

Lack of fluoride effect on disease and/or mortality rates

At levels of 1 mg/L of fluoride in drinking water, no effects have been established, either positively or negatively on disease or death rates. No differences in nephritis, coronary illness, allergic reactions or cirrhosis and includes: Downs Syndrome, senile dementia, nephrolithiasis, stillbirths and congenital abnormalities. It is suggested that fluoridation could therefore be ruled out as harmless to humans.

Optimal levels of fluoride ingestion

Fluoride exists in nature in compounds, released when water passes over rocks and soil, therefore fluoride is always present in small quantities in all water sources. Fluoride also exists in small quantities in food and beverages. Therefore, artificial fluoridation is a supplementation of naturally occurring fluoride. Intake of fluoride can occur from many sources including water, food, beverages, coal fires and gases produced from volcanic activity. Fluoride in water is the largest source and the only controllable element. Concentration of fluoride, controlled dose and dosage are not equal and must all be considered when discussing fluoride intake at safe levels. The pathways within the human body vary depending on age, weight and health status with lower and upper suggested levels available from public health bodies.

Fluoride concentrations

Fluoride concentrations are continuously and rigorously investigated to ensure human safety and good health. Safe levels of fluoridation are advised by: EU directives, World Health Organization, Environmental Protection Agency, United States Department of Health and Human Services, Center for Disease Control and Prevention to name a few. Optimal levels.

Introduction

Research into the beneficial effects of water fluoridation began in the early 1900's by Dr. McKay, a dental practitioner from Colorado Springs, United States of America and Dr. G.V Black, Dean of the Northwestern University Dental School in Chicago. With several patients presenting with brown stained permanent teeth Dr. McKay encouraged Dr. G.V. Black to embark on a joint investigation into this phenomenon. Their research led them to discover that the condition termed, 'mottled teeth', occurred due to developmental imperfections in the teeth. Currently termed 'dental or enamel fluorosis', Drs. McKay and Black suspected drinking water was influential and also noted that mottled teeth were resistant to decay (National Institute of Health 2014). In the 1930's it appeared from their investigations that exposure to high levels of fluoride in drinking water appeared to cause mottled teeth. Fluoride levels as high as high as 7.15 parts per million (ppm) were discovered in Arizona and 13.7 ppm in Bauxite . Upon investigation of other areas it was discovered that mottled teeth were more prevalent in areas with high fluoride. Further geographical studies in the 1930's by a U.S. Public Health Service dental officer, Dr. H. Trendley Dean and his associates, reported that the more severe forms of dental fluorosis did not appear to be caused by fluoride levels of up to 1.0 ppm in drinking water (Dean 1933). Based upon their investigations, Dr. G. J. Cox and associates at the Mellon Institute were the first to propose, in a paper, that adding fluoride to drinking water would be beneficial in preventing dental decay (Fluoride Facts 1993). In the 1940s, the first community wide water fluoridation program began in Grand Rapids, Michigan, in order to assess the beneficial effects of adding sodium fluoride to water supplies.

In the first half of the 20th Century, Epidemiological studies confirmed that naturally occurring fluoride in water could have a beneficial effect by reducing dental caries and also a detrimental effects on dental health, fluorosis (Parnell et al.2009). Extensive studies have shown over the past 50 years that individuals in areas of fluoridated drinking water have fewer dental caries. Naturally occurring in soil, water and plants concentration levels can occur between trace amounts to over 25mg/L. When this fluoride is ingested by humans there is some uptake by body tissues, particularly teeth and bones. It is now commonly accepted that dental enamel is protected through this deposition through a process of remineralisation and also by inhibiting demineralisation (Kumar, 2008). Resistance to decay occurs in post-eruptive teeth (teeth that have broken through the gum) when fluoride creates a surface resistance to acids formed by bacteria. This post-eruptive resistance is assisted through a consistent low level of fluoride present in the oral cavity (Pizzo et al. 2007). While the protective elements of fluoride are generally accepted for post-eruptive teeth, pre-eruptive (prior to the tooth being exposed through the gum) protective effects from fluoride remain

in contention and under debate. Pre-eruptive teeth remain susceptible to fluoride application through water fluoridation however, measuring the benefits remains particularly difficult. If the pre-eruptive tooth is exposed to excessive levels of fluoride during enamel formation , hypomineralisation of the enamel can occur (greater surface and subsurface porosity). This is also known as enamel fluorosis (Browne et al., 2005).

As a public health measure community water fluoridation is considered valuable for several reasons. Equal access to optimally fluoridated water can be achieved throughout communities regardless of socio-economic status, educational attainment or other social variables. Obtaining the benefits of water fluoridation does not require behavioural change from individuals within the community. Exposing the tooth to small amounts of fluoride may be effective in reducing dental decay if exposure occurs over the life span and in comparison to other forms of fluoride treatments, community water fluoridation is the thought to be the most cost effective treatment. In spite of the fact that the similar measurable advantages may have diminished in recent years as other fluoride sources have become accessible, the benefits of water fluoridation are still plainly clear (Fluoridation Facts 2005).

Preventing tooth decay through fluoridation of the public water supplies has been debated time and again, becoming one of the most controversial topics for several decades (Martin 1988). Disagreement continues to reign over the benefits and risks of fluoride, particularly in relation to prevention of tooth decay. While several countries may have reconsidered the use of fluoridated water, others continue to supply fluoridated drinking water to their communities. Consideration is given to the use of other sources of fluoride and raises the issue of the necessity of intentional water fluoridation and possibility of risk of over-exposure (CDC 2013). Anti-fluoridationists point to the reports on the health and environmental risks that are attached to fluoridating agents such as hydrofluorosilicic acid, sodium silicofluoride, disodium hexafluorosilicate or hexafluorosilicic acid, stating that proper assessments have not been undertaken. Indeed, they go on to suggest that such substances may have adverse health effects on humans including bone health (Scientific Committee on Health and Environmental Risks 2011). The debate continues, raising questions from the European Parliament, Ireland and the United Kingdom where intentional water fluoridation is still practiced.

Pioneering anti-fluoridationist, Gladys Caldwell was a proponent of fluoride as a pollutant in the 1950s. Publishing 'Fluoridation and Truth Decay' in 1974 she actively sought discontinuation of not only fluoride in drinking water but also industrial discharge of fluoride, fluoride in aerosols, gasoline and meats. Religious arguments also arose over fluoridation of water as 'socialized medication'.

While religious beliefs forbade the use of medication it was felt that fluoridation without consent violated human rights. In an Oregan court in 1955, it was ruled however that the freedom to believe is a protected right, the freedom to act on those beliefs is restricted by public interest. Fluoridation was deemed to be in the best interests of the public. Other opponents of water fluoridation disagreed with the argument for public interest supporting the communist theories that fluoridation of water was used to conquer territories and sterilize individuals. Joining the debate over fluoridation of water were consumers in the 1960's and 1970's who, made claims of misuse of tax funds. Water fluoridation they advised was toxic and ineffective and tax payers were being duped into paying for something they did not request. The most prominent during this time was Ralph Nader who fuelled the debate around cost-effectiveness of fluoridation of water (Reilly, 2007).

Raging through the 1980's arguments over the relationship between AIDS and fluoridation of water surfaced with claims ranging from the suppression of the immune system thereby decreasing resistance to AIDS, to those with AIDS or HIV positive being more susceptible to the disease. Entering the political domain, non-religious philosophical arguments again arose highlighting the question of civil liberties. Despite the governmental conclusion that fluoridation is in the interest of public health, anti-fluoridationists argued that fluoridation was dissimilar from other forms of medication. For example, chlorination of water supplies is deemed a legitimate responsibility of governments due to its ability to prevent life-threatening diseases. Fluoridation they advise is non-communicable and not life-threatening, therefore not a legitimate concern of governments and is considered nothing more than socialized dentistry. Concerns over the amount of control Governments can have over an individual's health become part of the anti-fluoridationists argument warning too much control of such socialized medication can lead to further infringements including the possibility of mass birth control or anti-hostility drugs. In the 1980s the term 'compulsory mass medication' enters the fluoridation vocabulary (Reilly, 2007).

Those in support of water fluoridation remain in the domain of dental, medical and scientific communities, however, support from a minority of scientists is gathering for those who oppose fluoridation practices (Martin, 1988). However, researchers continue to concentrate on the potential adverse and health impacts connected with introduction to fluoride in drinking water. A significant number of the studies have concentrated on high fluoride intake of natural occurring fluoride as opposed to artificial fluoridation levels. However in the 1993 NRC report, few instances of this extreme condition had been reported in the United States and it was not viewed as a public health concern (Tiemann 2013).

