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Community Water Fluoridation: An Evidence Review

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Introduction

Purpose of the Evidence Review

This review evaluates evidence on potential benefits and harms of community water fluoridation (CWF). The City of Phoenix is currently considering whether or not to continue its CWF program. Concerns have been raised about potential harms and questions have been asked about the effectiveness of CWF in an era where there is ready access to other fluoride containing products. The University of Arizona's Mel and Enid Zuckerman College of Public Health has conducted this evidence review to present to the City Council to assist with their deliberations. It is an assessment and summary of the scientific evidence on the benefits and harms of CWF.

Scope of the Evidence Review

The following key questions are addressed in this review:

1. What are the known benefits of CWF programs?
2. What are the known harms of CWF programs?

This review does not include cost benefit analyses of CWF programs.

Conflicts of Interest

The authors have no conflicts of interest.

Methods

Evidence Search and Strategy

Appendix 1 demonstrates what evidence based methodologists refer to as the pyramid of evidence. The quality of scientific evidence, which reflects the confidence in the findings, is higher at the top of the pyramid and is lowest at the bottom. Appendix 2 includes a description of scientific study types, in the order of their quality.

High quality systematic reviews are the highest level of evidence one can obtain from the scientific literature. A systematic review looks at and describes the totality of the scientific evidence. Each individual study is assessed for quality and potential biases and the result of the analysis of all studies is presented. Policy makers should be wary of advocates on any side of an issue (for or against) who present single studies (referred to as "cherry picking") to support their views. Individual studies rarely are definitive, especially if they are of low quality.

The first step in conducting a systematic review is to search the scientific literature to determine if a systematic review on the topic of interest has already been conducted. If it has, and it is of high quality, the current review needs only to search the scientific literature from the date of the published review to the present, to add any new information. Appendix 3 lists the criteria we

assessed to determine the quality of a systematic review. These criteria are based on the standards for reporting systematic reviews, established by the Institute of Medicine (IOM).¹

If no high quality systematic review exists on the topic, one must be conducted from the beginning. The steps involved include searching all pertinent scientific databases, creating criteria to use to determine which studies should be included, assessing each study and summarizing all of the findings. These same steps are followed to update existing systematic reviews. The IOM publication includes a description of methods that should be used to conduct a systematic review.¹

We conducted an initial literature search, looking for systematic reviews, using the following databases: The Cochrane Library, Ovid and PubMed MEDLINE, Web of Science, and Google Scholar Bibliographies. We found seven systematic reviews, four of which were of high or moderate quality.²⁻⁵ These are described in table 1. The two of low quality are included in the table 2, with reasons for rating them low.^{6,7} One review was a summary of three systematic reviews, all of which are included in the four we discovered.⁸

The dates of publication of the four systematic reviews were, 2000, 2002, 2006, and 2007. We therefore conducted a literature search for additional individual studies from 2007 to the present. The search was conducted in July and August of 2012, utilized the same databases as the search for systematic reviews. The search terms used are included in appendix 4.

Studies that met all of the following criteria were included:

1. English language
2. Human study
3. Were relevant to one of the key questions

Studies that were excluded include those that were:

1. Animal studies
2. Case studies
3. Editorials or opinions
4. Descriptions of biochemical and pathophysiological pathways
5. Not relevant to the key question

This update search uncovered only seven additional studies.⁹⁻¹⁵ They are all of low quality or did not add any significant new information for the key questions asked. They are listed in table 2. The results found from the four higher quality systematic reviews will therefore serve as the basis for the results presented below. All 4 reviews came to the same conclusions.

The overall quality of the evidence for each question has been graded using the GRADE methodology illustrated in Appendix 5. When considering the quality of the evidence on CWF it is important to remember the limitations of studies on this topic. Since CWF is a community level intervention it by nature is studied using observational studies, or controlled, before and after studies, since randomized, controlled clinical trials are not possible. Therefore, using the GRADE system of assessing evidence the quality of the

evidence starts out low to moderate, although it can be upgraded if specified criteria are met.

