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HEALTH TECHNOLOGY ASSESSMENT

Community Water Fluoridation Programs: A Health Technology Assessment Protocol

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Background and Rationale

Fluoride is a negative ion (F^-) of the element fluorine (F_2).[1] The term fluoride also refers to compounds containing F^-, such as NaF (sodium fluoride), CaF_2 (calcium fluoride), H_2SiF_6 (fluorosilicic acid), or Na_2SiF_6 (sodium fluorosilicate).[1] In water, these compounds dissociate to release F^-.[1]

Fluoride compounds exist in soil, air, plants, animals, and water.[2] In the early 20th century, it was discovered that people living in areas with high concentrations of naturally occurring water fluoride, such as Colorado Springs, US, had permanent brown stains on the surfaces of their teeth.[3] This discoloration later became known as dental fluorosis — a side effect of prolonged exposure to higher-than-recommended levels of fluoride that is characterized by decreased mineral content (hypomineralization) in tooth enamel.[4-7] Depending on the severity of the condition, discoloration can vary from mild (e.g., barely noticeable white flecks) to severe (e.g., brown stains).[5] Epidemiological studies in the 1930s and 1940s found that people living in areas with high levels of naturally occurring fluoride in water had a low incidence of dental caries (i.e., cavities and tooth decay) — a chronic and progressive disease of the mineralized and soft tissue of the teeth. This led to the controlled addition of fluoride (also known as artificial fluoridation) to community drinking water with low-fluoride levels for caries prevention.[8,9] In 1945, Brantford, Ontario became the first city in Canada and the third city in the world to implement drinking water fluoridation.[10,11]

According to the 2010 Health Canada Guidelines for Drinking Water Quality, the maximum acceptable concentration (MAC) of fluoride in drinking water is 1.5 parts per million (ppm) or mg/L. However, the optimal level of fluoride in drinking water for providing dental health benefits and minimizing dental fluorosis is recommended to be 0.7 ppm (reduced from a previous range of 0.8 ppm to 1.0 ppm).[2] Thus, community water fluoridation (CWF) in Canada is a process of controlling fluoride levels in the public water supply to reach the recommended optimal level of 0.7 ppm and not exceed the MAC of 1.5 ppm.[2]

There are several options to lower fluoride levels in water, including blending fluoride-rich water with fluoride-low water; selecting low-fluoride water sources; or removing excess fluoride by various technologies, such as activated alumina, reverse osmosis, lime softening, and ion exchange.[2] Most sources of drinking water in Canada have low levels of naturally occurring fluoride.[2] According to a Canadian survey conducted between 1984 and 1989, the average naturally occurring fluoride levels in drinking water ranged from less than 0.05 ppm in British Columbia and Prince Edward Island to 0.21 ppm in the Yukon.[2] Elevated levels of naturally occurring fluoride are relatively rare in Canada, although some individual communities in Quebec, Saskatchewan, and Alberta have fluoride concentrations in drinking water sources as high as 2.52 to 4.35 ppm.[2] The provincial and territorial data on drinking water in 2005 provided by the Federal-Provincial-Territorial Committee on Drinking Water showed that average fluoride concentrations in fluoridated drinking water across Canada ranged between 0.46 and 1.1 ppm.[2] As of 2007, about 45% of Canadians had been exposed to controlled drinking water fluoridation for the prevention of dental caries.[1,12] By 2011, many large Canadian cities had adopted water fluoridation; Vancouver, Regina, and Montreal were exceptions.[1] The decision to fluoridate drinking water is not regulated at the federal, provincial, or territorial level. It is regulated at the municipal level, where decisions are often taken by means of a community vote (i.e., by referendum or plebiscite).[1]

