SYSTEMATIC REVIEW

Public perceptions and scientific evidence for perceived harms/risks of community water fluoridation: An examination of online comments pertaining to fluoridation cessation in Calgary in 2011

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ABSTRACT

OBJECTIVES: To examine the perceived harms/risks of fluoridation as expressed in online forums relating to cessation and aftermath in Calgary, specifically, 1) which harms/risks are mentioned, 2) for those harms/risks, what kinds of evidence are cited, 3) to what extent is scientific literature cited, and what is its quality, and 4) for a subset of harms/risks, what is known from the broader scientific literature?

METHODS: Relevant online comments were identified through free-text Internet searches, and those explicitly discussing the harms/risks of water fluoridation were extracted. Types of evidence mentioned were identified, and the scientific papers cited were reviewed. Finally, the broader scientific literature on two of the harms/risks was reviewed and synthesized.

SYNTHESIS: We identified 17 distinct groups of harms/risks, which spanned human body systems, the environment and non-human organisms. Most often, no evidence was cited. When evidence was cited, types included individuals viewed as authorities and personal experiences. Reference to scientific articles was rare, and those papers (n = 9) had significant methodological concerns. Our review of scientific literature on fluoride and 1) thyroid functioning and 2) phytoplankton revealed some negative effects of fluoride at concentrations exceeding maximum recommended levels (>1.5 ppm).

CONCLUSION: The findings have implications for communication with the public about fluoridation. First, to the extent that the public consults the scientific literature, it is essential that the methodological limitations of a study, as well as its relevance to community water fluoridation, be widely and promptly communicated. Second, scientific evidence is only one component of why some people support or do not support fluoridation, and communication strategies must accommodate that reality.

KEY WORDS: Fluoridation; drinking water; safety; risk; evidence-based practice; public health

La traduction du résumé se trouve à la fin de l'article.

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Community water fluoridation refers to the controlled addition of industrial-grade fluoride compounds to public water supplies with the goal of preventing dental decay.[1] In Canada, the optimal fluoride concentration to promote dental health is 0.7 mg/L, with a maximum acceptable concentration (MAC) of 1.5 mg/L.[2] The evidence base for a beneficial effect of *fluoride* on tooth decay is substantial. In addition to its antibacterial activity against cariogenic bacteria, fluoride exerts a positive effect on tooth remineralization through its absorption into the surface of enamel crystals as it flows over the teeth, protecting against dissolution by bacterial acids.[3] Research also supports the benefits of *fluoridated water* for preventing tooth decay, in Canada[4,5] and and elsewhere. However, a systematic review of research on water fluoridation and health concluded that overall the evidence base is of low to moderate quality.[6]

Opposition to fluoridation has existed as long as the intervention itself, and the main reasons have not changed: skepticism about its effectiveness, concern about its potential harms and resistance to its intrusive nature. Recently, opposition has materialized in decisions by several communities in Canada to discontinue the practice.[7,8] While the proportion of Canadians exposed to community water fluoridation increased from 6% (1960) to 45% (2007), there has been a decline since 2007 because several large municipalities have discontinued the practice, including Calgary (2011), Waterloo (2010), Windsor (2013), Quebec City (2008) and Moncton (2012).

In terms of the risks/harms associated with fluoridation, research has consistently shown an association between fluoride exposure and risk of dental fluorosis (staining of the tooth enamel).[9] There is less support for other harms. The MAC of 1.5 mg/L set out by Health Canada was identified on the basis that it is "unlikely to cause adverse health effects", including immunotoxicity, developmental toxicity and/or neurotoxicity.[2]

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A recent report by Public Health England (PHE) confirmed the absence of association between fluoridation status and a range of adverse health outcomes.[10]

Despite these (and other) reports, there remains concern about various harms/risks of fluoridation among some members of the public.[11] Understanding these concerns is important from the point of view of public health communication. For example, if communication is premised on disseminating information from scientific studies, it may be less effective for those who are more influenced by other factors. Sandman describes this phenomenon in his discussion of hazard and outrage in the public perception of risk. Whereas experts may understand risk in terms of magnitude and the probability of an unfavourable event ("hazard"), the public may see risk as a combination of hazard and *outrage* factors (e.g., fear, dread, misery).[12]

In Calgary, fluoridation was discontinued in May 2011, following a City Council vote. Comments on online forums (i.e., online discussion sites where individuals can hold conversations in the form of posted messages) provide an opportunity to investigate what the public perceives to be the harms/risks of fluoridation. Decisions about fluoridation are made at the municipal level in Canada, within provincial guidelines (if any). Although a systematic study of fluoridation decision-making in Calgary in 2011 has not been undertaken, anecdotal reports suggest that important factors included the need for an infrastructure upgrade (and associated cost), efforts by a veteran councillor to revisit fluoridation, and a City Council characterized by several new councillors and a new mayor.[13–15] Unlike previous instances of fluoridation decision-making in Calgary (i.e., in 1989 and 1998), when a public vote (plebiscite) was undertaken, the 2011 decision was made by City Council. The decision-making process happened quickly, with limited public engagement and essentially none prior to January 2011.[13,14]

The study objective was to identify the health risks, perceived by some members of the public, associated with water fluoridation as expressed in online forums relating to its cessation and aftermath in Calgary (January 2011–) and to systematically examine their scientific basis. Research questions were as follows: 1) which harms/risks are mentioned, 2) for those harms/risks, what kinds of evidence are cited, 3) to what extent is scientific literature cited, and what is its quality, and 4) for a subset of risks/harms, what is known from the broader scientific literature?

METHODS

Identification of online comments about perceived harms/risks of fluoridation

A professional health sciences librarian was consulted to establish an optimal (sensitive and specific) search strategy. Three known links relating to fluoridation in Calgary were used to validate the search strategy; that is, we ensured that the search captured links known to be relevant.[7] The search was conducted in May 2014 and considered materials from January 2011 (as noted above, little if any discussion occurred before then) to May 2014.