Results

The results will be separated and presented in five categories: benefits, fluorosis, osteoporosis and fractures, cancers, other potential harms. Most of the studies of benefits and harms were conducted prior to the year 2000. However, there have been studies subsequent to that date and the results have been the same.

Benefits

There is high quality evidence that CWF programs reduce caries in children and adults. The presence of fluoride in community water supplies results in lower levels of caries, the addition of fluoride reduces the number of caries within a short period of time and the elimination of fluoride from a community water supply increases the number of caries within a short period of time. These results have been consistently found regardless of the date of the analysis showing that benefits persist even in an era of availability of fluoride from other sources.

The studies on this topic are either controlled, before and after analyses, or observational studies (cohort, cross sectional or ecological). However, the results are consistently found in multiple studies and there is a dose response (higher levels of fluoride and longer times of exposure result in fewer cavities) with the mean effect being in the range of a 25% reduction of caries. These findings justify the evidence being upgraded from moderate to high. We can have good confidence that these results are unlikely to be affected by future research.

Fluorosis

There is moderate quality evidence that CWF programs cause some degree of fluorosis (mottling or discoloration). Most of the studies on this issue are observational or before and after designs with significant flaws. However, the results are found consistently among studies and there is a dose response effect, with higher fluoride levels causing fluorosis in a higher proportion of the population. The evidence can therefore be upgraded from low to moderate. The best review estimates that at a fluoride concentration of 1.0 parts per million (ppm) about 4 % of the population would have fluorosis that would cause some aesthetic concern. There is no other known harm from this degree of fluorosis. We can have moderate confidence that this adverse effect is real, although of low prevalence and significance other than cosmetic.

Fractures

Four studies showed small increases and five studies showed small decreases in rates of fractures as a result of CWF. The majority of studies (20 of them) showed no effect. Most are low quality studies and there is significant heterogeneity among them. The summation of all studies indicates no effect of CWF on bone fracture rates, however the quality of the evidence is low.

Cancers

Out of 26 studies on this issue, one found a small increase in all cancers, another found a small decrease. One -third of these studies were of moderate quality with two-thirds being of low quality. Most found no differences in cancer rates. One study, out of 9 looking at bone cancers, found an increase among males, but this finding has not been replicated. The weight of the evidence points toward no cancer causation, with the quality of the evidence being moderate to low.

Other Potential Harms

There are over 30 studies looking at a variety of other potential harms from CWF. All are of low quality and all but two have had negative results. One found an elevated rate of Alzheimers and another an elevated rate of congenital malformations. Two studies out of 30 with positive findings is about what one would expect by chance, all studies are of low quality and none have been replicated.

As this report was being finalized an article appeared in the Arizona Republic regarding a possible link between CWF and thyroid disease. The study team conducted a quick review on this topic, which is described in appendix 6. There was no credible scientific evidence found linking CWF to thyroid disease. However, the review on this topic should not at this time be considered a complete systematic review.

Conclusions

The scientific evidence at this time provides high certainty that CWF benefits both children and adults with a reduction in tooth caries. There is moderate certainty that CWF causes tooth mottling in a small proportion of the population, which can have cosmetic consequences but no other known harm. There currently is no credible evidence of any other harms from CWF.