Daily intake levels of fluoride in humans vary depending on many factors, such as sources of fluoride (water, foods or beverages, or dental products), level of fluoride in water or foods, amount of water or food consumed, and individual characteristics and habits (e.g., dental hygiene).[1] About 75% to 90% of ingested fluoride is absorbed through the gastrointestinal tract; up to 75% is deposited within 24 hours in calcified tissues, such as bones and teeth, in the form of fluorapatite.[13,14] The rest is excreted, primarily in the urine, with small amounts also excreted in perspiration, saliva, breast milk, and feces.[13,14] In 2007, a dietary survey of the Canadian population estimated that the average intake of fluoride in children aged one to four years old in fluoridated and non-fluoridated communities was 0.026 mg/kg/day and 0.016 mg/kg/day, respectively.[1] The average dietary intake of fluoride in adults aged 20 years and older ranged from 0.038 mg/kg/day to 0.048 mg/kg/day in fluoridated communities, and 0.024 mg/kg/day to 0.033 mg/kg/day in non-fluoridated communities.[1] The recommended adequate intake (AI) of fluoride — that is, the amount sufficient to prevent dental caries — and the tolerable upper limit (UL) of fluoride intake vary by age, sex, and whether a woman is pregnant.[15,16] For instance, a child between four and eight years old with a standard body weight of 22 kg would require an AI of 1.1 mg/day and a UL of 4.4 mg/day.[15] For adults (≥ 19 years old) with a standard body weight of 76 kg (for men) and 61 kg (for women), the AI values are 4.0 mg/day and 3.0 mg/day, respectively.[15] The UL value is 10.0 mg/day for all adults based on the relationship between fluoride intake and skeletal fluorosis, a condition caused by excessive accumulation of fluoride in the bones.[15] The AI and UL values are similar for both pregnant and non-pregnant women.[15]

Dental caries are a common public health problem in Canada (five to eight times more common than asthma).[17] It affects about 57% of children aged six years to 11 years and 59% of adolescents aged 12 years to 18 years.[18] It has been estimated that the prevalences of coronary caries and root caries for Canadian adults aged 19 years and older are 96% and 14%, respectively.[18] Dental caries can result in pain, infection, premature tooth loss, and misaligned teeth.[19] Untreated dental caries in children are associated with poor overall growth, iron deficiency, behaviour problems, low self-esteem, and reductions in school attendance and performance.[20-25] In pregnant women, tooth decay and other dental health issues are risk factors for preterm low birth weight.[26,27] By adulthood, about 96% of Canadians have experienced dental caries, with a mean of 10.7 decayed, missing, or filled teeth.[18] Dental caries seem to affect higher proportions of Canadians when compared internationally, but the severity appears to be less than that in Australia and similar to that in the US.[18] In 2009, the cost of dental services was estimated to be higher than $12 billion in Canada — about $360 per Canadian, based on total national health expenditures estimated from both the private sector ($11.5 billion) and public sector ($0.7 billion).[28]

Fluoride prevents dental caries both systemically (pre-eruptive, or before the teeth emerge) and topically (post-eruptive, or on the tooth surface).[29,30] The systemic effect occurs through the incorporation of ingested fluoride into enamel during tooth formation, strengthening the teeth and making them more resistant to decay.[30-32] The major sources of systemic fluoride are fluoridated water, and foods and beverages prepared in areas with fluoridated water.[33,34] Fluoride from other sources, such as toothpastes, mouth rinses, gels, varnishes, or foams, provides a topical effect through direct contact with exposed tooth surfaces; this increases tooth resistance to decay against bacterial acid attack by inhibiting tooth de-mineralization, facilitating tooth re-mineralization, and inhibiting the activity of bacteria in plaque.[35] As well, after being absorbed systemically, a small portion of fluoride is excreted into the saliva, where it provides a topical effect from the continuous bathing of the teeth in saliva.[36]

While public and dental health agencies and organizations — and more than 60% of Canadians who were aware of CWF, based on a 2008 telephone survey[37] — view CWF as a cost-effective and equitable means of improving and protecting the dental health of populations, there continues to be opposition, resistance, and skepticism about it, especially in terms of human and environmental health.[1,38-40] There is a diversity of different perspectives on CWF, some of which centre on the scientific evidence of clinical benefit. Other arguments include the availability of alternative oral public health programs or interventions that avoid perceived concerns about CWF.[41] Alternative publicly funded oral public health programs, such as school-based topical fluoride varnishes, are available in communities across Canada. However, there is low uptake of these interventions, as school participation rates and target age groups vary across communities and municipalities within each jurisdiction. Furthermore, public health programming is often targeted toward youth, excluding adult and elderly populations. CWF, in contrast, is an intervention that reaches a broader population. Still others cite evidence of the potentially harmful side effects of fluoridation — such as fluorosis, impaired thyroid function, lower average intelligence quotients, and negative environmental impact[39,40] — as justification for water fluoridation cessation. Additional concerns name possible relationships between industry and fluoridation as worrisome.[39] Finally, an unsettled tension exists around the ethics of CWF in terms of distribution of benefits to all persons who consume fluoridated tap water, removing (or making very difficult) the ability to "choose" fluoridation.[39]

Within this context, some municipalities are choosing to cease water fluoridation, leading to its decline. Notably, large Canadian cities such as Calgary, Quebec City, Windsor, Moncton, and Saint John have discontinued their water fluoridation programs in recent years.[42-44] The impact of CWF cessation on dental health is unclear.