First, a series of free-text searches, using Google™, was conducted using 1) "fluorid Calgary" (~373,000 results), 2) "fluoride Calgary" (~182,000 results), 3) "fluoridation Calgary" (~24,600 results) and 4) "water fluoridation Calgary" (~12,300 results). Results were listed in order of relevance (i.e., default setting), with no additional filters. Beginning with the top result of each search, each webpage was opened to assess its content. Those webpages that allowed for public comments were included as a potential source. Webpages that did not allow for comments, or had zero comments, were excluded. In viewing multiple pages of results for each search, we observed that the relevance of comments to our study (fluoridation in Calgary) dropped after the 8th or 9th page. We therefore decided to examine all results within the first 10 pages for each search. Many items from the first search (i.e., using the search terms "fluorid Calgary") appeared again in subsequent searches. Duplicate items were omitted.

Next, for each webpage from the original searches, we pursued "related articles", "related links" and any additional webpages cited in the text. Related links that allowed for comments and had at least one comment were added as sources. Most "related links" had either already been identified in the original search, did not have the capacity for comments, had zero comments or were unrelated to water fluoridation. Finally, search engines available on the webpages of the Calgary Herald, the Calgary Sun, The Globe and Mail, the National Post, Canadian Broadcasting Corporation, Metro News, and Maclean's Magazine were used with the search terms "fluoride Calgary" and "fluoridation Calgary". Again, articles that had at least one comment and had not been previously identified were added to the list of sources.

Once an exhaustive list of sources had been assembled, a qualitative judgement was made regarding each source's specific relevance to fluoridation in Calgary. This was done independently by the two authors, with disagreements resolved by discussion. Only sources that pertained to Calgary were used in the next phase of the study.

User comments were extracted from each source. The date of entry of the comment was recorded (if available), along with the full comment text. Individual comments were rated on whether they mentioned the harms/risks of fluoride (yes/no) and on what specific harms/risks were mentioned. Comments that were in favour of water fluoridation or negative comments that did not mention any harms/risks were not considered further. At this stage, it was necessary to develop a working definition of "harms/risks". We operationalized the term to include any possible adverse health effects in humans, including harm to sensitive populations (e.g., children, individuals with existing health conditions); effects on animals; and effects on the environment (e.g., pollution and bio-accumulation). A subset of comments was examined independently by the two authors to gauge agreement and to refine the criteria for judgement in order to permit consistency. The two raters agreed on 94% of the comments (n = 86) from five randomly selected sources. Harms/risks were recorded verbatim, sorted into categories of similar terms, then further combined into groupings of thematically similar content.

Types of evidence included in online comments about perceived harms/risks of fluoridation

Next, for those user comments that mentioned the harms/risks of fluoridation (identified above), we extracted cited sources of evidence. In other words, we re-examined the comments to determine whether the user provided any evidence for his/her stated harm/risk. We deliberately adopted a broad conceptualization of evidence to include anything that the user identified as support for his/her position (i.e., not just scientific evidence). We grouped similar types of evidence together and computed the frequency of occurrence. For scientific papers (one type of evidence) cited, we retrieved and reviewed the original papers.

Review of scientific literature for a subset of harms/risks identified in online comments

To consider the broader evidence base, we selected a subset of two (for feasibility reasons) harms/risks groupings for a structured literature review: animals, environment and aquatic life (we focused specifically on aquatic life); and the endocrine system (we focused specifically on the thyroid gland). We selected these two topics because we wished to consider both human and non-human organisms, and to avoid duplication of recent published reviews (e.g., cognitive outcomes[16]). The breadth of the aquatic life search necessitated further focus: we decided to focus on phytoplankton. Other foci within aquatic life (e.g., amphibians) would have been equally good choices. Although scientific evidence does not resonate with everyone in terms of their views on fluoridation (i.e., it is not *sufficient*), it is nonetheless *necessary* to maintain an up-to-date knowledge base by reviewing and synthesizing published literature on specific topics identified by members of the public as areas of concern. A professional health sciences librarian was consulted in operationalizing and executing searches. Search details are provided in Appendix A. For both topics, we first reviewed titles and abstracts using the inclusion/exclusion criteria described in Appendix B. All titles and abstracts were reviewed by the first author (PP), and a subset was independently reviewed by the second author (LM) to assess and establish consistency.

Papers extracted from both searches were reviewed and summarized. The following information was extracted into a table: study objective, rationale, type of study design, study population (e.g., plant species or human sample), source of fluoride, concentration(s) and exposure time(s), methods, results and implications for community water fluoridation. Methodological limitations, as stated by the author, were also recorded. For each review, a synthesis focused on overall findings, key methodological limitations and relevance to fluoridation at recommended levels.

RESULTS

Of the 55 sources identified from the initial search as being potentially relevant and having comment capacity, 48 (87%) were related specifically to fluoridation in Calgary. Most sources were published or posted during 2013 (n = 24; 50%), 35% in 2011 (n = 17), 8% in 2012 (n = 4) and 6% in 2014 (n = 3). The degree of relevance was substantive in 46% of cases (n = 22) and constituted only a mention in the remaining 54% (n = 26). Sources were classified as 1) news/newspaper and magazine articles (n = 24; 50%), 2) blogs (n = 9; 19%), 3) public discussion forums (n = 7; 15%), 4) opinion articles or letters to the editor (n = 4; 8%) and 5) others, including petition, video, website and interview (n = 4; 8%). Of the news/newspaper and magazine articles, most were obtained from the National Post (n = 5; 21%) and MacLean's Magazine (13%). The number of user comments per source ranged from 1 to 824, with a mean of 69.

Identification of perceived harms/risks of fluoridation mentioned in online comments

In total, the 48 sources corresponded to 3,330 user comments. Of these, 356 (10.7%) mentioned the harms/risks of fluoride (based on our operational definition). Harms/risks were grouped into 56 categories, which in turn were further combined into 17 thematic groupings. Table 1 shows the 17 thematic groupings, the 56 original categories from which the groupings were formed, examples and the frequency of occurrence.

Types of evidence included in online comments about perceived harms/risks of fluoridation

Table 2 presents the types of evidence cited in user comments about the harms/risks of fluoride, along with examples and frequency of occurrence. Forty-two percent of comments (n = 176) did not cite any evidence. Of those comments that did, the most frequent evidence types were a person viewed as an expert or authority, a generic reference to research, and a website, including YouTube. Less frequently cited types included personal experiences, product labels and non-government or non-profit organizations.

Published literature represented 5.5% of all evidence cited, corresponding to nine papers.[16–24] These papers are summarized in Table 3. Overall, the papers have very significant methodological problems (e.g., no or limited details on methods, limited or unknown measurement of potentially important confounding variables), and their relevance to community water fluoridation at recommended concentrations is limited or unknown.