Table 1: Systematic Reviews Included in the Review

<i>Publication</i>	<i>Description</i>	<i>Significant Findings</i>	<i>Quality</i>
McDonagh MS, Whiting PF, Wilson PM, Sutton AJ, et al. Systematic review of water fluoridation. <i>BMJ</i> 2000;321(7265):855-859.	A systematic review consisting 214 articles from 25 distinct databases with a timespan from 1945 until February 2000. Reviewed the safety and efficacy of fluoridation of drinking water.	<ol style="list-style-type: none"> 1. Water fluoridation was associated with an increased proportion of children without caries and a reduction in the number of teeth affected by caries. There was a mean of 14% reduction in number of caries with a wide range of results from 0-64%. 2. A dose-dependent increase in dental fluorosis was found. At a fluoride level of 1 ppm an estimated 4% of exposed people would have fluorosis classified as aesthetically concerning. 3. An association between water fluoridation with other adverse effects was not found. 	<p>High Quality</p> <ul style="list-style-type: none"> • All quality criteria met
Truman BI, Gooch BF, Sulemana I, Gift HC, et al. Reviews of evidence on interventions to prevent dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries. <i>American Journal of Preventive Medicine</i> 2002;23(1):21-54.	A systematic review of effectiveness, applicability, other positive and negative effects, economic evaluations, and barriers to use of selected population-based interventions intended to prevent or control dental caries, oral and pharyngeal cancers, and sports-related craniofacial injuries. This review was completed by the Task Force on Community Preventive Services. Thirty articles were reviewed on the topic of CWF of which 21 were deemed appropriate according to the strict inclusion criteria.	<ol style="list-style-type: none"> 1. CWF results in a mean 41% reduction in caries. 2. Stopping CWF results in a median of 18/% increase in caries in 6-10 years. 3. Fluorosis is the only adverse effect proven to be caused by CWF. 	<p>Moderate to High Quality.</p> <ul style="list-style-type: none"> • Meets all the quality criteria. • Latest reviewed content included in the review regarding in CWF is from 1997. • Includes assessment of the evidence for other interventions. Those are not assessed here. • Did not independently assess harms. Relied on other systematic reviews for this.
Griffin SO, Regnier E, Griffin PM, Huntley V. Effectiveness of fluoride in preventing	A systematic review of the effects of CFW and other fluoride supplementation programs on preventing	<ol style="list-style-type: none"> 4. 1. CWF programs are effective in preventing caries in adults. They result in about a 25% reduction in 	<p>Moderate Quality</p> <ul style="list-style-type: none"> • Assessed only benefits, not harms.

caries in adults. J Dent Res 2007;86:410-415.	caries in adults. Included 20 studies , 9 involved CWF.	caries for adults who have lived in communities with CWF.	<ul style="list-style-type: none"> Searched only a limited number of data sets. No evidence that unpublished studies were sought.
Yeung CA. A systematic review of the efficacy and safety of fluoridation. Evidence-Based Dentistry 2008;9(2):39-43.	A systematic review on the health benefits and harms of water fluoridation. The review includes 77 articles from 3 distinct databases published between 1996 to 2006. The review was commissioned by the Australian National Health and Medical Research Council.	<ol style="list-style-type: none"> CWF is effective in preventing caries. No estimate on the amount of reduction. Flourosis can be caused by CWF but is usually mild. Occurs in about 4% . There is no proven association between CWF and osteoporosis, fractures, cancers, or any other adverse effect. 	Moderate to High Quality. <ul style="list-style-type: none"> Met all quality criteria except for searching only a limited number of databases. Addressed other caries prevention interventions which are not assessed in this report.
Parnell C, Whelton H, O'Mullane D. Water Fluoridation. European Archives of Paediatric Dentistry. 2009;10(3):141-148.	A review of the evidence from three systematic reviews on the effectiveness and safety of water fluoridation.	<ol style="list-style-type: none"> This article summarizes three systematic reviews that are included in this table. 	Quality criteria not appropriate as this was a summary of 3 systematic reviews.