A request has been submitted to CADTH for a Health Technology Assessment (HTA) that would comprehensively review the evidence and other considerations related to CWF. The review is not intended to be a comprehensive assessment of all interventions for caries prevention. In contrast to other public health programs, such as school programs, water fluoridation, where available, has the potential to reach a broader population. Alternatives available at the population level, such as fluoridated milk or fluoridated salt, are either unavailable in Canada, not publicly funded, or do not eliminate other concerns that have been raised with the use of fluoride. The HTA will focus exclusively on CWF, and will not examine the effectiveness of other sources of fluoride, including fluoridated dental products, fluoridated salts, and fluoride supplements. Furthermore, we will not compare the clinical effectiveness of CWF to these other sources of fluoride.

This HTA is intended to provide guidance to policy- and decision-makers at the municipal levels to help orient discussions and decisions about water fluoridation in Canada. The HTA will seek to address the following policy question:

Policy Question

Should community water fluoridation be encouraged and maintained in Canada?

Objective

The aim of this HTA is to inform the policy question by assessing the clinical effectiveness and safety of CWF as well as the related economic considerations, social dimensions,

implementation issues, environmental impact, and ethical considerations. Analyses of the evidence related to these considerations are presented in different chapters of the HTA, each with specific and different research questions and methodologies.

Research Questions

The HTA will address the following research questions:

Clinical Review

1. What is the effectiveness of community water fluoridation (fluoride level between 0.4 ppm and 1.5 ppm) compared with non-fluoridated drinking water (fluoride level < 0.4 ppm) in the prevention of dental caries in children and adults?
2. What are the effects of community water fluoridation cessation (fluoride level < 0.4 ppm) on dental caries in children and adults compared with continued community water fluoridation (fluoride level between 0.4 ppm and 1.5 ppm), the period before cessation of water fluoridation (fluoride level between 0.4 ppm and 1.5 ppm), or non-fluoridated communities (fluoride level < 0.4 ppm)?
3. What are the negative effects of community water fluoridation (at a given fluoride level) compared with non-fluoridated drinking water (fluoride level < 0.4 ppm) or fluoridation at different levels on human health outcomes?

Economic Analysis

4. From a societal perspective, what is the budget impact of introducing water fluoridation in a Canadian municipality without an existing community water fluoridation program?
5. From a societal perspective, what is the budget impact of ceasing water fluoridation in a Canadian municipality that currently has a community water fluoridation program ?

Social Dimensions

6. How is community water fluoridation conceptualized, communicated, and enacted by public health practitioners, municipal decision-makers, and members of the general public who may be affected by its implementation or cessation?

Implementation Issues

7. What are the main challenges, considerations, and enablers related to implementing or maintaining community water fluoridation programs in Canada?
8. What are the main challenges, considerations, and enablers related to the cessation of community water fluoridation programs in Canada?

Environmental Assessment

9. What are the potential environmental (toxicological) risks associated with community water fluoridation?

Ethical Considerations

10. What are the major ethical issues raised by the implementation of community water fluoridation?

11. What are the major ethical issues raised by the cessation of community water fluoridation?
12. What are the major ethical issues raised by the legal, social, and cultural considerations to consider for implementation and cessation?

An analytic framework for the HTA and a discussion of how the research questions will be addressed can be found in Appendix 1.

Methods

To inform the preparation of this protocol, a preliminary scoping review of existing HTAs and systematic reviews was conducted. This protocol was developed a priori, and will be followed throughout the HTA process. This protocol has also been prospectively registered in the PROSPERO database (https://www.crd.york.ac.uk/PROSPERO/); any deviations will be disclosed in the final report. Likewise, any updates will be made to the PROSPERO submission.

Clinical Review

The clinical review will attempt to answer the following research questions:

1. What is the effectiveness of community water fluoridation (fluoride level between 0.4 ppm and 1.5 ppm) compared with non-fluoridated drinking water (fluoride level < 0.4 ppm) in the prevention of dental caries in children and adults?
2. What are the effects of community water fluoridation cessation (fluoride level < 0.4 ppm) on dental caries in children and adults compared with continued community water fluoridation (fluoride level between 0.4 ppm and 1.5 ppm), the period before cessation of water fluoridation (fluoride level between 0.4 ppm and 1.5 ppm), or non-fluoridated communities (fluoride level < 0.4 ppm)?
3. What are the negative effects of community water fluoridation (at a given fluoride level) compared with non-fluoridated drinking water (fluoride level < 0.4 ppm) or fluoridation at different levels on human health outcomes?