Review of scientific literature for a subset of harms/risks identified in online comments

Detailed information about all studies retrieved is available as supplemental online material. Attributes of studies are summarized in Table 4. Table 5 shows the correspondence among different units of fluoride, to permit comparison across studies.

Fluoride and Aquatic Plant Life

The search yielded 2,594 unique citations. After applying inclusion and exclusion criteria, we arrived at 15 papers for in-depth review. Four of these were either unavailable in English or could not be retrieved (via Interlibrary Loan), reducing the final set to 11 papers (see Table 4 and Supplementary Table 1).

Collectively, the papers may be summed up as follows: at elevated concentrations (i.e., >2 mg/L) and in some species (e.g., *Chlorella pyrenoidosa*), the fluoride ion produces visible toxic effects in algae and phytoplankton. These effects include inhibition of growth, photosynthesis, respiration, cell division

Table 1. Harms/risks mentioned in online comments pertaining to community water fluoridation cessation in Calgary, January 2011–May 2014, ordered by frequency

Thematic grouping	Original harm/risk category	Example terms	Frequency (%) of mention (total = 639)
Generic: toxic/poisonous/chemicals/ hazardous/contaminant (including deadly)	Chemicals including build-up in body Contaminant Death Hazardous Noxious Poison Toxic	"Contaminant" "Deadly poison" "Toxic" "May be fatal if swallowed or inhaled" "Noxious waste"	187 (29.3%)
Generic: unhealthy/damaging to health	Dangerous, detrimental Epidemic Harmful Multiple body systems Overexposure Sick people Side effects Unhealthy	"Dangerous substance" "Detrimental substance" "Harmful side effects" "Serious abnormalities of several body systems" "Health problems" "Linked to several serious health conditions"	83 (13.0%)
Dental, including but not limited to fluorosis	Dental fluorosis Dental, not fluorosis	"Staining of teeth due to mottling of tooth enamel" "Discoloration" "Rotting" "Not good for porcelain caps as it makes them crack over time" "Weakens teeth"	66 (10.3%)
Behavioural and cognitive	Attention deficit hyperactivity disorder Alzheimer's Anti-depressant Autism Depression Dyslexia Energy IQ Irritability Concentration	"Inability to concentrate" "Lowered IQ" or "IQ reduction" "Anti-depressant effect on people" "Makes you a slug" "Effects on mental performance"	50 (7.8%)
Generic: children, elderly	Children – generic Elderly people – generic	"Harm to young children" "Overexposure in formula-fed infants" "The elderly" "Affects seniors" "Babies"	38 (5.9%)
Animals, environment and aquatic life	Animals Environment	"Spinal collapse in guppies" "Cattle dropped dead" "Harms salmon and other aquatic life" "Harm to the downstream environment" "Damaging environmental pollutant"	37 (5.8%)
Bones and skeleton	Skeletal fluorosis Bone problems (break, fracture) Arthritis	"Degenerative problems in bone, bone tissue" "Broken hips from brittle bones" "Painful and debilitating fluorosis in the joints" Arthritis as "subclinical skeletal fluorosis" "Affects skeleton"	36 (5.6%)
Endocrine system	Pineal gland Thyroid	"Thyroid suppressant" "Goitre development" "Pineal gland damage" "Suppresses thyroid by competing with iodine for absorption in the thyroid" "Overactive thyroid"	36 (5.6%)
Cancer	Cancer	"Rats started to develop small tumours in their brains… tumours developing in their stomach lining" "Bladder cancer" "Bone cancer" "Carcinogenicity" "Osteosarcoma"	34 (5.3%)
Brain and central nervous system (CNS)	Brain and CNS Neurotoxin	"Destroys the brain" "Calcinates parts of the brain" "Abnormal development of the central nervous system in fetuses and young children" "Neurotoxin which impairs brain function" "Central nervous system effects"	24 (3.8%)

Continues

Table 1. Continued

Thematic grouping	Original harm/risk category	Example terms	Frequency (%) of mention (total = 639)
Urinary system	Bladder Dehydration Kidney disease	"Those with kidney impairment" "Anyone with kidney stones" "Stress on the kidneys" "Serious bladder problems and surgeries" "People on kidney dialysis"	23 (3.6%)
Immune system	Allergy Immune system Irritation Oxidative stress Sensitivity Ulcers	"The immune compromised" "Allergic reactions" "Causes irritation to skin, eyes" "Causes oxidative stress by interfering with the body's defence mechanisms against reactive oxygen species" "Mouth ulcers"	8 (1.3%)
Digestive system	Digestive system Liver	"Upset stomach" "Digestive systems of fluoride poisoning" "Stomach problems" "Not good for your liver" "Nausea"	6 (0.9%)
Others	Diabetes Genetic Hair	"People with diabetes" or "Diabetics" "Genetic damage" "Hair loss"	4 (0.6%)
Circulatory system	Cardiovascular system	"Coronary artery disease" "Scarring arterial walls" "Affects circulatory system" "Harmful to many arteries" "Affects heart"	3 (0.5%)
Respiratory system	Respiratory and related	"Chronic cough" "Affects respiratory system"	2 (0.3%)
Pregnancy and related	Pregnancy and related	"Sudden infant deaths" "Anemia in pregnant women" "Premature births" "Low baby birth weight"	2 (0.3%)

and protein synthesis, and reduced cellular ATP (adenosine triphosphate) levels, enzyme activity (e.g., enolase) and metabolism. However, the toxic effects are variable, exhibiting fluctuations with fluoride concentration, exposure time, temperature, water pH, water composition (e.g., the presence of other ions), water hardness and season. Many of the studies suggest that fluoride could combine with other constituents present in water (e.g., calcium, magnesium), mediating or enhancing toxicity.

In some cases, positive effects of fluoride were observed. There is minimal growth enhancement observed in some species, suggesting that fluoride may be a nutritional requirement for these plant forms (e.g., *Anabaena fertilissima*). Further, some species demonstrate resistance to extreme fluoride levels, hence their use in de-fluoridation experiments (e.g., *Amphidinium carteri*).