Cancer

The relationship between fluoridation and cancer is one that has been reported as a concern. In the early 1990s, using laboratory animals, two studies were undertaken to assess the cancer-causing nature of sodium fluoride. A principle study was undertaken by The National Toxicology Program (NTP) of the National Institute of Environmental Health Sciences with the second study supported by the Proctor and Gamble Company. In both studies, extremely high concentrations of sodium fluoride were ingested by rats and mice (25, 100 and 175 ppm) with a total of eight individual sex/species being used for the analysis. Within the eight groups, seven did not display any evidence of malignant tumor development. Male rats, however, from the NTP study, indicated a minor increase in neoplasms (osteosarcomas or cancerous tumors of the bone), (Bucher et al. 1991). The Ad Hoc Sub-committee on Fluoride of the U.S. Public Health Service addressed both studies in combination and expressed their concern stating that a secure relationship between fluoride and cancer could not be established from the animal studies (United States Public Health Service 1991). NTP researchers also inferred from this study, that levels of sodium fluoride beneath 175 mg/L in drinking water over a two-year period would not be expected to bring about any bone diseases in rats or mice. As indicated by the Agency for Toxic Substances and Disease Registry (ATSDR), both studies had issues that restricted their assessment in demonstrating whether fluoride can result in cancer causation in humans (United States Public Health Service 2003). Because of the concerns raised by the NTP 1990 study, The Environmental Protection Agency asked for the Nation Research Council (NRC) to survey the available toxicological and exposure data on fluoride to establish if the drinking water standard of 4 mg/L was sufficient to secure optimal wellbeing within the public domain (National Research Council 1993).

Subsequently, in a study by Moss et al. (1995) an analysis of bone cancer was undertaken in Wisconsin. Cases and matched controls were obtained from the cancer registry with controls experiencing other forms of cancer. The study included 167 cases, with 989 controls matched by age (±7 or 5 yrs), sex and race. Researchers did not detect a relationship between fluoridation at the time of diagnosis and bone cancer. While it is suggested that younger age groups are more susceptible to fluoride exposure, the researchers did not report the duration or timing of exposure. Fluoridated versus non-fluoridated areas were analyzed however no histories were taken from individuals under study so fluoride exposure assessment was based only on residence at time of diagnosis. The sample size is considerably small with no analysis by sex and age groups were too broad.

Mahoney et al. (1991) conducted a comparison of incidence rates between counties in New York State. The population included 10 million (between 1955 and 1987 for some analyses, 1976 - 1987 for others). Fluoridated versus non-fluoridated cities were compared with three counties considered non-fluoridated. All ages ranges were included in the study with a male versus female analyses. Mahoney et al. (1991) concluded their study indicated statistically significant increases in incidence rates of osteosarcoma in those over 35 years of age. However, they also acknowledged there were no increases in fluoridated areas compared to non-fluoridated areas. While those living in areas without fluoridated water were assigned as 'non-fluoridated' counties assigned as 'fluoridated' were in fact on average 56% fluoridated, an inaccurate assignment. New York City was also excluded, an area of 100% fluoridated water with the highest population on non-whites. According to Gelberg's 1995 study from the same NY Cancer Registry, non–whites had significantly higher rates of osteosarcoma, also, Freni (1992) found that amongst registries in the Unites States (US), Canada, Northern Europe, the United Kingdom (UK), Australia and New Zealand the greatest increase in young males with cancer occurred in NYC. By excluding NYC, Mahoney deprived this study of a large population. This study also used a large age range category. From inexact fluoridation classification and wide age range this study had a high degree of misclassification which limited its statistical power.

While Hoover (1990) reported higher incidence rates of osteosarcoma in males under the age of 20 years when comparing fluoridated and non-fluoridated communities, Eyre et al. (2009) found that young males consuming fluoridated drinking water above 0.7 mg/L showed no increase in osteosarcoma. Further studies conducted by The Harvard Fluoride Osteosarcoma study also limited their research to participants under the age of twenty. Conducted across 11 hospitals in the United States of America, fluoride exposure levels were measured from several sources including municipal, private well and bottled drinking water. Age was also taken into consideration during the time of exposure. 103 cases were matched with 215 controls with municipal fluoride levels determined by contacting local, regional and national registries. Well water was analyzed and bottled water was given a value of 0.1 mg/L. Variations in consumption were taken into consideration due to local climate with warmer climates estimated at 0.07 mg/L while cooler climates were estimated at 1.2 mg/L, CDC optimal target levels. Topical exposures such as toothpaste and fluoride supplements were also included in the study. A statistically significant increase was reported for osteosarcoma in males who were exposed to the highest level of the CDC optimal target level between the ages of six and eight. After adjustments were made for the use of topical fluorides and socio-economic status, the increase in risk remained (Bassin 2006). Further research was suggested based on this intermediate evaluation and primary conclusions. The retrospectively collected data raises concern

for the findings along with findings based on an intermediate evaluation. Further research would be necessary to confirm or refute the observations in relation to fluoride exposure and osteosarcoma. SCHER agrees that epidemiological studies do not indicate a clear link between fluoride in drinking water, osteosarcoma and cancer in general. There is no evidence from animal studies to support the link, thus fluoride cannot be classified as carcinogenic.

Examining whether living in areas of higher water fluoride concentration increased the risk of primary bone cancer, Blakey et al. (2013) analyzed data obtained from population-based cancer registries in Great Britain (GB) for patients diagnosed with osteosarcoma or Ewing sarcoma during 1980–2005. 2566, (1493 males, 1073 females) osteosarcoma and 1650, (988 males, 662 females) Ewing sarcoma cases were included in the study. Cases were further divided into age groups 0–14, 15–29 and 30–49 years at diagnosis. Fluoride level in drinking water was continuously monitored and required to be less than 1·5 ppm on a 3–month average basis. The findings from this study provide no evidence that higher levels of fluoride (whether natural or artificial) in drinking water in GB lead to greater risk of either osteosarcoma or Ewing sarcoma. Limitations include, small area population study not allowing for individual fluoride dosage and an assumption that water fluoride levels remained unchanged within the study time-frame.

An alleged connection between water fluoridation and increased cancer mortality, occurring in the 1970's raised concerns over public health and wellbeing and heightened controversy over water fluoridation practices. Although, few in number, reports have argued that cancer mortality was higher in territories with fluoridated drinking water than in non fluoridated regions. These discoveries were disproved by various researchers who indentified issues with the study's methodologies (Congressional Research Council 2013). However, it remains imperative that such issues are addressed and to this end research continues to analyze and examine the likelihood of a relationship between fluoridated water and cancer occurrence within human populations. In 1982 and 1985, available scientific studies were gathered and reviewed by Independent expert panels, culminating in the conclusion that such studies did not provide any solid confirmation of a relationship between fluoride in drinking water and danger of cancer (United States Public Health Service 1991). However, as indicated by the 1993 NRC fluoride review, all except one of these studies were ecological studies; that is, they were either geographic correlation or time-line studies that addressed exposures to fluoridated water at the group level as opposed to individual exposures. As a result, the translation of the information was constrained by the failure to measure singular fluoride exposures over time, or to measure exposure to other hazardous components, for example,

smoking or other cancer causing substances. Other examinations of this issue have seen researchers at the National Research Council (NRC), assessing the relationship between drinking water fluoridation and the number of deaths occurring due to cancer in the United States, by area. After analyzing more than 2.2 million cancer death records, NCI scientists suggested no link can be established between increased risk of cancer death and fluoridated drinking water. With more than 50 epidemiological studies combined in the 1993 study, it was suggested that any link to cancer causing effects must be extremely weak due to the absence of any positive results (National Research Council 1993). Despite the fact that NRC alleged that the information did not show a relationship between fluoridated drinking water and cancer, it did propose that more research ought to be attempted particularly investigating exposure to fluoride on an individual level rather than population exposure.