Study Design

To reduce redundancy in research and leverage existing published research, updates to two previously published systematic reviews identified through our initial systematic scoping will be conducted. While other related reviews have been published in the past decades,[45-50] in accordance with recent guidance documents, these two reviews have been identified as the most recent, comprehensive, and relevant to our policy question.[51] Further, their methodological quality was considered sufficient to warrant an update as compared to a *de novo* review; details of methods and results are reported transparently and comprehensively to facilitate the updating process.

To address the research questions related to the effects of CWF (Questions 1 and 3), an update of the 2016 Australian National Health and Medical Research Council (NHMRC) review by Jack et al.[52] will be conducted. To address the research question related to the impacts of CWF cessation on dental caries (Question 2), the 2016 systematic review by McLaren and Singhal will be updated.[42]

The NHMRC review process included two main parts. The first, an evaluation of the dental effects of water fluoridation, consisted of an overview of reviews and a systematic review of the primary studies on the effects of water fluoridation on dental caries, and a critical appraisal of the evidence on the role of water fluoridation in the development of dental fluorosis included in a 2015 Cochrane review.[46] The second part consisted of a systematic review of other (non-dental) health effects of water fluoridation. The 2016 NHMRC review is an update of a 2007 NHMRC review, which included publications from 1996 onward.[45] The time frame for the literature search strategy of the 2016 NHMRC review for dental caries (Question 1) was between October 1, 2006 and November 12, 2015; for other health outcomes of water fluoridation (Question 3), it was between October 1, 2006 and October 14, 2014. The search period of the systematic review by McLaren and Singhal 2016[42] was from inception of databases to September 29, 2014. Therefore, the search period of the current review will be from January 1, 2014 onwards.

The protocol for the clinical review was developed in consideration of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) checklist[53] for guidance on clarity and completeness.

Literature Search Strategy

The literature search will be performed by an information specialist using a peer-reviewed search strategy. The clinical search strategy is presented in Appendix 2.

For the clinical search, published literature will be identified by searching a relevant selection of CADTH subscription databases: MEDLINE (1946–) with in-process records and daily updates; Embase (1974–); the Cochrane Central Register of Controlled Trials; the Cochrane Database of Systematic Reviews; the Cochrane Methodology Register; the Database of Abstracts of Reviews of Effects and the HTA database via Ovid; the Cumulative Index to Nursing and Allied Health Literature (CINAHL) (1981–) via EBSCO; PubMed; and Scopus. The search strategy will comprise both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords.

The search strategies developed for the Australian NHMRC 2016 review[52] relevant to research questions 1 and 3, and the search strategy developed for the systematic review by McLaren and Singhal 2016[42] relevant to research question 2, will be restructured and additional subject headings and keywords incorporated to produce a single broad search strategy. This single strategy will be used to identify literature relevant to all three research questions. The main search concepts will be fluoridation and fluoride in water. To keep the search broad, search concepts for dental caries, cessation, and health outcomes will not be integrated into the search strategy. While the original searches for NHMRC 2016[52] and McLaren and Singhal[42] included multiple databases, the databases used for the clinical search will be limited to those recommended in the Cochrane Handbook[54] and supplemented with other databases to which CADTH has access.

Retrieval will be limited to documents added to the databases since January 1, 2014 to capture studies after the literature searches for NHMRC 2016[52] and McLaren and Singhal 2016[42] were conducted. Conference abstracts will be excluded from the search results. No methodological filters or language limits will be applied.

Regular alerts will be established to update the searches until the publication of the final report. Regular search updates will be performed on databases that do not provide alert services. Studies identified in the alerts that meet the selection criteria of the review will be incorporated into the analysis if they are identified prior to the completion of the stakeholder feedback period of the final report. Any studies that are identified after the stakeholder feedback period will be described in the discussion, with a focus on comparing the results of these new studies with the results of the analysis conducted for this report.

Grey literature (literature that is not commercially published) will be identified by searching the *Grey Matters* checklist (https://www.cadth.ca/grey-matters), which includes the websites of HTA agencies, clinical guideline repositories, systematic review repositories, economics-related resources, public perspective groups, and professional associations. Google and other Internet search engines will be used to search for additional Web-based materials. These searches will be supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry.

Study Eligibility

The eligibility criteria for clinical studies are outlined in Table 1.