Overall, levels of fluoride pollution assessed in the studies reviewed do not seem to pose an immediate threat to the viability and growth of algae and phytoplankton provided sufficient nutrients are available. However, an important limitation is that all studies were carried out in conditions of sufficient nutrients, thus it is important to consider the implications of nutrient insufficiency on toxicity.

Overall, study quality was poor. Most reviews did not include a description of the search strategy, inclusion/exclusion criteria or method of analysis. Frequently, tested fluoride concentrations and exposure times were not justified, and the rationale for the experiments was limited or absent. Most studies did not make explicit references to community water fluoridation.

Fluoride and Thyroid

The initial search of seven databases yielded 955 unique abstracts. After applying inclusion and exclusion criteria, we arrived at 27 papers for in-depth review (see Table 4 and Supplementary Table 2).

Collectively, the papers may be summed up as follows:

Human studies Even at more elevated concentrations (e.g., 4.0 ppm), the fluoride ion did not show toxic effects on the thyroid gland nor did it clearly affect levels of thyroid hormones. Specifically, few studies report serum levels of thyroid hormones (T3, T4, thyroid stimulating hormone) outside the normal range; few studies report any clinical manifestations of thyroid enlargement (e.g., total thyroid volume is not different in children exposed to high [e.g., 4.6 mg/L] and normal [e.g., 0.19 mg/L] fluoride levels); and goitre prevalence does not seem to correlate with fluoride levels in water.

There were numerous methodological limitations identified in human studies, relating especially to a lack of control for other variables (e.g., fluoride consumption in food, presence of other ions and contaminants in water).

Animal studies Animal models testing extremely high fluoride concentrations (e.g., 40–500 ppm) report lower thyroid hormone levels when compared with controls, although these findings are not consistent across studies or species (i.e., rats, mice and rabbits). Most animal studies do not translate their findings to humans. The range of fluoride that showed adverse effects on the thyroid (30–500 ppm) among animals were in all cases substantially higher than recommended concentrations for

Table 2. Types of evidence cited in online comments, ordered by frequency

Type of evidence	Examples and/or sample quotes	Frequency (%) of mention (total = 416)
None (no evidence)	N/A	176 (42.3%)
Person viewed as an expert or authority, including personal expertise and credentials	"Dr. James Beck" "Christopher Bryson (journalist)" "14 Nobel prize winners in either medicine or chemistry" "I am a practicing dental hygienist" "I'm a nutritionist that practices alternative medicine"	53 (12.7%)
Generic reference to research	"Feel free to ask for sources" "Read the facts about what happens to kids who get too much fluoride before the age of 8" "Numerous scientific studies" "According to new research" "More and more science is showing"	30 (7.2%)
Website, including YouTube	http://slweb.org/bibliography.html ("A Bibliography of Scientific Literature on Fluoride") http://www.nofluoride.com/presentations/Nobel%20Prize%20Winners.pdf ("14 Nobel Prize Winners who object to fluoridation") www.fluoridealert.org (Website of The Fluoride Action Network) http://en.wikipedia.org/wiki/Dental_fluorosis (Wikipedia page for dental fluorosis) http://cof-cof.ca/convincing-canadian-studies-demonstrating-water-fluoridations-questionable-merit/ (A list of "Convincing Canadian studies demonstrating water fluoridation's questionable merit")	30 (7.2%)
Personal experience	"We have lost 8 horses and 4 dogs from the consumption, accumulation and systemic effects of this product" "It destroyed my thyroid" "I've started to lose a lot of hair…my thyroid started acting up and I developed a goitre" "I've been fighting health problems" "I don't use tap water for the guppies either, it was causing their spines to collapse"	25 (6.0%)
Government report or organization, including government acts and regulations	"Food and Drug Act" "The Safe Drinking Water Act (2002)" "The Ontario Safe Drinking Water Act, Section 19, in effect January 2013" National Research Council "The Canadian Health Measures Survey (CHMS) released data …"	23 (5.5%)
Study or article in peer-reviewed journal	"Sawan, et al. (Toxicology 2/2010): Water fluoride chemicals boost lead absorption in lab animals' bones, teeth and blood" "Tang el al., "Fluoride and Children's Intelligence: A Meta-analysis" in Biological Trace Element Research"	23 (5.5%)*
My own research/reading	"I have done extensive research on fluoride" "I read an article" "I have read reports"	17 (4.1%)
Product label	"If you look at the bag labels Sodium Fluoride you will see the skull and cross bones" "Warning labels on toothpaste" "Material Safety Data Sheet"	13 (3.1%)
Documentary, magazine, or book	"Christopher Bryson's 'The Fluoride Deception'" The Case Against Fluoride "Book published in 1961, The Fluoridation Experiment, by Exner, Waldbott & Rorty" "Time magazine listed fluoride as one of the 'Top Ten Common Household Toxins' and described fluoride as both 'neurotoxic and potentially tumorigenic if swallowed.'"	13 (3.1%)
NGO/non-profit organization	The Council of Canadians (Windsor Chapter) Sierra Club Columbia Riverkeepers The Canadian Association of Physicians for the Environment The National Kidney Foundation	11 (2.6%)
Newspaper	"Editorial that appeared in the Windsor Star" "Howard University's student newspaper, The Hilltop"	2 (0.5%)

* Corresponds to 9 separate published articles, some of which were mentioned multiple times.

controlled water fluoridation. There were numerous methodological limitations identified in animal studies, relating especially to a lack of rationale for fluoride concentrations and mode of administration.

DISCUSSION

Overall, the main conclusions are threefold. First, according to online comments surrounding fluoridation cessation in Calgary, Alberta, in 2011, concerns about a wide range of harms/risks of fluoridation were expressed. These concerns relate to the health of humans (diverse body systems), the environment, and non-human organisms.