Table 2: Publications After 2007 and Systematic Reviews Not Included

<i>Publication</i>	<i>Description and Design of Study</i>	<i>Findings</i>	<i>Quality</i>
Systematic Reviews			

<p>Newburg E. Effectiveness of water fluoridation. <i>Journal of Public Health Dentistry</i> 1989;49(5):279-289.</p>	<p>A review of 95 published articles in the MEDLINE database with the MeSH headings, “fluoridation” and “dental caries” from 1945 until 1983.</p>		<p>Low Quality</p> <ul style="list-style-type: none"> This review was conducted in 1989, before standards for systematic reviews had been developed. It meets only 1 of the quality criteria for systematic reviews.
<p>Pizzo G, Piscopo M, Pizzo I, Giuliana G. Community water fluoridation and caries prevention: a critical review. <i>Clin Oral Invest.</i> 2007;11:189-193.</p>	<p>A review of the current role of community water fluoridation in preventing dental caries. A search for original articles in the MEDLINE database published from January 2001 to June 2006.</p>		<p>Low Quality. Did not meet any of the quality criteria for systematic reviews.</p>
<p>Studies published 2007-Present</p>			
<p>Amini H, Taghavi SM, Amini M, Ramezani Mehrian M, Mokhayeri Y, Yunesian M. Drinking Water Fluoride and Blood Pressure? An Environmental Study. <i>Biological trace element research</i> 2011:1-7.</p>	<p>A retrospective ecological study on the relationship of fluoride in ground water resources of Iran with the blood pressure of Iranian residents.</p> <p>Data sets from previously published studies were employed for this ecological study.</p>	<p>1. A statistically significant correlation between Fluoride concentration in ground water sources and rates of hypertension in males and females.</p>	<p>Very Low Quality..</p> <ul style="list-style-type: none"> Ecological study design with potential for ecological fallacy. There was no controlling for confounding variables. Large risk of bias in data collection.
<p>Comber H, Deady S, Montgomery E, Gavin A. Drinking water fluoridation and osteosarcoma incidence on the island of Ireland. <i>Cancer Causes and Control</i> 2011:1-6.</p>	<p>This is an ecological study looking at osteosarcoma between 1994-2006 in Ireland. Data from the Northern Ireland Cancer Registry (NICR) and the National Cancer Registry of Ireland (NCRI) on osteosarcoma incidence in the above mentioned populations were used to estimate incidence rates in areas with and without drinking water fluoridation.</p>	<p>1. There was no significant difference in any incidence rates of osteosarcoma between fluoridated and non-fluoridated areas for either males or females.</p>	<p>Very Low Quality.</p> <ul style="list-style-type: none"> Ecological study design. Mentioned limitation: the rarity of the condition [osteosarcoma] and difficulty detecting significant differences in incidence rates. Methodology is not fully described in this article.