Evaluations were undertaken by McDonagh et al. (2000) from the same set of urban communities in the USA, 10 fluoridated and 10 non-fluoridated. These urban areas were initially chosen and investigated by Yiamouyiannis and Burk (1977). All studies utilized before and after study designs contrasting tumour occurrence prior to and after the introduction of water fluoridation in 10 of the 20 study areas. In the first study, Yiamouyiannis discovered a positive relationship between cancer occurrence and increased water fluoride, however, criticisms of this study include the exclusion of demographic characteristics between the two communities at baseline and for inadequately accounting for changes that occurred in age and gender from baseline to final study years. Yiamouyiannis grouped men and women together and also whites and non-white. The age ranges were broad (0-24, 25-44, etc.). The information appears to show the non-white population over the age of 65 years increased faster in the fluoridated area than in the non-fluoridated area (Doll 1977). In alternate studies where the use of standardization to control for age, sex and ethnic groups were utilized, no relationship was found between cancer mortality and water fluoridation in the chosen urban communities. However, criticisms of such studies ensued by Yiamouyiannis claiming data included the in Doll's (1977) analysis were supplied by the National Cancer Institute (NCI) and contained an information transcription error. This they advised was repeated in the paper (Yiamouyiannis, 1977). Yiamouyiannis also contended that the investigation was not conducted properly based on the grounds that 90- 95% of the accessible information were excluded and that the choice of the year 1970 as one of the study years was unsuitable as fluoridation of the control group had officially begun. This had indeed just been begun in two of the urban communities a few months before the 1970 information were gathered. Doll advocated the decision of 1970 as a year for which more precise population information were accessible. Smith (1980) utilized the remedied

NCI figures within a comparable analysis and furthermore neglected to locate any relationship between water fluoridation and cancer mortality in the chosen urban areas.

Realizing in 2002 that a number of new studies in relation to the impact of fluoride on bone had been conducted since the implementation of the fluoride standard in 1986, EPA advised a new investigation was warranted.

Again it was requested of the NRC by the EPA to review all available toxicological and epidemiological information on fluoride. Additionally, the fluoride risk assessment would be updated and NRC would provide a scientific evaluation of EPA's current drinking water standards for fluoride. NRC then released 'Fluoride in Drinking Water: A Scientific Review of EPA's Standards' in March 2006 (National Research Council 2006). While the responsibility of the NRC was to evaluate the sufficiency of EPA drinking water guidelines rather than address inquiries with respect to health risks or benefits of fluoridation, they did however conclude from the review of available studies that the literature does not clearly or plainly show that fluoride either is or is not cancer-causing in humans

Bone Health

Once Fluoride ions are integrated into bone, its mineral structure becomes altered. Because bone strength is thought to derive mainly from the interface between collagen and the mineral, alteration in mineralization affects bone strength (Pratushaet al. 2011). Long term exposure of bone to high levels of fluoride can result in skeletal fluorosis. Reports have been cited of skeletal fluorosis with severe crippling in China, India and Africa where fluoride levels are extremely high, a result of drinking water and indoor burning of fluoride rich coal. Reports are less common in Ireland and are limited to those working within the aluminium industry, fluorospar processing and superphosphate manufacturing (Hodge and Smith 1977). The study design for most of the available studies is not suitable for estimating the dose- response relationship and development of a No-observed-adverse-effect level (N/LOAEL) for skeletal fluorosis because of other factors such as nutritional status and climate influence water intake (World Health Organization 2002). In the body, almost all fluoride is associated with hard tissue, however, while some areas reach natural fluoride levels of 20mg/L, skeletal fluorosis is quite rare with only 5 cases confirmed over a period of 35 years.

It is suggested that the fluoride ion taken up by bone decreases throughout the growth phase of the skeleton in children over 15 years by as much as 50%. With a large number of epidemiological studies completed investigating the effects of fluoride on bone fractures, there appears to be no

obvious association between the risk of bone fracture and fluoridation (McDonagh et al. 2000). It has been suggested by AU-NHMRC (2007) that water fluoridated to levels of 0.6 to 1.1 mg/L may actually lower overall risk of bone fracture in agreement with IPCS (World Health Organization 2002). It has been hypothesized by NRC (2006) that a water concentration ≥4 mg fluoride/L can in fact weaken bone and increase the risk of bone fractures. There are few reports of skeletal fluorosis in the European Union (EU) with the SCHER report advising that due to lack of data, evaluation of the risk of bone fracture at current levels in fluoridated areas cannot be undertaken.

Jones et al (1999) conducted a systematic review incorporating 21 observational studies to determine the association between water fluoridation and fracture risk within populations. In general they compared fluoridated with non-fluoridated areas, however, some fluoridation levels were as high as 4 or 5 ppm, higher than optimal levels of fluoridation. Included in the review were English articles published between 1966 and November 1997. While there were no other inclusion and exclusion criteria stated, the review was thought to be of fair to good methodological quality. Upon consideration of the relevant studies, Jones et al. (1999) determined that there was no effect of fluoride upon fracture risk, advising that water fluoridated at optimal levels to prevent dental caries appears to have little or no effect on fracture risk.

Demos et al. (2001) also undertook a review of the literature published in English between 1991, following the NHMRC report up to December 1998. Including animal (n=6) and human studies (n=27). Investigating fracture, bone mass density (BMD) and bone strength, Demos et al. (2001) concluded that water fluoridated at optimal levels of 1ppm does not increase the incidence of bone fractures or decrease bone mass density. In addition, there appears to be no association or a slight beneficial effect between water fluoridation and bone strength. Included in the 27 human studies were: 6 ecological, 4 cross- sectional, 1 ecological & cross-sectional, 3 cohort, 12 clinical trials, 1 case- control. While slight benefits are reported by some to the trabecular bone in the spinal column (Pak et al 1994) it is thought to be controversial due to inconsistent results. Such benefits do not appear consistent across bone structures in the body which are mostly comprised of cortical bone. However in area where fluoridation levels were high, an increase in cortical bone fracture was reported (Riggs et al, 1994). Necessary in establishing a link between fluoride and bone fracture includes amongst others, differences in stages of osteoporosis, the fluoride dosage and the study design.

It has been found that fluoride absorbs more rapidly in growing bone than after peak bone mass has been achieved. This may account for no differences found in BMD of white women 65 and over with the same length of exposure to optimally fluoridated drinking water. Singlephoton absorptiometry

was used to take measurements at the distal and proximal radius and the calcaneus. The Lumbar spine and the proximal femur were measured using dual X-ray absorptiometry. Residential histories were assessed to ascertain duration of fluoride exposure. Findings concluded no differences in BMD across fluoride exposure strata, this may be due to exposure to fluoridated water after the age of 34 at which age peak skeletal mass would have occurred (Cauley 1995).

The studies, for the most part, have largely demonstrated that fluoride ingestion at high levels has an impact on skeletal tissues (skeletal fluorosis) and also that these impacts are more serious as this exposure to fluoride increases. While extremely mild skeletal fluorosis, characterised by slight increases in bone mass, crippling skeletal fluorosis, produces more extreme symptoms such as bone deformations, calcification of ligaments, lack of mobility and pain

Questions associated with fluoridation of water that have been the subject of exploratory examination, often concern the danger of bone fractures in older females. In the 1980's and 1990's, various community level studies analyzed rates of fracture, age and gender specifics in fluoridated and non-fluoridated groups. A few of these studies showed that increases in bone fracture occurred when introduction to fluoridated water occurred. A few studies demonstrated that water fluoridation decreased the danger of fracture and a few studies discovered no impact, then again, a shortcoming of these studies was that they were focused around communities as opposed to individuals. To enhance our understanding of this subject, a 2000 study was undertaken to analyze the relationship between utilization of fluoridated water and fractures in individual women. The population under study included older white women and suggested that water fluoridation may decrease the danger of fractures of the hip and vertebrae within this group (Phipps et al. 2000).

The frequency of hip fracture is emphatically connected with age and sex, accordingly any study exploring the rate of hip fractures ought to control for these variables. Other confounding factors that may affect the relationship between water fluoride levels and hip fracture frequency include; body mass index (BMI), ethnicity, calcium intake, certain medications, non-water fluoride intake and the menopausal status of women.

Apart from fluorosis, bone health and development (excluding bone cancer) were the most often cited studies on health risks of water fluoridation, according to The York Report (McDonagh et al. 2000). Again, low levels of validity were reported all but one being level C (lowest quality of evidence, high risk of bias). Retrospective and prospective cohort designs were included, with some including the appropriate analyses to control for potential confounding factors. Based on its review

of 18 studies The York Review concluded that there is no clear association of hip fracture with water fluoridation. As fluoridation of drinking water (1 mg/L) has been established as an efficient way of decreasing dental caries more studies on the potential risk or benefits with regard to fractures are of great importance.

In 2007, reviews examining the potential association between water fluoridation and fracture were identified by the NHMC (AU-NHMRC 2007). Identified studies were published post 2000 following the McDonagh review. One such review examined the association of fluoride levels and bone fracture at population level comparing areas that were fluoridated (in some parts up to 4 or 5 ppm) with areas of no fluoridation. English language papers covering 1966 – November 1997 were included and results pooled. While there was substantial diversity between the studies, fluoridated water was considered to be of relative risk, indicating that fluoridated water at levels considered optimal for preventing dental caries and even higher, has neither a positive or harmful effect on bone fracture risk. The review was considered to be of good quality.