Second, a large proportion of comments about harms/risks did not provide any supporting evidence, and of those that did, the sources of evidence were diverse, with scientific research infrequently cited. The nine scientific papers cited were found to have very significant methodological limitations and at best only very limited relevance to community water fluoridation at recommended concentrations. Perhaps most troubling is that, in many cases, information that would permit some readers to

Table 3. Summary of published scientific papers* cited in online comments

Citation (#)	Synopsis	Key issues/concerns
Choi et al.[16]	Systematically reviewed research on fluoride and neuro-developmental delays published between 1980 and 2011, including studies from rural China that examine naturally occurring high levels of fluoride. Studies contained high and reference exposure groups (final *n* = 27; 2 from Iran and the rest from China). Overall results support association between high fluoride exposure and lower intelligence (based on standardized mortality ratio, pooled risk ratio). Finding was robust to different study exclusions.	Quality of original studies is quite poor (e.g., information on child's sex and parental education was not reported in >80% of studies, and only 7% [*n* = 2] of studies reported household income; most reports were fairly brief and complete information on covariates was not available; most studies did not report age adjustment of the cognitive test scores). All original studies appear to be cross-sectional comparisons of fluoridated and non-fluoridated groups. Fluoride concentrations in the high exposure group were in most cases higher than recommended (0.7 ppm) and maximum (1.5 ppm) levels: range >2 to 11 ppm.
Duan et al.[17]	Various tests (i.e., cognitive ability, electroencephalograph, neurological history taking and physical examinations) were administered among three groups of individuals: 1) *n* = 72 men with chronic industrial fluorosis who worked or had worked in the electrolysis workroom at an aluminum production facility; 2) *n* = 43 men who had worked in same environment for less time and whose condition did not meet the diagnosis for industrial fluorosis; and 3) *n* = 42 healthy persons. Economic status, lifestyle habits and other factors were similar across groups. Across tests, the worst outcomes were observed in group A (longest exposure) followed by group B (shorter exposure), and the best results were in group C (healthy group). Exposure was confirmed by air quality tests in the facility and from fingernail samples.	Paper was translated from Chinese by the Fluoride Action Network. No information on how participants were sampled/selected within each group. Though authors report that economic status, lifestyle habits and other factors were similar across the groups, no data are presented, and there is no information on how these were measured nor what "lifestyle habits" and "other factors" entail. Limited information is provided on the tests and what the results mean (e.g., from the electroencephalogram, the proportion moderately abnormal and mildly abnormal are reported for each group, but it is not clear what these categories mean or how they were assigned). Whether the findings have relevance to fluoridated drinking water and to what extent is unclear.
Gazzano et al.[18]	Review article (134 references) anchored in the observation that fluoride's behaviour in the human organism makes it a classic example of a double-edged sword. The rationale for the article appears to be the proposed insertion of fluoride in the preparation of biomaterials to improve their integration in the bone, which demands understanding of the safety of fluoride in terms of prolonged exposure to living tissue. The review covers the following areas: 1) fluoride metabolism and types of exposure; 2) mechanisms of fluoride action on dental caries onset; 3) fluoride application in caries prevention; 4) effects of fluoride on bone; 5) acute and chronic effects of fluoride; 6) activation of G proteins and kinases and inhibition of phosphatases; 7) fluoride inhibition of many other enzymes; and 8) fluoride and oxidative stress. Concludes by presenting a model for "Is there a unifying hypothesis for fluoride effects?"	No methods section; it is unclear how the authors selected the studies reviewed. Article is very technical, therefore not accessible to a non-expert reader.
Grandjean & Landrigan[19]	Review (115 references) that is an update of a 2006 review of the developmental neurotoxicity of industrial chemicals. The 2006 report identified five industrial chemicals that could be reliably classified as neurodevelopmental toxicants: lead, methylmercury, arsenic, polychlorinated biphenyls and toluene. The authors are concerned that subclinical toxicity may be widespread before it is realized that concentrations thought to be safe are shown, by epidemiological research, to be too high. They also cite examples of early warning signs of subclinical neurotoxicity being ignored or dismissed. Fluoride is recognized as one of the "newly recognized developmental neurotoxicants". This is based entirely on the Choi[16] paper above.	Search/selection methods are only briefly described. Because the identification of fluoride as a newly recognized developmental neurotoxicant is based entirely on Choi,[16] this paper suffers from the same limitations as above in terms of the low/unknown quality of the original studies. The section on "newly recognized developmental neurotoxicants" begins with a paragraph about "powerful epidemiological methods" such as prospective birth cohort studies, which gives the misleading impression that the information that follows is based on those methods. The studies in the Choi paper,[16] as noted above, are all cross-sectional, mostly do not include any covariate information and pertain to higher than recommended fluoride levels.
Justus & Krook[20]	Authors build on another paper recently published in the same journal, which demonstrated fluoride poisoning in horses that consumed artificially fluoridated water. This paper focuses on allergy as another expression of fluorosis in horses. The horses were not likely exposed to other sources of fluoride. Over the years, 2 of 11 horses exposed to the water developed allergy (skin lesions), and the two cases are presented. In the first horse, for example, the lesions were reduced when the horse consumed snow instead of fluoridated water and disappeared when it consumed water from a different source. Eventually, the horse was taken off fluoridated water altogether and the lesions ceased entirely.	The paper is an account of a personal experience; as such, it lacks the systematic nature of rigorous research, and thus it is more difficult to rule out alternative explanations.
Sandhu et al.[21]	The study aimed to examine serum fluoride, among other things, in 25 osteosarcoma patients as well as age- and sex-matched controls with 1) bone-forming tumours other than osteosarcoma (*n* = 25) and 2) musculoskeletal pain (*n* = 25). Found that serum fluoride levels were significantly higher in the osteosarcoma group than in the two control groups. The authors acknowledged studies that show a link between fluoride in drinking water and osteosarcoma as well as those that did not show a link.	The age- and sex-matching is only mentioned in the abstract (not in the methods section). No information about how the individuals were sampled/selected. No other information about the three groups (covariates) to permit assessment of how similar/different they were on other variables. Conclusion is thus overstated: "this report proves a link between raised fluoride levels in serum and osteosarcoma". Implications for fluoridated drinking water at recommended levels are unclear.
Sawan et al.[22]	Authors aimed to test whether administration of fluorosilicic acid could increase blood lead content and mineralized tissue lead concentration in rats exposed to low levels of lead from the beginning of gestation (silicofluoride is the fluoride compound used most commonly for fluoridated water in the US, Canada and other countries). The fluoride concentration for the control and lead-only groups was 1 mg/L; for the fluoride and fluoride + lead group it was 100 mg/L. The authors note that this fluoride concentration produces plasma fluoride levels that are comparable to those commonly found in humans chronically exposed to 8 mg/L in drinking water (which far exceeds recommended and	The fluoride concentration far exceeds recommended (0.7 mg/L) and maximum (1.5 mg/L) levels for drinking water. Relevance of findings to community water fluoridation is minimal, if any.