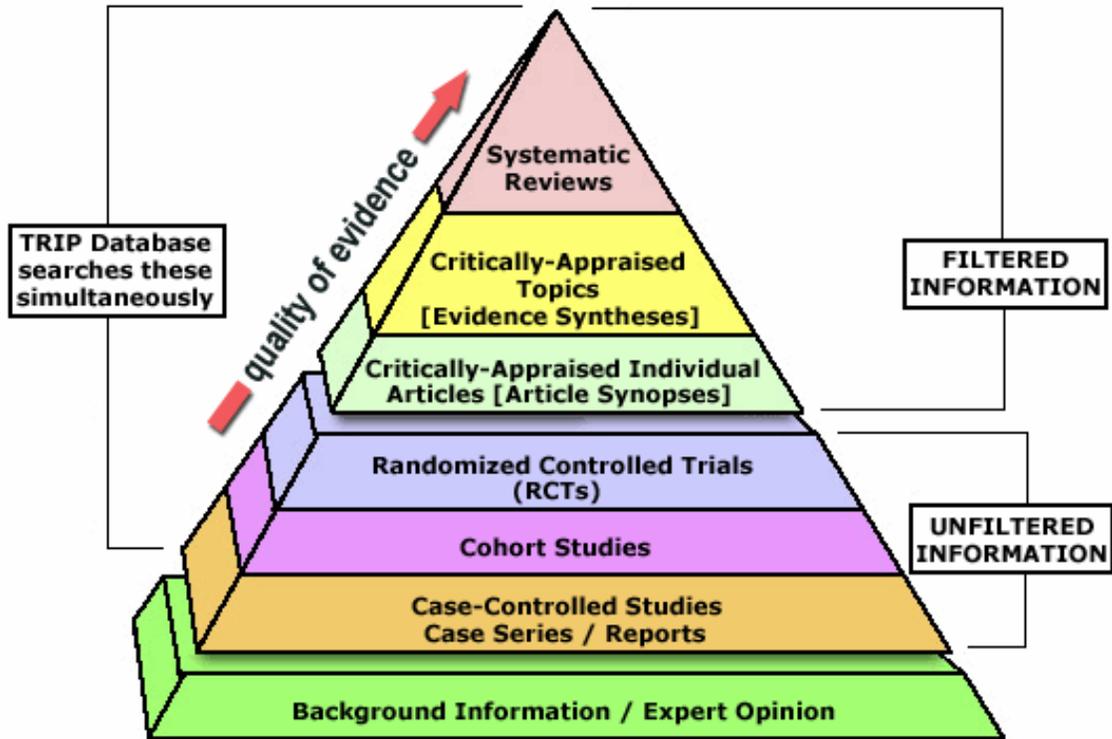
<p>Evans R, Hsiau A, Dennison P, Patterson A, Jalaludin B. Water fluoridation in the Blue Mountains reduces risk of tooth decay. <i>Australian Dental Journal</i> 2009;54(4):368-373.</p>	<p>Two cohorts of students were studied in Australia. In one cohort a CWF program was instituted, not in the areas of the other cohort. A survey in 1993 was disbursed amongst the students enrolled in eighteen schools that asked information regarding residential history, sources of drinking water pertinent to the study, and fluoride toothpaste exposure. In 2003 the survey was again disbursed amongst the children attending the same schools. At the 1993 survey, 2204 students between the ages of 4-12 years participated while in 2003, only 1963 children ages 5-13 years participated in the survey. A comparative analysis was employed to identify trends.</p>	<p>1. Water fluoridation reduced the DMFT (Decayed, Missing, Filled Teeth) incidences in children. Caries reduction occurred in the Blue Mountains as a direct benefit of water fluoridation. This finding is consistent with the literature.</p>	<p>Moderate Quality.</p> <ul style="list-style-type: none"> • Methodology is not fully explained. • Large sample sizes, applicable results. • Long time period between data collection year and publication year. • While the variable of interest was measured by examiners, they were probably not blinded to the cohorts. • No harms were studied.
<p>Frazao P, Peres M, Cury J. Drinking water quality and fluoride concentration. <i>Rev Saude Public</i> 2011;45(5).</p>	<p>A review analyzing the benefits and harms of fluoride concentration in drinking water in Brazil. Analysis is specific to Brazil. Systematic reviews studies; official documents and meteorological data were examined.</p>	<ul style="list-style-type: none"> • The article references publications listed in table 1 and reiterates those findings and applied them to policy in Brazil. 	<p>Quality raking does not apply as this is a review article with no new information.</p>
<p>Ismail AI, Hasson H. Fluoride supplements, dental caries and fluorosis: A systematic review. <i>The Journal of the American Dental Association</i> 2008;139(11):1457-1468.</p>	<p>A systematic review of the literature on the effectiveness of fluoride supplements in caries prevention and the risk for fluorosis.</p>	<p>Publication does not address the key question of CWF. It addressed oral FI supplementation.</p>	<p>No quality assessment performed.</p>
<p>Levy M, Leclerc BS. Fluoride in drinking water and osteosarcoma incidence rates in the continental United States among children and adolescents. <i>Cancer Epidemiology</i> 2011.</p>	<p>Ecological study design. States were the unit of analysis. The cumulative osteosarcoma incidence rate data from the CDC Wonder database for 1999–2006, categorized by age group, sex and states was compared to. data on the estimated percentage of the population served by community water systems who received naturally occurring or adjusted fluoridated water. System.</p>	<p>1. There was no correlation between the water fluoridation status in states and the osteosarcoma incidence rates during childhood and adolescence.</p>	<p>Very Low Quality.</p> <ul style="list-style-type: none"> • Ecological study design with a large unit of analysis (states)