Comparisons between areas of varying fluoride exposure on BMD and bone fracture were also considered. Exposure levels were often considerably higher than that found in EU countries and were characteristically extracted from developing countries where water was consumed from ground water wells on a population level. Alarcon-Herrera et al. (2001), a cross-sectional study, looked at children in the Guardiana valley in Mexico, an area of high natural levels of fluoride (1.5 - 5.5 ppm) against a control exposure of 1ppm. 1437 individuals (N=1437) participated with 902 adults (n=902) and 333 children (n= 333). Participants were long term residents. They found a strong linear correlation between the severity of dental fluorosis and the incidence of bone fractures in children and adults, however, participants self-reported fractures that were not the result of trauma with no medical intervention. There is little or no reporting of confounding factors or demographics. Sowers et al. (2005) collected data from 1300 female residents of 3 small communities in Iowa where the water fluoride concentrations were 1ppm or 4ppm. The study was predominantly cross-sectional although fractures were recorded longitudinally over a 4 year period. Fractures were self-reported every 6 months with 87% medically verified. Women were selected via a census with no other criteria specified. Results suggest that over the 4 year period, bone fracture or BMD did not appear related to fluoride concentrations amongst female residents in either community

A third study conducted by Li et al. (2001) compared several exposure levels, some low and some high against an optimal exposure. A cross-sectional study with 8266 participants (n=8266) from six Chinese populations were recruited randomly from communities. Participants were 50 years or older who resided in their community for at least 25 continuous years. Participants were grouped together

according to fluoride exposure which was confirmed by chemical analysis. Group 1: 0.25–0.34 ppm, Group 2: 0.58–0.73 ppm, Group 3: 1.00–1.06 ppm (considered the optimal group), Group 4: 1.45–2.19 ppm, Group 5: 2.62–3.56 ppm and Group 6: 4.32–7.97 ppm. Fractures were self-reported and verified by medical records or x-ray. Those in the extremely low (group 1) and extremely high group (group 6) had significantly higher overall fracture rates, while those in the control group had the lowest overall fracture rate. The control group was not considered however to be significantly different from group 2 or group 4. Hip fracture was also deemed significantly higher in group 6 than in the control group. Amounts of fractures per person was collected but not used in the analyses, only one fracture per person was included (occurrence or no occurrence). Notably, subjects were randomly recruited from their communities with no detail of how this was undertaken or whether the selection process was equal across groups. As with other self-reported studies, self-reporting can result in under-reporting. The conclusion of previous systematic reviews that intentional water fluoridation that occurs at levels recommended and implemented by Australia have no negative effect on fracture risk were supported by Li et al (2001). In fact, the results of Li et al (2001) provide some suggestion that fluoridation to optimal levels of 1 ppm may be preferable to no fluoridation or extreme high concentrations. However, as this study represents a low level of evidence, in the face of many potentially confounding factors, this relationship should be interpreted with caution.

It is suggested through epidemiological data that over longer periods of time, a smaller intake of fluoride at a younger age may be beneficial for bone health. Osteoporosis is considered a process of aging, typically from age forty onwards, that is almost irreversible. While fluoride intake may not completely avert the onset of osteoporosis, it may be helpful to identify preventative measures that can be put in place and therefore reduce treatments needed (Richmond 1985)

Neurotoxicity

Limited data is available regarding fluoride exposure and neurotoxicity. Some studies conducted on animals involved rats being exposed to high doses of fluoride, 7.5 mg per kilogram of body weight for six weeks. The results included female rats exhibiting signs of hyperactivity and deficiencies in cognition (Public Health Service 2003). Other studies exposing female rats to doses as high as 11.5 mg per kilogram of body weight for eight months showed no significant differences in ability to perform tasks or adjust their appetitive-based responses (Whitford et al. 2009). Alternative responses have been suggested regarding the effects of fluoride exposure including its effects on the thyroid, however, long term studies conducted on animals appear inconsistent with no conclusive evidence on fluoride effects on thyroid function.   While fluoride does not appear to impede the

iodine uptake by the thyroid, long term exposure to high fluoride levels appear to be related to increased fluoride levels in the thyroid glands of some animals (European Food Safety Authority 2005).

Data on neurotoxicity of fluoride exposure for humans is also limited. Studies such as those conducted by Tang et al. (2008) involving schoolchildren exposed to high levels of fluoride in China and India are often cited as evidence of neurotoxicity resulting in lowered IQ, impaired thyroid function and deterioration of the central nervous system. Several issues however are raised regarding the controls of water quality in these areas which may be contaminated with chemicals such as arsenic. There is little or no control for confounding factors such as socio-economic status, income, education or nutritional status. Outcomes of IQ have been cited as five times more likely in areas of high fluorosis and high fluoride exposure, however, areas using fluoridated drinking water have been compared to areas burning coal for domestic fuel, indicating poor methodological design (European Food Safety Authority 2005).

Other studies conducted on IQ and fluoride exposure were also conducted in China by Wang et al. (2007). In the Shanxi province, 720 children between the ages of eight and twelve exposed to fluoride levels between 0.5 mg/L (control group n=196) and 8.3 mg/L were investigated. Children in the high fluoride area were sub divided into low (n=253), medium (n=91) and high (n=180) arsenic exposure groups. Children in high fluoridated areas were reported as having significantly reduced IQ in comparison to the control group. Socio-economic or genetic factors were not accounted for but were expected to have minimal influence on outcomes. Mexico has also been the focus for intelligence and fluoride/arsenic exposure studies in children (Rocha-Amador et al. 2007). A cross-sectional design included 3 rural areas with varying fluoride and arsenic levels in drinking water. Fluoride levels ranged from: 0.8 mg/L to 5.3 mg/L and 9.4 mg/L. The three communities were comparable in relation to their general demographic, ages of children and length of time lived in the area. While three hundred and eight children (n=308) were eligible for the study one hundred and fifty five children (n=155) were randomly selected to participate. IQ assessment was blinded to fluoride or arsenic levels and confounding factors were considered such as education, flooring material used in the household, crowding and drainage. Questionnaires regarding type of water used for cooking (tap or bottled water) and health conditions were distributed. After adjusting for confounding factors, including arsenic, an inverse association was noted between fluoride in drinking water and IQ. From available studies on fluoride and neurotoxicity, it is clear that they do not support impairment of IQ at permitted EU levels, neither does it suggest an effect on thyroid function. The Scientific Committee on Health and Environmental Risks (2011) acknowledges that

due to limited data in relation to fluoride in drinking water and its effects on IQ and thyroid function at current levels permitted in the EU it is not possible to establish any firm conclusions.

Fluoride, like all supplements and minerals has a level of intake that is harmful or toxic. Levels of fluoride intake considered dangerous for people are at the level of 2.5 to 5 g, if ingested at one time. This is the equivalence of 42 to 84 mg/Kg for a 60 Kg adult or 5 to 10 g intake of sodium fluoride. Exploratory studies investigating the effects of ingesting large doses of fluoride included two people who consumed 114mg fluoride in one dosage. Reported impacts on health included slight sickness and intestinal distress that was experienced for approximately five hours in one case and 24 hours in the other. Other symptoms included; increases in salivation for around 30 minutes and stopped in one and a half hours, a tingling sensation in the hands and feet went on for around one week in one study participant. At 1 mg F/L an adult (60 to 72 Kg) ingests around 0.028 to 0.033 mg/Kg from 2 L of water (Richmond 1985)

Reproductive and developmental effects

Animal studies

The effects of fluoride exposure on the reproductive system are mostly animal studies dealing with male mice or rats. According to Gupta et al. (2007), male rats who received doses of 2, 4 and 6 mg/L in drinking water for six months showed signs of adverse effects on fertility and reproductive systems. Over and eight week period, male Wistar rats receiving fluoride in drinking water at levels of 5 mg per kilogram of body weight for 8 weeks also showed signs of reduced fertility and reproductive ability in comparison to control groups. Reduced male fertility it was suggested was due to 'sub-chronic exposure to fluoride' causing 'oxidative stress damage and loss of mitochondrial trans-membrane potential' (Izquierdo- Vega et al. 2008). Contrary to such findings, Chioca et al. (2012) upon investigating the effects of fluoride exposure on sperm production and sperm morphology in rats found no observable differences among the groups of rats. With 10, 70 day old Wistar rats per group in the experimental group, each received 50 or 100 parts per million of sodium fluoride. 1.54 ppm were received by the control group. The treatment was completed in a 30 day cycle. Findings would indicate that exposure to fluoride at the doses used did not cause any impairment to male rat reproductive function, no differences were found between experimental or control group. Findings from Sprando et al. (1998) where male rats received between 25 and 250 ppm sodium fluoride during a 14 week treatment and Collins et al (2001) where male rats received up to 250 ppm, are in agreement with Chioca et al. (2012). No adverse effects were found on the

reproduction of male rats. It must be noted however, male rats in Chioca et al's 2012 study were exposed to levels of fluoride over a 30 day period, while the complete cycle of spermatogenesis occurs over a 58 day period. Therefore, in order to assess the full extent of fluoride effects a testicular histology should be investigated. Overall, fluoride doses used in these studies were high making observed effects irelevant for the European situation.