Continues

Table 3. Continued

Citation (#)	Synopsis	Key issues/concerns
	maximum levels). Higher blood lead concentrations were reported in the fluoride + lead group compared with the lead-only group, and lead concentrations in calcified tissues were significantly higher in the fluoride + lead group than in the lead-only group. No significant differences in fluoride concentrations in calcified tissues were found between these groups.	
Susheela et al.[23]	Article examined (among other things) whether, among anemic pregnant women with urinary fluoride beyond 1.0 mg/L, an intervention to reduce fluoride intake reduced pre-term births and low birth weight. The intervention included counselling on how to avoid fluoride in water and food. Eligible women were randomly assigned to intervention vs. control groups. Information on confounding factors was gathered: diet, economic status, literacy status, employment status, first pregnancy, miscarriage and other problems, other ailments, and use of folic acid and iron supplements. The intervention group, compared with the control group, had higher (better) hemoglobin and higher birth weight/lower% low birth weight.	The paper is poorly written/organized, so is difficult to follow. Unclear whether the effect is attributable to the reduction in fluoride, the improved nutrition or a combination of the two. Although covariate data were collected, it does not appear that the authors examined whether results could be explained by covariates (though random allocation is a strength).
Tang et al.[24]	A systematic review of studies from China, written in English or Chinese, on the association between fluoride and intelligence/IQ, published between 1988 and 2008 (the "earlier review" cited by Choi[16]. Among the 16 included "case control" studies, the authors found that children in fluoridated areas had increased risk of lower IQ (meta-analysis, sensitivity analyses).	No information at all on covariates/confounders in original studies or any other methodological detail of the original studies.

* All studies are published in peer-reviewed journals.

gauge the validity of the study was missing entirely, for example, studies having no description of how the participants were sampled, or the absence of a methods section altogether. These are not minor concerns; they are egregious methodological flaws that make it very difficult (in some cases impossible) to have confidence in the reported results.

Third, for the two examples for which we systematically examined the broader research literature, the evidence likewise did not support the perceived harms/risks. On the contrary, the scientific evidence points towards the safety of fluoride at recommended levels (0.7–1.5 mg/L) with respect to these specific harms/risks. Overall, these findings are consistent with Sandman's concept of "outrage", whereby perception of risk, for some members of the public, is influenced by factors other than scientific evidence.

The findings have implications for communication with the public about fluoridation. First, scientific evidence is only one component of why some people support or do not support fluoridation strategies. Communication strategies must accommodate that reality by, for example, incorporating techniques that are not dismissive of expressed concerns. Excellent resources are available for this (e.g., the US-based Campaign for Dental Health, http://ilikemyteeth.org/). Second, to the extent that members of the public consult the scientific literature, it is essential that methodological assessment of new studies, including their relevance to community water fluoridation, is promptly performed and widely disseminated. There are excellent examples of this as well, such as appraisals performed by Peel Public Health in the Peel Region of Ontario (e.g., http://bit.ly/1aLhom8).

Table 4. Attributes of the final set of papers from the aquatic plants/phytoplankton (n = 11) and thyroid (n = 27) literature searches (see Supplementary Tables 1 and 2 for details of individual studies)

Topic of review	Publication years (range)	Main countries of origin	Study type	Fluoride forms administered/ tested	Levels/concentration of fluoride and exposure times	Measured parameters
Fluoride and aquatic plants/ phytoplankton	1962–1999 (55%) 2000–2011 (45%)	Canada (45%) India (18%) Other (36%)	Experimental (55%) Review (36%) Observational (9%)	Sodium fluoride (NaF), hydrogen fluoride (HF) and ammonium fluoride (NH_4F) (only NaF is commonly used for water fluoridation).	0 to 1900 mg/L Exposure times ranged from hours (minimum 5) to days (maximum 36).	Growth (measured as cell number and/or absorbance), oxygen exchange, ATP levels, chlorophyll content, enzyme activity (i.e., carbonic anhydrase) and respiratory activity.
Fluoride and thyroid	1960–1999 (56%) 2000–2014 (44%)	India (30%) Tunisia (11%) China (11%) United States (7%) Switzerland (7%) Turkey (7%) Other (26%)	Observational (44%) Experimental (48%) Review (8%)	Sodium fluoride (NaF) Naturally occurring fluoride (e.g., studies of children in areas of high naturally occurring fluoride in the water).	0 to 500 ppm	Thyroid volume, thyroid weight, thyroid hormone levels in serum (T3, T4, and thyroid stimulating hormone), clinical thyroid enlargement and goitre prevalence.

Table 5. Unit conversion chart (for fluoride concentrations)

Standard unit	Equivalent unit	Recommended fluoride concentration in drinking water (converted)
1 mg/L	1 ppm	0.7–1.5 ppm
	0.05 mM	0.035 mM–0.075 mM
	50 µM	35 µM–75 µM

One limitation of our study is that the comments we examined are limited to a small segment of the population during a particular time frame and do not represent those of the public as a whole. They do, however, resemble the broad cross section of risks/harms identified in other times and places.[11] Although those who are strongly opposed to fluoridation and who may thus contribute to online fora are thought to constitute a small minority of the population, they may have disproportionate impact on plebiscite outcomes, and thus it is important to identify, understand and find ways to address their expressed concerns. Second, because the search was conducted in May 2014, some of the information posted at the time of the 2011 Calgary plebiscite may no longer be available online, and unfortunately we do not know the extent to which this occurred. A third limitation is that for feasibility reasons our broader literature review focused on only two specific harms/risks among the many identified in this study. Although scientific evidence does not resonate with everyone in terms of influencing support for/opposition to fluoridation (i.e., it is not *sufficient*), it is nonetheless *necessary* for informed discussion and decision-making, and thus periodic review and synthesis of existing research on specific harms/risks and fluoride is important; this was the reasoning behind our two reviews (for which recent published reviews do not exist). Fourth, the nature of the evidence base and our review methods are such that potential biases may be present. Most notably, we excluded articles published in non-English language (the proportion of non-English articles on fluoride appears to be non-negligible). Additionally, we did not perform a formal risk of bias assessment, opting instead to focus on major methodological limitations and relevance to community water fluoridation.