<p>Neidell M, Herzog K, Glied S. The association between community water fluoridation and adult tooth loss. American journal of public health 2010;100(10):1980.</p>	<p>Ecological study using the county as the unit of analysis. Two data sources used: the 1995 through 1999 Behavioral Risk Factor Surveillance System, merged with data from the 1992 Water Fluoridation Census.</p>	<ol style="list-style-type: none"> 1. CWF levels in respondent's county of residence at the time of birth were significantly inversely related to tooth loss. For every 4 individuals that currently live in a county that fluoridated at their times of birth, 1 individual had 1 more tooth than if those individuals had not lived in a county that fluoridated. 2. The impact of CWF exposure is larger for individuals of lower socioeconomic status (SES) than for individuals of higher SES. Lower-SES individuals may be less able than are higher-SES individuals to compensate for the occurrence of dental caries through dental interventions. 	<p>Very Low Quality.</p> <ul style="list-style-type: none"> • Ecological study design. • Potential confounding not controlled for
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Appendix 1: Evidence Pyramid



Appendix 2: Taxonomy of Study Designs

BOX 1 Taxonomy of study designs to assess the effectiveness of an intervention

Experimental designs

A study in which the investigator has control over at least some study conditions, particularly decisions concerning the allocation of participants to different intervention groups.

1. Randomised controlled trial

Participants are randomly allocated to intervention or control groups and followed up over time to assess any differences in outcome rates. Randomisation with allocation concealment ensures that on average known and unknown determinants of outcome are evenly distributed between groups.

2. Quasi-randomised trial

Participants are allocated to intervention or control groups by the investigator, but the method of allocation falls short of genuine randomisation and allocation concealment (e.g. allocated by date of birth, hospital record number, etc.)

3. Non-randomised trial/quasi-experimental study

The investigator has control over the allocation of participants to groups, but does not attempt randomisation (e.g. patient or physician preference). Differs from a 'cohort study' in that the intention is experimental rather than observational.

Observational designs

A study in which natural variation in interventions (or exposure) among study participants is investigated to explore the effect of the interventions (or exposure) on health outcomes.

4. Controlled before-and-after study

A follow-up study of participants who have received an intervention and those who have not, measuring the outcome variable both at baseline and after the intervention period, comparing either final values if the groups are comparable at baseline, or change scores. It can also be considered an experimental design if the investigator has control over, or can deliberately manipulate, the introduction of the intervention.

5. Concurrent cohort study

A follow-up study that compares outcomes between participants who have received an intervention and those who have not. Participants are studied during the same (concurrent) period either prospectively or, more commonly, retrospectively.

6. Historical cohort study

A variation on the traditional cohort study where the outcome from a new intervention is established for participants studied in one period and compared with those who did not receive the intervention in a previous period, i.e. participants are not studied concurrently.

7. Case-control study

Participants with and without a given outcome are identified (cases and controls respectively) and exposure to a given intervention(s) between the two groups compared.

8. Before-and-after study

Comparison of outcomes from study participants before and after an intervention is introduced. The before and after measurements may be made in the same participants, or in different samples. It can also be considered an experimental design if the investigator has control over, or can deliberately manipulate, the introduction of the intervention.

9. Cross-sectional study

Examination of the relationship between disease and other variables of interest as they exist in a defined population at one particular time point.

10. Case series

Description of a number of cases of an intervention and outcome (no comparison with a control group).