Human studies

No evidence to suggest fluoride effects on human reproductive hormones or fertility were discovered in the National Health Service review on water fluoridation (McDonagh et al. 200). With human studies limited and of poor quality, risk assessment would be considered to be of limited value. Conclusions drawn from studies available suggest that fluoride concentrations permitted in the EU do not have an adverse effect on human reproductive capabilities.

Dental caries/fluorosis

Know as The York Report, this was commissioned by the Department of Health in the United Kingdom from York University (McDonagh 2000). The purpose of this report was to complete an expert review of the safety and efficacy of fluoride in drinking water. An assessment was made on the positive and negative health effects of fluoridated water supplies. In total, 214 epidemiological studies were included in the report and published between the years 1966 and May 1999. The search for literature was conducted via 25 electronic databases, the world wide web with further information requested from authors if necessary. The report focused mainly on outcomes of decayed, missing, filled primary and permanent teeth and the proportion of children without dental caries in areas of fluoridated and non-fluoridated areas. Measurements in changes from baseline to final examination were examined with approximately 12.5% of children exposed to levels of 1ppm experiencing aesthetically related fluorosis. This evidence was cited as showing clear benefits for dental caries, however, it was noted that such benefits should be considered alongside the increase in the appearance of fluorosis. The York Report also made note that there did not appear to be any other undesirable effects. The studies included in The York Report were considered to be of low to moderate quality, i.e., they did not include evidence of a high quality with unlikely bias, however, the conclusion did advise that areas with water fluoridation showed an increase in children without dental caries and a reduction in children with dental caries. Study designs included in the report consisted of 45 controlled before-after studies, 102 cross sectional studies, 47 ecological studies, 13 cohort (prospective or retrospective)

As per the York Report (2000), dental fluorosis is the most commonly studied unfavourable consequence resulting from water fluoridation. While 88 of the included studies on dental fluorsis were included in the report they were considered of low quality (high likelihood of bias and lack of control for confounding factors), a significant dose-response relationship was observed between water fluoride concentration and the fluorosis prevalence. While The York Reports findings on caries reduction were supported by National Health and Medical Research Council (2007) and Parnell, Whelton and O'Mullane (2009), consideration must be given to the vigour applied to each study and the findings must therefore be viewed cautiously based on the quality of data obtained.

Lack of fluoride effect on disease and/mortality rates

At levels of 1 mg/L of fluoride in drinking water, no effects have been established, either positively or negatively on disease or death rates. Such claims are supported by USA city wide studies documenting the changes in cancer death rates and heart disease with no differences occurring. No differences in nephritis, coronary illness, cirrhosis or cancer from all causes were also cited. Levels of fluoridation in such areas varied from 2 to 10mg/L in drinking water, occurring naturally and reached approximately 7million residents. With no changes in health risks occurring between cities, it is suggested that fluoridation could therefore be ruled out as harmless to humans. Anti-fluoridationists often cite studies showing increases in the incidence of Down's Syndrome births, cardiovascular disease and cancer to support their opposition to fluoridation of water supplies, however, it must be noted that such studies overlook vital and critical variables. For instance, older populations in fluoridated areas compared to younger populations in non-fluoridated areas are more likely to die from heart disease, therefore skewing results in favour of non-fluoridation. Such amendments must be made, including those of sex, race and socio-economic factors to address such queries fairly (Richmond 1985). Whiting et al (2001) conducted a systematic review commissioned by the UK Department of Health to examine the effects of water fluoridation on the incidence of Down's syndrome. Six ecological studies were included, all published between 1957 and 1980, all were deemed to have low validity scores. None of the studies had prospective follow-up, incorporated blinding, had a baseline survey or stated how the level of water fluoride was calculated. Confounding factors such as maternal age and race were discussed in some papers.

Study designs utilized in researching other possible effects of fluoridation measure populations rather than individual exposure, as such, population exposure to other factors associated with the outcome under investigation may differ. Therefore, all confounding factors must be accounted and

controlled for during the analysis. For example, maternal age is a confounding factor for Down's syndrome. Populations with a higher average maternal age in areas where water fluoridation is also higher may lead to an apparent association to be found. While studies have been found to consider maternal age, only two studies were found to control for this possible confounding factor, Erikson (1976 and 1980). Both of these studies found a non-significant association of water fluoride level with Downs syndrome. Other studies conducted by Rapaport (1957) rather than controlling for maternal age, studied the age differences between two different areas. Maternal age was found to be higher in the areas of high fluoridation, however, rates of Down's syndrome were found to be lower in this area and higher in low fluoridated areas with lower maternal age. Also reported by Rapaport (1963), while considering maternal age, found the rate of Down's syndrome births to be higher in areas of high fluoridation where the mother's age was greater than or equal to forty years, however no measures of the significance of this association was presented. Comparisons of maternal age in two areas was also conducted by Needleman (1974) who found the mean maternal age in high fluoride areas to be 34 and low fluoride areas to be 33.2, suggesting this was sufficient to justify differences found in incident rates of Down's syndrome found in the study.

Small study numbers, study designs and low quality create difficulties in interpreting data effectively. While studies are considered low grade with high level of bias, all results should be interpreted with caution. Lack of control for confounding factors was also evident throughout many studies. Future studies of other effects of water fluoridation needs to ensure higher quality research with confounding factors taken into consideration. Overall, the studies examining other possible negative effects provide insufficient evidence on any particular outcome.

Various outcomes were also investigated by The York Report through a total of 33 studies. Outcomes included Down's Syndrome, senile dementia, IQ and mortality. A variety of methodologies were included such as: ecological, cross sectional, case control and retrospective cohort studies. Study quality was level C (lowest quality of evidence, high risk of bias). None of the studies had a prospective follow up or incorporated any form of blinding, however, increased incidence of Alzheimer's disease was reported by Forbes (1997) and also decreased incidence on impaired mental functioning. Decreases were also reported for congenital malformations in one of two sets of data by Erickson (1976). Increases in incidences of goitre and mental retardation were reported by Lin (1991) on examination of a combination of low-iodine/high fluoride. Fewer cases in areas of fluoridated water were reported for degenerative dementia (Still 1980) and cognitive impairment (Flaten 2001), however, the statistical significance of this effect was not provided.

Since the publication of the McDonagh (2000) and Whiting (2001) reviews, the National Health and Medical Research Council (2007) investigated three other published articles that related to other potentially negative effects of fluoride. In summary, the additional studies do not suggest an increased risk of other adverse events with the level of fluoridation used in optimally fluoridated areas such as Ireland. The study of Singh et al (2001) investigated the occurance of nephrolithiasis (urinary stone disease). Comparisons were drawn between areas where fluoride levels in drinking water ranged from 3.5 to 4.9 ppm to areas of low fluoride concentration of 0.5 ppm. Kidney stone prevalence was considered to be 4.6 times higher in areas with higher fluoridation levels. This study however, involved fluoride concentrations that would not be observed in optimally fluoridated areas, the level of evidence and quality of the study is also considered to be poor.

Supporting the conclusions of the Whiting systematic review, Lowry (2003) indicates there are no differences in the occurrences of stillbirths and congenital abnormalities in fluoridated and non-fluoridated areas. It is suggested by Kaipio et al (2004) however, that there may be a small protective effect in relation to coronary heart disease mortality. It must be noted however, that this ecological study must be interpreted with caution due to its many potential biases. It may be possible that the beneficial effect on coronary heart disease mortality may occur indirect, due to the beneficial effects of fluoride on dental infections.

Allergic reactions

Often cited to confirm claims of allergic reactions to fluoride in water is Feltman's (1961) study on prenatal and postnatal ingestion of fluorides. Documented as confirming causation of eczema in children and adults through medically documented, double blinded clinical trials it is discussed as proving the dangers of water fluoridation (Connett 2010). However, further investigation into such claims has been made by the United States Public Health Service. They requested the American Academy of Allergy to perform an evaluation of allergic reactions to fluoridated water. Reports were firstly reviewed for claims of allergic reactions and secondly, clinical and scientific information were evaluated to determine if there was enough information to classify such responses as allergies. While several symptoms such as nausea, epigastric distress and skin rashes were cited within the articles reviewed, including Feltman (1961), the American Academy of Allergy reported there was no evidence the immunological mediated reactions had been presented with insufficient clinical and laboratory evidence to support any claims of causation from fluoridated water (Public Health Service 1971).