Important directions for future research on the subject of public perceptions and fluoridation include analysis of comments in favour of fluoridation, including how disagreements play out in online forums; research into the development and testing of public health communication messages that reflect our findings here; and ongoing systematic reviews of research on other perceived harms/risks that showed up in our sample of comments, such as fluoride's impact on amphibians, issues of the industrial source of fluoride (e.g., sodium fluorosilicate) and concerns about arsenic contamination and lead leaching.

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RÉSUMÉ

OBJECTIFS : Examiner les dangers et les risques perçus de la fluoration discutés sur les tribunes en ligne portant sur l'arrêt et les répercussions de la fluoration à Calgary, plus précisément : 1) quels dangers et risques on mentionne; 2) pour ces dangers et risques, quels genres de données probantes on cite; 3) la mesure dans laquelle on cite des articles scientifiques, et leur qualité; et 4) pour un sous-ensemble de dangers et de risques, ce que l'on sait d'après la littérature scientifique en général.

MÉTHODE : Nous avons repéré les commentaires en ligne pertinents au moyen de recherches en texte libre sur Internet, et nous en avons extrait

ceux qui traitent explicitement des dangers ou des risques de la fluoration de l'eau. Nous avons identifié les types d'éléments probants mentionnés et examiné les communications scientifiques citées. Enfin, nous avons examiné et résumé la littérature scientifique en général sur deux de ces dangers ou risques.

SYNTHÈSE : Nous avons cerné 17 groupes distincts de dangers et de risques pour les systèmes et appareils du corps humain, pour l'environnement et pour les organismes non humains. Le plus souvent, aucune donnée probante n'était citée. Lorsqu'on citait des données probantes, elles pouvaient être attribuées à des personnes considérées comme des autorités ou à des expériences personnelles. Il était rare que l'on fasse référence à des articles scientifiques, et ces articles (n = 9) présentaient des problèmes méthodologiques importants. Notre examen de la littérature scientifique sur le fluorure par rapport 1) au fonctionnement de la thyroïde et 2) au phytoplancton a mis au jour quelques effets néfastes du fluorure à des concentrations supérieures aux niveaux maximum recommandés (>1,5 ppm).

CONCLUSION : Nos constatations ont des conséquences pour la communication avec le public au sujet de la fluoration. Premièrement, dans la mesure où le public consulte la littérature scientifique, il est essentiel que les contraintes méthodologiques d'une étude, ainsi que sa pertinence pour la fluoration municipale de l'eau, soient largement et rapidement communiquées. Deuxièmement, les preuves scientifiques ne sont qu'une des raisons pour lesquelles certaines personnes sont pour ou contre la fluoration, et les stratégies de communication doivent tenir compte de cette réalité.

MOTS CLÉS : fluoration; eau potable; sécurité; risque; pratique fondée sur des éléments probants; santé publique

Appendix A

Search Strategy: Fluoride and Pollution/Aquatic Life (July 2014)

Databases

Aqualine
Biological Abstracts (OVID to 2005)
CAB Abstracts
Environment Abstracts
Environment Complete
Environmental Sciences and Pollution Management
MEDLINE
Pollution Abstracts
ToxLine
Web of Science
Zoological Record

Total abstracts (before de-duplication): 4155
Total abstracts (after de-duplication): 2594

Search strings and total number of results by database:

Aqualine

1. TI (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales) OR AB (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales)
2. TI (fluoride* or fluoridation) OR AB (fluoride* or fluoridation)
3. 1 and 2
4. Limit 3 to scholarly peer review journals

Total: 293 results

Biological Abstracts (OVID to 2005)

1. (algae or Aquatic life* or Aquatic mammal* or aquatic organism* or aquatic plants or Fish or Salmon or Water plants or water pollut*).tw.
2. (dolphin* or sharks or tuna or whales).tw.
3. 1 or 2
4. fluorid*.tw.
5. 3 and 4

Total: 437 results

CAB Abstracts

1. exp Fishes/
2. exp Aquatic organisms/
3. exp Cetacea/
4. (algae or Aquatic life* or Aquatic mammal* or aquatic organism* or aquatic plants or Fish or Salmon or Water plants or water pollut*).tw.
5. (dolphin* or sharks or tuna or whales).tw.
6. water pollution/ or exp water pollution, chemical/
7. exp algae/
8. exp aquatic plants/
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. fluorid*.tw.
11. 9 and 10

Total: 878 results

Environment Abstracts

1. TI (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales)
2. TI (fluoride* or fluoridation)
3. 1 and 2
4. Limit 3 to scholarly peer review journals

Total: 11 results

Environment Complete

1. TI (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales) OR AB (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales) OR SU (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales)
2. TI (fluoride* or fluoridation) OR AB (fluoride* or fluoridation) OR SU (fluoride* or fluoridation)
3. 1 and 2
4. Limit 3 to Scholarly Peer Reviewed Journals

Total: 444 results

Environmental Science and Pollution Management

5. TI (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales) OR AB (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales)
6. TI (fluoride* or fluoridation) OR AB (fluoride* or fluoridation)
7. 1 and 2
8. Limit 3 to scholarly peer review journals

Total: 514 results

MEDLINE

1. exp Fishes/
2. exp Aquatic organisms/
3. exp Cetacea/

4. (algae or Aquatic life* or Aquatic mammal* or aquatic organism* or aquatic plants or Fish or Salmon or Water plants or water pollut*).tw.
5. (dolphin* or sharks or tuna or whales).tw.
6. water pollution/ or exp water pollution, chemical/
7. 1 or 2 or 3 or 4 or 5 or 6
8. exp Fluorides/ae, to [Adverse Effects, Toxicity]
9. Fluoridation/ae [Adverse Effects]
10. fluorid*.tw.
11. 8 or 9 or 10
12. 7 and 11

Total: 358 results

Pollution Abstracts

1. TI (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales) OR AB (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales)
2. TI (fluoride* or fluoridation) OR AB (fluoride* or fluoridation)
3. 1 and 2
4. Limit 3 to scholarly peer review journals

Total: 21 results

ToxLine

1. (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales)
2. (fluoride* or fluoridation)
3. 1 and 2
4. Limit 3 to scholarly peer review journals