Table 1: Selection Criteria for Clinical Review

Population	Human populations of any age Subgroups: • Age (e.g., 0 years to 9 years, 10 years to 17 years, 18 years and older, and ≥ 65 years) • Geographic location (e.g., remote, rural, and urban) • Socio-economic status (e.g., high, mid, and low in terms of education or household income)[a]
Intervention or Exposure	Q1: Natural or artificial water fluoridation (fluoride level 0.4 ppm to 1.5 ppm)[b] Q2: Cessation of water fluoridation (fluoride level < 0.4 ppm) Q3: Water fluoridation at any level[c]
Comparator	Q1: Non-fluoridated water (fluoride level < 0.4 ppm) Q2: Continued water fluoridation (fluoride level 0.4 ppm to 1.5 ppm), before cessation of water fluoridation, or non-fluoridation community Q3: Non-fluoridated water (fluoride level < 0.4 ppm) or different fluoride levels in drinking water
Outcomes	**Clinical effectiveness (Q1 and Q2):** Any measure of dental outcomes including but not limited to: • Mean dmft or DMFT • Mean dmfs or DMFS • Mean dfs or DFS • Proportion of children with or without caries in primary teeth • Proportion of individuals with or without caries in permanent teeth • Hospital admissions for dental surgery under general anesthesia **Negative effects (Q3):** Any measure of adverse health outcomes associated with water fluoridation, including but not limited to: • Dental fluorosis • Skeletal fluorosis • Bone development and bone fracture • Thyroid function • Cancer • Neurodevelopment • Mortality • Other negative effects

Time Frame	January 1, 2014 to present
Study Designs	Primary studies of any design: RCTs as well as comparative observational studies (including concurrent or historical cohort studies, case-control studies, interrupted time series, cross-sectional studies, ecological studies, and before-and-after studies)

DFS = decay, and filled (permanent) tooth surfaces; dfs = decay, and filled (primary) tooth surfaces; DMFS = decay, missing/extracted, and filled (permanent) tooth surfaces; dmfs – decay, missing/extracted, and filled (primary) tooth surfaces; DMFT = decay, missing/extracted, and filled (permanent) teeth; dmft = decay, missing/extracted, and filled (primary) teeth; NHMRC = National Health and Medical Research Council; ppm = part per million; Q = question; RCT = randomized controlled trial.

[a] As defined by the included studies.

[b] The average fluoride concentration in fluoridated drinking water across Canada ranges from 0.46 ppm to 1.1 ppm. The fluoride level of 0.4 ppm was chosen to mark the cut-off between non-fluoridated and fluoridated water. This level is in line with that set in the NHMRC 2016 and other previous systematic reviews.

[c] Fluoride at any level will be applied for the intervention of question 3 with the intent to capture all adverse health outcomes potentially associated with water fluoridation.

Full-text published or unpublished studies in English or French that meet the criteria outlined in Table 1 will be included. Conference abstracts, duplicates of publication of the same study, narrative reviews, letters, editorials, laboratory studies, and technical reports will be excluded.

For questions related to the effectiveness of CWF and the impact of fluoridation cessation on dental caries (i.e., questions 1 and 2), studies will be excluded if they assessed the impact of a fluoride level in community drinking water greater than 1.5 ppm, based on Health Canada guidance on the maximum acceptable level in drinking water,[2] or if they assessed the effects of fluoride from sources other than drinking water, such as supplements, toothpastes, mouth rinses, salt, milk, diet, soil, air. Participants of any age in any jurisdiction who resided in a fluoridated and non-fluoridated community, whether in conjunction with other sources of fluorides (e.g., fluoridated toothpaste) or without, will be included. In addition to the absence of a limit on participants' age, there will be no limits regarding geographic location, socio-economic status, or ethnicity.

For the question related to the effectiveness of CWF on dental caries (question 1), a fluoridated-water community (artificially or naturally fluoridated) will be compared with a non–fluoridated-water community (fluoride level < 0.4 ppm) or with the same community before the introduction of water fluoridation. In addition, studies will be also included if they compared participants' percentage exposures to CWF. For instance, a study will be considered for inclusion when comparing 100% (or any percentage) lifetime exposure with 0% (or any percentage lower than 100%) lifetime exposure to water fluoridation. The effect of CWF will not be compared with the effects of fluoridation from other fluoridated products, as they will be considered as confounding variables. Confounding variables of interest include oral health habits (i.e., brushing teeth, flossing, using mouthwash, etc.), diet, socio-economic status, and the presence of other public health programming. As in the exclusion criteria of the National Health and Medical Research (NHMRC) 2016 review,[52] studies that did not conduct multivariable analysis to control for confounding variables will be excluded. Given the widespread use and availability of fluoridated toothpaste in both fluoridated and non-fluoridated communities, the effect of water fluoridation will be considered to be above and beyond the effect of fluoridated toothpaste. In addition to the confounding variables listed above, the presence of other public health interventions, such as school-based varnish programs, will also be taken into consideration. Where possible, data will be extracted to inform a subgroup analysis of the effect of other public health interventions, particularly in communities without water fluoridation.