Appendix 3

Systematic Review Quality Criteria

- Adequate number of databases searched
- Unpublished studies searched
- Inclusion and exclusion criteria spelled out
- More than one reviewer assessing articles
- Each study assessed for quality using standard tool
- Data from multiple studies combined if possible
- Overall summary assessment of evidence quality presented
- Both potential benefits and potential harms included

Appendix 4 Search Terms

Initial Terms used

1. water supply
2. dental caries
3. fluoridation

Mesh Terms

Health Care Category

Environmental and Public Health

Public Health Dentistry

Fluoridation [Major Topic]

- fluoridation/adverse effects
- fluoridation/instrumentation
- fluoridation/trends
- fluoridation/utilization

Mesh Terms

Diseases Category

Stomatognathic Diseases

Tooth Diseases

Tooth Demineralization

Dental Caries

- dental caries/prevention and control

Mesh Terms

Health Care Category

Environment and Public Health

Public Health

Sanitation

Sanitary Engineering

Water Supply

- water supply/fluoridation

Appendix 5: GRADE Method of Assessing Evidence

Study Design	Quality of Evidence	Lower if	Higher if
Randomized trial →	High	Risk of bias -1 Serious -2 Very serious	Large effect +1 Large +2 Very large
	Moderate	Inconsistency -1 Serious -2 Very serious	Dose response +1 Evidence of a gradient
Observational study →	Low	Indirectness -1 Serious -2 Very serious	All plausible confounding +1 Would reduce a demonstrated effect or
	Very low	Imprecision -1 Serious -2 Very serious Publication bias -1 Likely -2 Very likely	+1 Would suggest a spurious effect when results show no effect

Owens DK, Lohr KN, Atkins D, et al. Grading the strength of a body of evidence when comparing medical interventions. In: Agency for Healthcare Research and Quality. Methods Guide for Comparative Effectiveness Reviews. Rockville, MD. Available at: <http://effectivehealthcare.ahrq.gov/healthInfo.cfm?infotype=rr&ProcessID=60>.

Appendix 6 Additional Search on Thyroid Disease

After this evidence report was completed, the authors read an article in the Arizona Republic that described a citizen that claimed her thyroid disease was caused by fluoride in the drinking water and that she has uncovered information on the internet to substantiate her claim. Since none of the systematic reviews found for this report mentioned thyroid disease the authors conducted a separate search using the terms “fluoride” and “thyroid” using the databases Medline/Ovid and the Cochrane Library.

The search found 14 articles. Two were not related to the topic and mentioned fluoride only superficially, one was a letter to the editor commenting on one of the other articles, and one was a hypothesis presentation with no data. Of the remaining 10, five were animal studies in which either rats or dogs were given fluoride at 200 or more times the level in drinking water, with four demonstrating some effect on thyroid function and one showing no effect. Two articles had to be ordered from an outside library and could not be obtained by the time this report was completed. They will be reviewed once they arrive. Both appeared to be correlational (ecological studies). That left three articles to review.

Two studies were correlational (ecological) and are very low quality.^{1,2} One was conducted in Nepal the other in South Africa. Both were small studies in communities with low levels of iodine. The study in Nepal found a correlation between community water fluoride levels and rates of goiters in children, but the differences in the water fluoride levels was very small and all water sources contained very low levels of fluoride. The study in South Africa found no correlation between community water fluoride levels and rates of goiter but did find two towns with high rates of goiter and high levels of fluoride in the water.

The remaining study is a small clinical trial using sodium fluoride to treat osteoporosis, providing fluoride at much higher levels than is present in drinking water, and testing thyroid function after 3 and 6 months.³ No effect on thyroid function was found. This article was only available as an abstract and is not pertinent to the question about CWF.

In reviewing the references for the two correlational studies 6 older correlational studies were discovered with one published in the 1930's, one in the 1940's, two in the 1950's, and two in the 1960's. The authors will obtain those studies and review them. The citations state that they have conflicting results.

In conclusion, no credible evidence was found of any adverse effects of CWF on thyroid function in humans. This review, however, is not a complete evidence report. The authors would be happy to conduct a more complete assessment of this question if the Council requests it.

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