Total: 335 results

Zoological Record

1. (algae or Aquatic life* or Aquatic mammal* or aquatic organism* or aquatic plants or Fish or Salmon or Water plants or water pollut*).tw.
2. (dolphin* or sharks or tuna or whales).tw.
3. 1 or 2
4. fluorid*.tw.
5. 3 and 4

Total: 26 results

Web of Science (Science Citation Index and Social Science Citation

Index)

1. SU (algae or aquatic life* or aquatic mammal* or aquatic organism* or aquatic plants or fish or salmon or water plants or water pollut* or dolphin* or sharks or tuna or whales)
2. SU (fluoride* or fluoridation)
3. 1 and 2

Total: 838 results

Search Strategy: Fluoride and Thyroid (July 2014)

Databases

MEDLINE
PubMED
EMBASE
Global Health
CINAHL
ToxLine
Web of Science

Total abstracts (before de-duplication): 1616
Total abstracts (after de-duplication): 955

Search strings and number of results by database:

MEDLINE

1. exp Fluorides/ae, to [Adverse Effects, Toxicity]
2. Fluoridation/ae [Adverse Effects]
3. fluorid*.tw.
4. 1 or 2 or 3
5. Thyroid Gland/
6. exp Thyroid Diseases/
7. (euthyroid* or goiter* or goitre* or hyperthyroid* or hypothyroid* or thyroid* or thyrotoxicos*).tw.
8. 5 or 6 or 7
9. 4 and 8
10. limit 9 to animals
11. limit 9 to (animals and humans)
12. 10 not 11
13. 9 not 12

Total: 144 results

PubMED

1. Fluorides[MeSH] OR Fluoridation[MeSH]
2. fluorid*[tiab]
3. 1 or 2 or 3
4. Thyroid Gland[MeSH]
5. Thyroid Diseases[MeSH]
6. (euthyroid* or goiter* or goitre* or hyperthyroid* or hypothyroid* or thyroid* or thyrotoxicos*)[tiab]
7. 5 or 6 or 7
8. 4 and 8

Total: 400 results

EMBASE

1. fluoridation/ae [Adverse Drug Reaction]
2. fluoride/ae, to [Adverse Drug Reaction, Drug Toxicity]
3. fluorid*.tw.

4. 1 or 2 or 3
5. exp thyroid gland/
6. exp thyroid disease/
7. (euthyroid* or goiter* or goitre* or hyperthyroid* or hypothyroid* or thyroid* or thyrotoxicos*).tw.
8. 5 or 6 or 7
9. 4 and 8

Total: 326 results

Global Health

1. exp thyroid gland/
2. exp thyroid disease/
3. (euthyroid* or goiter* or goitre* or hyperthyroid* or hypothyroid* or thyroid* or thyrotoxicos*).tw.
4. 1 or 2 or 3
5. fluoride/ or fluorides/
6. fluoridation/
7. fluorid*.tw.
8. 5 or 6 or 7
9. 4 and 8

Total: 138 results

CINAHL

1. (MH "Fluoridation") OR (MH "Fluorides+")
2. TI fluorid* OR AB fluorid*
3. 1 or 2
4. (MH "Thyroid Neoplasms") OR (MH "Thyroid Diseases+") OR (MH "Thyroid Hormones+") OR (MH "Thyroid Gland") OR (MH "Hypothyroidism+") OR (MH "Hyperthyroidism +") OR (MH "Graves' Disease+") OR (MH "Goiter+") OR (MH "Thyrotoxicosis+")
5. TI (euthyroid* or goiter* or goitre* or hyperthyroid* or hypothyroid* or thyroid* or thyrotoxicos*) OR AB (euthyroid* or goiter* or goitre* or hyperthyroid* or hypothyroid* or thyroid* or thyrotoxicos*)
6. 4 or 5
7. 3 and 6

Total: 17 results

Toxline

1. SU fluorid*
2. SU (euthyroid* or goiter* or goitre* or hyperthyroid* or hypothyroid* or thyroid* or thyrotoxicos*)
3. 1 and 2

Total: 411 results

Web of Science (Science Citation Index)

1. TOPIC fluorid*
2. TOPIC (euthyroid* or goiter* or goitre* or hyperthyroid* or hypothyroid* or thyroid* or thyrotoxicos*)
3. 1 and 2

Total: 180 results

Appendix B

Inclusion/Exclusion Criteria

A. Inclusion/Exclusion Criteria: Fluoride and Aquatic Life

1. Must include a specific, named harm vs. generic "pollution" or "contamination" or "accumulation".
2. Harmful outcome must pertain to aquatic plants and/or phytoplankton.
3. If study pertains to aquatic animals (e.g., salmon) or non-aquatic life, such as humans or sheep, exclude.
4. Fluoride vis-à-vis specific, named harm must be primary (vs. peripheral) focus. For example, if fluoride is one of a number of compounds being studied, exclude.
5. Focus must be on the direct effect of fluoride on the specific harm, versus interactive effect. For example, if the focus is how fluoride interacts with aluminum, exclude.
6. All forms (i.e., ions, compounds) and sources (i.e., "natural" and artifical, e.g., industrial waste, controlled addition at water systems) of fluoride should be considered for inclusion.
7. If primary focus is processes of defluoridation, exclude.
8. Must be original, empirical research (letters to the editor, editorials and commentaries are excluded).

B. Inclusion/Exclusion Criteria: Fluoride and Thyroid

1. Fluoride must be primary focus (vs. peripheral). For example, if fluoride is one of a number of factors being studied, exclude, unless it is a study of a range of outcomes related to either naturally high fluoride levels in a region's drinking water or artificially fluoridated water. Include if fluoride is one of only TWO compounds under investigation.
2. Focus must be on the direct effect of fluoride on the specific harm, versus interactive effect.
3. The specific harm must be explicitly related to the thyroid. If the paper considers the effects of fluoride on multiple organs/systems, exclude, unless the thyroid is one of only TWO systems being investigated (e.g., skeleton and thyroid).
4. Must be human science focused (have human application) versus veterinary sciences or related (e.g., tadpoles).
5. Exclude papers that are mechanism-focused.
6. If the study considers the effects on thyroid hormones, include if focus is on production; exclude if focus is on circulating hormones without direct reference to the thyroid or production of the hormones.
7. Must be original, empirical research (letters to the editor, editorials, and commentaries are excluded).