For the question related to the impact of fluoridation cessation on dental caries (question 2), a community where water fluoridation was discontinued will be compared with a fluoridated

community, a non-fluoridated community, or the same community at a period before the cessation of water fluoridation.

For the question related to the effects of CWF on human health (question 3), a community where people are exposed to any level of fluoride in drinking water will be compared with a non-fluoridated community (< 0.4 ppm) or a community with different concentrations of fluoride in its drinking water. For outcomes, any measure of dental caries and adverse health outcomes as a result of fluoridated water exposure or non-exposure will be considered. For the purpose of updating the evidence in the literature, comparative primary studies of any study design will be considered.

Study Selection

DistillerSR[55] will be used to manage the selection process. Two reviewers will independently screen titles and abstracts of all citations retrieved from the literature search relevant to research questions 1 to 3, followed by an independent review of the full-text articles, based on the pre-determined selection criteria outlined in Table 1. The two reviewers will then compare their included and excluded studies from their full-text reviews and resolve any disagreements through discussion until consensus is reached, involving a third reviewer if necessary. The study selection process will be presented in a PRISMA flowchart.

The draft list of included studies will be posted for stakeholder review for 10 business days, during which time feedback and any additional studies identified for potential inclusion will be reviewed. Final lists of included and excluded studies (with reasons for exclusion) will be presented in the final report.

Data Extraction

Data extraction for included studies will be conducted using standardized data abstraction forms similar to those in the NHMRC 2016 report[52] (Appendix 4), which have been designed to collect relevant information from primary studies.

Two reviewers will pilot the data extraction form, in duplicate, on three randomly selected studies. Following calibration, data from each included study will be extracted by one reviewer and verified by a second reviewer. Disagreements will be resolved through discussion until consensus is reached, involving a third reviewer if necessary. Data will not be extracted from figures if they do not explicitly provide relevant, numerical data. In instances where a lack of clarity is identified in any included report of findings, authors will be contacted by email to request any missing information. If any authors cannot be contacted, the results will be described without actual numerical values.

Quality Assessment of Included Studies

The National Institute for Health and Care Excellence (NICE) checklists, which were designed for public health intervention studies, will be used to assess the quality of primary studies of CWF.[56] One generic checklist will be used to assess the quality of quantitative intervention studies, such as randomized controlled trials (RCTs), case-control studies, cohort studies, controlled before-and-after studies, and interrupted time series.[56] The other checklist will be used to assess the quality of quantitative studies reporting correlations and associations, such as cross-sectional and ecological studies.[56] The quality assessment checklists for primary studies are presented in Appendix 5.

Potential confounding factors to be considered in the primary studies will be age, sex, medical history, socioeconomic factors (e.g., income, education), other dental public health programming, and lifestyle factors, including tooth brushing, fluoride from other sources (e.g., fluoridated toothpaste, fluoride tablets, food, tea, coal smoke), and dietary habits (e.g., sugar consumption, water consumption). Studies that did not record, include, or adjust for any of those confounders in the analysis will be considered to have a potentially high risk of bias.

Two researchers will pilot the assessment of the risk of bias, in duplicate, on three randomly selected studies. Following the calibration, the risk of bias of the remaining studies will be independently assessed by two reviewers. Disagreements between reviewers regarding assessment of risk of bias will be resolved through discussion and consensus; a third researcher will be consulted when necessary. The findings of the risk of bias assessments for each included study will be tabulated and an assessment of the risk of bias across studies summarized. These assessments will not be used to further include or exclude studies.

Data Analysis

A narrative synthesis will be conducted. Most studies identified in the systematic reviews conducted by NHMRC 2016[52] and McLaren and Singhal 2016[42] are of ecological and cross-sectional design, highly heterogeneous, and affected by multiple confounding variables. Based on the initial scoping during the development of this protocol, it is anticipated that studies identified in this review will also be of similar study design and that the number of studies identified in this review will be much smaller compared with the large body of evidence found prior to 2014. Taken together, a meta-analysis is not expected to be warranted in this review due to the substantial heterogeneity and quantity of new evidence; instead, a narrative synthesis of the results of the updated SRs and primary studies will be discussed alongside study characteristics, study quality, and the summary tables of the findings.