What is Fluoride?

The element fluorine produces the fluoride ion. Within the earth's crust, fluorine is the 17th most abundant element. Fluorine is a gas that exists as a compound existing only in combination with other elements therefore fluorine does not occur freely in nature. Fluorine is considered to be the lightest member of the halogen group and is one of the most reactive of all chemical elements. It is not, therefore, found as fluorine in the environment (World Health Organization 2006). As water passes over rock formations it comes into contact with fluoride compounds. This interaction causes the breakdown of the fluoride compounds releasing the fluoride ions present. Therefore, small amounts of fluoride ions exist within all water sources, including oceans. Fluoride is also present to some degree in foods and beverages however the concentrations within these vary greatly (Shattuck 2000). Fluoride, however acquired, whether added artificially under controlled conditions or occurring naturally by water seeping over rocks and soil, is identical. Artificial fluoridation is simply a supplementation of naturally occurring fluoride that is present in all water sources. The three main fluoride compounds used to fluoridate drinking water include sodium fluoride (NaF), hydrofluosilicic acid or hexafluorosilicic acid (H_2SiF_6) and sodium silicofluoride (Na_2SiF_6). All of these compounds fully mix (dissociate) in water. Hydrolysis in water yields six fluoride ions and silicon dioxide.

Once consumed in appropriate quantities, any nutrient, including fluoride is considered safe and effective. Over 50 years of scientific research and evaluation has failed to confirm the lack of benefits and safety of fluoridation of water supplies. While fluoridation of water supplies is considered beneficial to communities by the majority of health professionals, a few supporters of non-fluoridation of water continue to speak out against the limitations on freedom of choice. Such concerns may arise from the extraction of scientific research out of context or misinterpretation of the findings.

The effects of fluoride are dependent on the intake from several sources including, food, air, burning of coal fires, from gases produced by volcanic activity and water with water being the main and largest resource. Fluoride, therefore is available in various concentrated forms within nature. However, air is typically responsible for only a small fraction of total fluoride exposure (NRC 1993). Concentration of fluoride in water sources, however, is considered a controlled variable measured in mg/L. This is not the same as controlling the dose which is measured in mg/day (Connett 2010) Consumption of 1L of water at optimal fluoridated levels of 1ppm equates to the ingestion of approximately 1.68 to 1.98mg of fluoride (Richmond 1985)

Young children, on average, consume less than half a litre of water per day which is considered to equate to 0.05mg of fluoride at optimal levels of 1ppm. Their dietary intake of fluoride in areas with optimally fluoridated water is considered to be 0.05mg per day also. In order to establish possible harm from fluoride intake, we must account for a person's body weight. The dose divided by a person's bodyweight is called the dosage and this is measured as mg/kg/day. Safe dosage therefore will vary between infants, young children and adults. As a practical example, a sufficient intake of fluoride for a child within the age range of 9 – 13 years weighing 40kg (88lbs) is 2mg. Calculated at 0.05mg/kg/day this is well below the recommended upper tolerable level of 10mg/kg/day equal to 400mg, as considered by The Institutes of Medicine (1997). Australia and New Zealand's nutrient reference values for fluoride are very similar (NHMRC 2006). Dietary fluoride intakes for adults are considered to be approximately 1.4 to 3.4mg/day. Dietary Reference Values (DRV) were replaced with Dietary reference intakes (DRI), by the Food and Nutrition Board of the Institute of Medicine in 1997.

Once ingested, fluoride enters the blood stream via the stomach and small intestine causing a blood spike. Peak concentration is reached within 60 minutes and declines rapidly within 3 to 6 hrs. Approximately 50% of fluoride is absorbed by young or middle-aged adults, taken up by hard tissues in the body including teeth and bone. This occurs within 24 hours although age and skeletal maturity will affect retention with younger bone retaining great levels of fluoride than older bones. The kidneys will excrete any waste. It must be advised however, that those with impaired kidney function may not effectively deal with fluoride excretion. Nonetheless, no cases of dental or skeletal fluorosis has been cited for those experiencing impaired kidney function. This may be an area that requires further investigation.

Population subgroup	Upper Limit (mg/day)
Infants 0-6 months	0.7
Infants 7-12 months	0.9
1-3 years	1.3
4-8 years	2.2
9-13 years	10.0
14-18 years	10.0

Adults 19 years including   10.0

pregnant women

The Institutes of Medicine in the United States in 1997 produced tolerable upper limit guidelines

Australia and New Zealand nutrient reference values for fluoride are highly similar (NHMRC 2006).

Fluoride concentrations

The fluoride level for natural and artificial fluoridated water , available for human consumption was

determined by the Council Directive 98/83/EC of 3rd November 1998 (Council Directive 98/83/EC). A

level of less than 1.5mg/L was determined as a safe level of fluoridation in drinking water. This level

has been reduced even further by the United States Department of Health and Human Services who

recommended a fluoride level in water of 0.7 mg/L . This they advised would create a balance

between protecting dental health and limiting any unwanted adverse health effects (Center for

Disease Control and Prevention 2014).

In 2006 a guidance value was set by the World Health Organization for fluoridated water. Based on

2 litres of water consumption a day, naturally occurring fluoride in drinking water should not exceed

1.5mg/L while artificially fluoridated water should not exceed levels of 1mg/L (WHO 2006).

Monitoring of fluoride intake is regularly conducted by relevant authorities and bodies to ensure

human safety and improvements in public health. Upper tolerable levels (UL) were set during the

most recent assessment by the European Food Safety Authority (EFSA 2005a), calcium fluoride and

sodium monofluorophosphate as a source of fluoride (EFSA 2008a, EFSA 2008b) also, fluoride in

dental products were assessed by the Scientific Committee on Consumer Products (SCCP 2009). The

United States Environmental Protection Agency's (EPA) water standards for fluoride were also

reviewed by the United States National Academies of Science in 2006 (NRC 2006). In 2011, to attain

an update on recommended levels, The Scientific Committee on Health and Environmental Risks

(SCHER), SCCP, EFSA's panel on dietetic products, nutrition and allergies (EFSA NDA) and EFSA's

panel on contaminants in the food chain (EFSA CONTAM) collaborated to ensure safety for public

consumption. A review of the relevant scientific information was gathered, via a public call for

submissions. SCHER included papers submitted by various stakeholders, reviews and articles

published in peer-reviewed journals and reports from several regulatory agencies and other

organizations (SHER 2011). A period of three months was agreed for public consultation on the

published preliminary opinion which was then discussed at a public hearing along with additional

material received. Using a weight-of-evidence approach, all studies including epidemiological, cell culture studies and experimental human and animal studies looking at the health risks of fluoridation of drinking water were evaluated. All evidence was then weighed together across all areas to produce a combined assessment. The Irish Expert on Fluorides and Health (2013) states that as of July 1st 2007, the level of fluoride in Irish drinking water is set between 0.6 and 0.8ppm (Irish Expert Body on Fluorides and Health 2013).

Concerns become elevated when several sources of fluoride are used in conjunction with each other, for example fluoridated water and toothpaste. Upon investigation of fluoride intake from all sources including: fluoridated water, food and toothpaste – it is suggested by SCHER that intake is still below the upper tolerable intake level (UL) for adults and children over the age of twelve in the majority of areas within the EU. Exceptions include those living in areas of naturally occurring fluoridated water with levels above 3mg/L who also have a high intake of water-based beverages. This UL is based on a maximum water intake of 1L a day for children aged between 6 – 12 years with no more than 1.5 mg/L being consumed, while also using fluoridated toothpaste. In children between the ages of 1 – 6 years, UL is considered to be exceeded if more than 0.5L of water is consumed per day plus the use of fluoridated toothpaste. There is no UL specified for children under the age of 1 year. It is expected that fluoride exposure will exceed 0.8mg/kg/day when fluoride levels in drinking water exceed 0.8mg/L. The committee determined that the UL could be exceeded for children between the ages of six to twelve if they consumed more than 1 litre of water a day and brushed their teeth with adult strength toothpaste (0.15%) whilst unsupervised. For children between the ages of one to six UL may be exceeded if more than 0.5 litres of water were consumed alongside brushing with adult strength toothpaste (0.15%) whilst unsupervised and finally for children below the age of six months who were receiving infant formula, UL would be exceeded if infant formula was reconstituted with water containing fluoride levels higher than 0.8 mg/L. The safe level for children under six months is considered by the UK's Department of Health to be 0.22 mg/kg/day.