The findings will be presented by outcomes, starting with the findings of the systematic reviews followed by the results for the primary studies identified in the updated search. Summary tables will be made to include the findings of the updated systematic reviews together with those identified in this review. For the interpretation of the results, the evidence of each outcome will be presented together with the risk of bias and the applicability of the included studies to the Canadian context. Risk of bias in each study will be assessed and the quality of each study classified as high, acceptable, or low based on the internal validity of the study results (i.e., how well the study minimized sources of bias by adjusting for potential confounders) and the generalizability of the findings to Canadian population. Applicability will be judged by the review authors based on comparability with the Canadian context, including fluoride levels in fluoridated and non-fluoridated water, socio-economic factors, and similarity of dental and health care systems to Canada.

For each outcome table, a narrative summary will be prepared to describe results within and across studies. Within the summary, attention will be paid to describing the direction and size of the observed effect and consistency in effect across studies. When differences are observed, an attempt will be made to explain those differences by study and patient characteristics. Findings related to subgroups will be presented and described narratively, depending on the availability of the data.

Economic Analysis

Systematic reviews of economic evaluations for CWF have found that fluoridating community drinking water is a cost-saving technology for preventing caries.[57,58] From the perspective of a municipal decision-maker who needs to decide whether to implement or cease using this technology, the value for money and impact on public health may not be the only considerations. This decision involves considerable costs and budget implications. In light of the existing literature on this topic and the need to provide additional information to decision-makers on the financial impact of the decision, this economic analysis will focus on budget impact analyses to address the following research questions:

4. From a societal perspective, what is the budget impact of introducing water fluoridation in a Canadian municipality without an existing community water fluoridation program?
5. From a societal perspective, what is the budget impact of ceasing water fluoridation in a Canadian municipality that currently has a community water fluoridation program?

For question 4, the analysis will estimate the budget impact of introducing a CWF program compared with leaving water unfluoridated in municipalities that have naturally low levels of fluoride in their drinking water. Question 5 will be addressed by estimating the budget impact of discontinuing current CWF programs compared with maintaining them in municipalities that have existing water fluoridation programs. Given that water fluoridation is a public health initiative, the population of interest in both questions will be residents of Canadian municipalities. Potential sensitivity analyses will explore how the municipal population size may influence the findings observed. The budget impact analyses will be conducted in accordance with the latest International Society for Pharmacoeconomics and Outcomes Research (ISPOR) principles of good practice.[59]

The analyses will be conducted from a Canadian societal perspective. Consistent with the perspective taken, the costs associated with introducing, maintaining, operating, or discontinuing a CWF program (e.g., construction, labour, and supply costs) and the costs associated with accompanying changes in dental caries will be considered. These costs may potentially include, but will not be limited to: health care costs (e.g., caries treatments), lost productivity costs, transportation costs incurred for health care visits, and the environmental costs of water fluoridation. We will consult with the clinical experts involved in this review and other stakeholders involved in water fluoridation to identify relevant outcomes to consider. Costs will be reported in 2017 Canadian dollars and extracted from Canadian sources where available. If necessary, older costs will be converted to 2017 Canadian dollars using the consumer price index.[60] As the costs listed above are accrued to different payers, the budget impact analyses will also report total cost results disaggregately by payer (e.g., municipalities, departments of health, individuals, private health insurances); this will highlight the impacts of water fluoridation on budget expenditures and savings on different members of Canadian society.

A longer-than-conventional time horizon for budget impact analyses[59] will be used to consider the long-term population impacts pertaining to decisions about CWF. For question 4 (i.e., introduction of a CWF program), a 20-year time horizon was selected to reflect the suggested design period of water treatment plants[61] and capture the budget impact over the expected lifespan of a CWF infrastructure. For question 5 (i.e., cessation of a CWF program), a 20-year time horizon was also selected to broadly reflect the time frames recommended for Canadian municipal asset management plans.[62-65] The analyses will

further report a breakdown of costs, by year, to facilitate a deeper understanding of the budget impact over time.

All assumptions and limitations of the analyses will be identified in the report; where possible, any uncertainty in the structure and parameters of the analyses, including the time horizon, will be evaluated through sensitivity analyses. Depending on the availability of data, the analyses will also explore and incorporate any identifiable sources of heterogeneity, such as age, geography (i.e., urban, rural, or remote), and socio-economic status.