Monitoring and assessing fluoride effects efficiently is somewhat problematic due to limited availability, quality and accuracy of exposure information. It is suggested by SCHER that additional research is necessary at realistic EU exposure levels in order to obtain data on potential adverse health effects. Therefore recommendations include developing and validating new biomarkers for long-term exposure to fluoride. While developing standardized methods of exposure assessment, all routes of exposure to fluoride must be integrated. More must be done to collect the bioavailability of fluoride and fluoride in food products and finally to conduct epidemiological studies, taking

advantage of the existing mother-child cohorts to investigate the role of fluoride intake on incidence of dental fluorosis and dental health.

Conclusion

REFERENCES:

Alarcon-Herrera, M. T., MartIn-Dominguez, I. R., Trejo-vasquez, R. and Rodriguez-Dozal, S. 2001. Well-water fluoride - dental fluorosis and bone fractures in the Guadianna valley of Mexico. *Fluoride*, 34(2), pp.139-149.

American Dental Association 2005. *Fluoridation Facts* [Online]. Available from: http://www.ada.org/~/media/ADA/Member%20Center/FIles/fluoridation_facts.ashx [Accessed 5 July].

AU-NHMRC 2007. A *systematic review of the efficacy and safety of fluoridation. PART A: review of methodology and results.* Canberra: Robert Garran Offices.

Bassin, E. B., Wypij, P., Davis, R. B. and Mittleman, M. A. 2006. Age-specific fluoride exposure in drinking water and osteosarcoma (United States). *Cancer Causes Control*, 17, pp.421–428.

Blakey, K., Feltbower, R. G., Parslow, R. C., James, P. W., Gómez P. B., Stiller, C., Vincent, T. J., Norman, P., McKinney, P. A., Murphy, M. F., Craft, A. W. and McNally, R. J. 2014. Is fluoride a risk factor for bone cancer? Small area analysis of osteosarcoma and Ewing sarcoma diagnosed among 0-49-year-olds in Great Britain, 1980-2005. *The International Journal of Epidemiology*, 43(1), pp. 224 – 234.

Browne, D, Whelton, H. and O'Mullane, D. 2005. Fluoride metabolism and fluorosis. *Journal of Dentistry*, 33, pp.177-186.

Bucher, J. R., Heitmancik, M. R., Toft, J. D., Persing, R. L., Eustis, S. L. and Haseman, J. K. 1991. Results and conclusions of the National Toxicology Program's rodent carcinogenicity studies with sodium fluoride. *International Journal of Cancer,* 9(48), pp.733-737.

Cauley, J. A., Murphy, P. A., Riley, T. J. and Buhari, A. M. 1995. Effects of fluoridated drinking water on bone mass and fractures: the study of osteoporotic fractures. *Journal of Bone Mineral Research*, 10(7), pp.1076-1086.

Center for Disease Control and Prevention 2014). *Community Water Flouoridation* [Online]. Available from: http://www.cdc.gov/fluoridation/faqs/ [Accessed 2 August 2014].

Chioca, L. R., Müller, J. C., Boareto, A. C., Andreatini, R. and Dalsenter, P. R**.** 2012. Sodium fluoride does not alter sperm production or sperm morphology in rats. *Brazilian Archives of Biology and Technology*, 55(2), pp.257-262.

Collins, T. F., Sprando, R. L., Black, T. N., Shackelford, M. E., Bryant, M. A., Olejnik, N., Ames, M. J., Rorie, J. I. and Ruggles,D. I. 2001. Multigenerational evaluation of sodium fluoride in rats. *Food and Chemical Toxicology,* 39(6), pp.601–613.

Congressional Research Service 2013. *Fluoride in drinking water: a review of fluoridation and regulation issues* [Online]. Available from: http://fas.org/sgp/crs/misc/RL33280.pdf [Accessed 10 July 2014].

Connett, P., Beck, J. and Micklem, H. S. 2010. *The case against fluoride: how hazardous waste ended up in our drinking water and the bad science and powerful politics that keep it there*. USA: Chelsea Green Publishing Company.

Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. Official Journal of the European Communities. Available from: URL: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:330:0032:0054:EN:PDF [Accessed 2 August 2014].

Dean, H. T. 1933. Distribution of mottled enamel in the United States. *Public Health Reports (1896-1970),* 48(25), pp.703-734.

Demos, L. L., Kazda, H., Cicuttini, F. M., Sinclair, M. I. and Fairley, C. K. 2001. Water fluoridation, osteoporosis, fractures--recent developments, *Australian Dental Journal*, 46(2), pp.80-87.

Doll, R. and Kinlen, L. 1977. Fluoridation of water and cancer mortality in the U.S.A. *Lancet,* 1(8025), pp.1300-1302.

European Food Safety Authority 2005a. Scientific opinion of the panel on dietetic products, nutrition, and allergies on the tolerable upper intake level of fluoride. *The EFSA Journal*, 192, pp.1-65.

European Food Safety Authority 2008a. *Calcium fluoride as a source of fluoride added for nutritional purposes to food supplements scientific opinion of the panel on food additives and nutrient sources added to food*. The EFSA Journal, 882, pp.1-15.

European Food Safety Authority 2008b. *Scientific opinion of the panel on food additives and nutrient sources added to food on sodium monofluorophosphate as a source of fluoride added for nutritional purposes to food supplements*. The EFSA Journal, 88, pp.1-18.

Eyre, R., Feltblower, R. G., Mubwandarikwa, E., Eden, T. O. B. and McNally, R. J. Q. 2009. Epidemiology of bone tumours in children and young adults. *Pediatric blood & cancer,* 53(6), pp. 941-952.

Flaten, T. P. 2001. Aluminium as a risk factor in Alzheimer's disease, with emphasis on drinking water. *Brain Research Bulletin,* 55(2), pp.187–196.

Freni S. C. and Gaylor, D. W. 1992. International trends in the incidence of bone cancer are not related to drinking water fluoridation. *Cancer,* 70(3), 611-618.

Gelberg, K. H., Fitzgerald, E. F., Hwang, S. and Dubrow, R. 1995. Fluoride exposure and childhood osteosarcoma: a case-control study. *American Journal of Public Health*, 85(12), pp.1678-1683.

Gupta, R. S., Khan, T. I., Agrawal, D. and Kachhawa, J. B. S. 2007. The toxic effects of sodium fluoride on the reproductive system of male rats, Toxicology and Industrial Health, 23(9), PP.507–513.

Hodge, H.C. and Smith, F.A. 1977. Occupational fluoride exposure. *Journal of Occupational Medicine,* 19(1), pp.12-39.

Hoover, R. N., Devesa, S. S., Cantor, K. P., Lubin, J. H. and Fraumeni J. F. 1990. Time trends for bone and joint cancers and osteosarcomas in the Surveillance, Epidemiology and End Results (SEER) Program [Online]. Available from: http://www.fluoridealert.org/wp-content/uploads/nci-1990.pdf [Accessed 20 July 2014].

Institute of Medicine 1997. *Dietary reference intakes (DRIs): Tolerable upper intake levels, vitamins [*Online]. Available from: http://iom.edu/Activities/Nutrition/SummaryDRIs/~/media/Files/Activity%20Files/Nutrition/DRIs/ULs%20for%20Vitamins%20and%20Elements.pdf [Accessed 5 August 2014].

Institute of Medicine 1997. *Dietary reference intakes (DRIs): Estimated average requirements [Online]. Available from:* http://www.nal.usda.gov/fnic/DRI/DRI_Tables/recommended_intakes_individuals.pdf *[Accessed 5 August 2014].*

Izquierdo-Vega, J. A., Sánchez-Gutiérrez, M. and Del Razo, L. M. 2008. Decreased in vitro fertility in male rats exposed to fluoride-induced oxidative stress damage and mitochondrial trans-membrane potential loss. *Toxicology and applied pharmacology*, 230, pp.352–357.

Jones, G., Riley, M., Couper, D. and Dwyer, T. 1999. Water fluoridation, bone mass and fracture: a quantitative overview of the literature. *Australian and New Zealand Journal of Public Health*, 23(1), pp.34-40.

Kaipio, J., Nayha, S. and Valtonen, V. 2004. Fluoride in the drinking water and the geographical variation of coronary heart disease in Finland. *European Journal of Cardiovascular Prevention and Rehabilitation,* 11(1), pp.56-62.

Kumar, J. V. 2008. Is water fluoridation still necessary? *Advances in Dental Research,* 20(8), pp.8-12.
Li,Y., Liang, C., Slemenda, C. W., Ji, R., Sun, S., Cao, J., Emsley, C.L., Wu, Y., Ying, P., Zhang, Y., Gao, S., Zhang, W., Katz, B. P., Niu, S., Johnston, C. C. Jr. 2001. Effect of long-term exposure to fluoride in drinking water on risks of bone fractures. *Journal of Bone and Mineral Research*, 16(5), pp.932-939.

Lin Fa-Fu, Aihaiti, Zhao Hong-Xin, Un Jin, Jiang Ji-Yong, Maimaiti and Aiken. *The relationship of a low-iodine and high fluoride environment to subclinical cretinism in Xinjiang* [Online]. Available from: http://www.poisonfluoride.com/pfpc/lin-1991.pdf [Accessed 25 July 2014].

Lowry, R., Steen, N. and Rankin, J. 2003, Water fluoridation, stillbirths, and congenital abnormalities. *Journal of Epidemiology and Community Health,* 57(7), pp.499-500.

Mahoney, M. C., Nasca, P. C., Burnett, W. S., Meius, J. M. 1991. Bone cancer incidence rates in New York State: time trends and fluoridated drinking water. *American Journal of Public Health* 81(4), pp. 475-479.

Martin, B. 1988. Analyzing the fluoridation controversy: resources and structures. *Social Studies of Science*, 19, pp.331-363.

McDonagh, M. S., Whiting, P. F., Wilson, P. A., Sutton, A. J., Chestnutt, I., Cooper, I., Misso, K., Bradley, M., Treasure, E. and Kleijnen, J. Systematic Review Of Water Fluoridation. *British Medical Journal*, 321(7265), pp. 855-859.

Moss, M. E., Kanarek, M. S., Anderson, H. A., Hanrahan, L. P. and Remington, P. L. 1995. Osteosarcoma, seasonality and environmental factors in Wisconsin, 1979-1989. *Archives of Environmental Health,* 50(3), pp.235 -241.

National Research Council 1993. Health effects of ingested fluoride [Online]. Available from: http://www.nap.edu/openbook.php?isbn=030904975X [Accessed 18 July 2014].
National Research Council 2006. Fluoride in drinking water: a scientific review of EPA's standards [Online]. Available from: URL: http://www.nap.edu/catalog/11571.html [Accessed15 July 2014].

Pak, C. Y. C., Sakhaee, K., Piziak, V., Peterson, R. D., Breslau, N. A., Boyd, P., Poindexter, J. R., Herzog, J., Heard-Sakhaee, A., Haynes, S., Adams-Huet, B. and Reisch, J. S. 1994. Slow-release sodium fluoride in the management of postmenopausal osteoporosis: a randomimized, controlled trial. *Annals of Internal Medicine,* 120(8), pp.625-632.

Parnell, C., Whelton, H. and O'Mullane, D. 2009. Water fluoridation. *European archives of Paediatric Dentisty*, 10(3), pp.141-148.

Phipps, K. R., Orwoll, E. S., Mason, J. D. and Cauley, J. A. 2000. Community water fluoridation, bone mineral density and fractures: prospective study of effects in older women. *British Medical Journal*, 321(7265), pp. 860-864.

Pizzo, G., Piscopo, M. R., Pizzo, I and Giuliana, G. 2007. Community water fluoridation and caries prevention: a critical review. *Clinical Oral Investigation*, 11, pp.189 - 193.

Public Health Service 1971. *No evidence of allergy to fluorides in optimally fluoridated water – American Academy of allergy* [Online]. Available from: http://www.dentalwatch.org/usphs/ppb-24.pdf [Accessed 28 July 2014].

Public Health Service 2003. *Toxicological profile for fluorides, hydrogen fluoride and fluorine* [Online]. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp11.pdf [Accessed 20 July 2014].

Reilly, G. A. The task is a political one: the promotion of fluoridation. *IN:* Ward, J. W. and Warren, C. (eds.) S*ilent victories: the history and practice of public health in twentieth-century America.* New York**:** Oxford University Press, pp. 323 – 340.

Richmond, V. L. 1985. Thirty years of fluoridation: a review. *The American Journal of Clinical Nutrition,* 41, pp 129-138.

Rocha-Amador, D., Navarro, M. E., Carrizales, L., Morales, R. and Calderón, J. 2007. Decreased intelligence in children and exposure to fluoride and arsenic in drinking water. *Cadernos De Saude Publica,* 23(4), pp.579-587.

Scientific Committee on Consumer Products 2009. *Clarification on the opinions SCCNFP/0653/03 and SCCP/0882/05 on the safety of fluorine compounds in oral hygiene products for Children under the age of 6 Years* [Online]. Available from: http://ec.europa.eu/health/archive/ph_risk/committees/04_sccp/docs/sccp_o_169.pdf [Accessed 2 August 2014].

Scientific Committee on Health and Environmental Risks 2011. *Critical review of any new evidence on the hazard profile, health effects, and human exposure to fluoride and the fluoridating agents of drinking water*. Dublin: Stationery Office.

Shattuck, A. 2000. *The fluoride debate a response to the American Dental Association's booklet fluoridation facts* [Online]. Available from: http://www.fluoridedebate.com/Download/fluoridedebate.pdf [Accessed 2 August 2014].

Singh, P. P., Barjatiya, M. K., Dhing, S., Bhatnagar, R., Kothari, S., and Dhar, V. 2001, Evidence suggesting that high intake of fluoride provokes nephrolithiasis in tribal populations. *Urological Research*, 29(4), pp.238-244.

Smith, A. 1980. An examination of the relationship between fluoridation of water and cancer mortality in 20 large US cities. *New Zealand Medical Journal*; 91(661), pp.413-416.

Sowers, M. F., Whitford, G.M., Clark,M.K. and Jannausch, M.L. 2005. Elevated serum fluoride concentrations in women are not related to fractures and bone mineral density. *Journal of Nutrition,* 35(9), pp. 2247-2252.

Sprando, R.L., Collins, T.F.X., Black, T., Olejnik, N. And Rorie, J. Testing the potential of sodium fuoride to affect spermatogenesis: a morphometric study*, Food and Chemical Toxicology,* 36(12), pp.1117-1124.

Tang, Q., Du, J., Heng-hui Ma, H., Jiang, S. and Zhou, X. 2008. Fluoride and Children's Intelligence: A Meta-analysis. *Biological Trace Element Research,* 126, Pp. 115–120.

The Irish Expert Body on Fluorides and Health 2013. *FAQ on Fluoride and Water Fluoridation* [Online]. Available from: http://www.fluoridesandhealth.ie/faq/ [Accessed 2 August 2014].

US Public Health Service 1991. Review of fluoride: benefits and risks [Online]. Available from: http://www.dentalwatch.org/fl/phs_1991.pdf [Accessed 19 July 2014].

US Public Health Service 2003. *Toxicological profile for fluorides, hydrogen fluoride, and fluorine* [Online]. Available from: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=212&tid=38 [Accessed 15 July 2014].

Wang, S.X., Wang, Z.H., Cheng, X.T., Li, J., Sang, Z.P. and Zhang, X.D. 2007. Arsenic and fluoride exposure in drinking water: children's IQ and growth in Shanyin County, Shanxi province, China. *Environmental Health Perspectives,* 115(4), pp.643-647.

Whitford, G.M., Sampaio, F.C., Pinto, C.S., Maria, A.G., Cardoso, V.E., Buzalaf, M.A. 2008. Pharmacokinetics of ingested fluoride: lack of effect of chemical compound. *Archives of Oral Biology,* 53(11), pp.1037-41.

Whitford, G.M., Whitford, J.L., Hobbs. S.H. 2009. Appetitive-based learning in rats: lack of effect of chronic exposure to fluoride. *Neurotoxicology and Teratology,* 31(4), pp.210-215.

Whiting, P., McDonagh, M. and Kleijnen, J. 2001. Association of Down's syndrome and water fluoride level: a systematic review of the evidence. *BMC Public Health,* 1(6), p.6.

World Health Organization 2006. *Fluoride in drinking water*. UK: IWA Publishing.

World Health Organization 2006. *Guidelines for drinking-water quality.* Geneva: World Health Organization.

World Health Organization 2002. *Fluorides – Environmetal Health Criteria* [Online]. Available from: http://whqlibdoc.who.int/ehc/WHO_EHC_227.pdf [Accessed 20 July 2014].

Yeung, C.A., Hitchings, J.L., Macfarlane, T.V., Threlfall, A.G., Tickle, M., Glenny, A.M. 2005. Fluoridated milk for preventing dental caries. *American Dental Journal*, 50(4), pp. 286-287.

Yiamouyiannis, J. and Burk, D. 1977. Fluoridation *and cancer age dependence of cancer mortality related to artificial fluoridation* [Online]. Available from:

http://www.fluorideresearch.org/103/files/FJ1977_v10_n3_p095-148.pdf [Accessed 25 July 2014].