Social Dimensions

The goal of this review is to offer insight into the social dimensions of the policy question:

Should CWF be encouraged and maintained in Canada?

As this is a normative question for which there may well be no singular response, this review will focus on foregrounding varied understandings of and interactions with CWF (CWF) as a way of providing greater analytical depth to a complex policy question.

CWF may well be viewed as a "wicked problem" — one that, rather than indisputably serving a public good, involves a complex array of policy actors and interests, a breadth of scientific and technical expertise, and a range of ethical and social values and perspectives, and cannot be resolved by science alone.[66]

To unpack this complexity surrounding policy-making with regards to CWF, our review will explore how CWF is talked about and understood by a number of the diverse parties involved. Part of this exercise will be a directed effort to examine the ways in which cases for or against CWF are made and in which contexts. These social dimensions — i.e., how CWF "plays out" in various communities — can help inform what CWF might mean to some people and what policies pertaining to CWF (both investment and divestment) could confront. We will conduct an interpretive synthesis of primary qualitative and mixed-methods studies of any design as well as surveys and grey literature (e.g., policy briefs, position papers, manuscripts, and municipal minutes). Although there are a number of methods we could choose from, such as meta-ethnography,[67,68], we will draw on the Dixon-Woods et al.[69] approach of Critical Interpretive Synthesis (CIS), as CIS allows the use of both qualitative and quantitative studies in the analysis. While our interests lie primarily in qualitatively oriented studies and grey literature, by incorporating mixed-methods studies and surveys, we will have a greater understanding of the broad strokes surrounding the issue of CWF.

Another key reason for choosing CIS stems from our interest in examining the issue of CWF as more than a passive conduit of "data." While other methods of interpretive synthesis (e.g., meta-ethnography) may assess how individual studies relate to and translate into one another,[68] we want to understand how various modes or methods of examination may influence the discourse on CWF. Plainly stated, we are interested less in how included studies speak to each other and more in how study approaches change what is at stake in CWF. With an "explicit orientation toward theory generation,"[69] CIS approaches analysis in much the same way as primary qualitative research, where the object of analysis is seen to exist in relation to contexts outside itself. As such, the resultant interpretation will be an attempt to address both the prominent concerns with CWF as a public health measure as well as the "problematics" and "assumptions"[69] informing these concerns.

CIS also allows for a level of fluid exploration of the issue at the centre of inquiry. As such, although the following protocol outlines a general course of action, it should be noted that the process for this review will be iterative, dynamic, recursive, and emergent. This is consistent with epistemological and methodological orientations of qualitative research, in which the series of neatly organized procedural stages adopted within traditional systematic reviews are replaced by a sporadic series of fits and starts. Where these iterative processes may become necessary are indicated throughout this protocol.

Our review question serves as a guiding compass.[70] Rather than honing in on a pre-set, precisely defined research question, our question is broad and flexible (or, as Greenhalgh and colleagues would describe it, "fuzzy"[69]) approach as a way of remaining attuned to the complexity of the policy question and allowing for a deeper understanding of the resultant policy challenges related to the implementation or cessation of CWF. The question that will guide the initial stages of this research is:

6. How is community water fluoridation conceptualized, communicated, and enacted by public health practitioners, municipal decision-makers, and members of the general public who may be affected by its implementation or cessation?

Following our interest in the broad question of how CWF is conceptualized, communicated and enacted, the following secondary questions will guide our initial exploration:

- How has CWF emerged historically as a prominent dental public health measure?
- What sorts of publics are imagined to interact with CWF and what are the differences or similarities between them?
- How are decayed, missing or extracted, and filled permanent and primary teeth enacted within conversations by public health officials and members of the general public surrounding CWF?

Other questions may emerge as the research continues.

Literature Search Strategy

The literature search will be performed by an information specialist using a peer-reviewed search strategy.

Information related to social dimensions will be identified by searching the following bibliographic databases: MEDLINE (1946–) with in-process records and daily updates; BIOSIS Previews (1989 to 2010) and ERIC (1965–) via OVID; CINAHL (1981–) via EBSCO; PubMed; and the Social Sciences and Humanities segment in Scopus. The search strategy will comprise both controlled vocabulary, such as the National Library of Medicine's MeSH, and keywords. The main search concepts will be fluoridation and fluoride in water.

Methodological filters will be applied to limit retrieval to qualitative studies or studies relevant to social dimensions. No date limit will be applied. The search will also be limited to English- or French-language publications.

Regular alerts will be established to update the searches until the publication of the final report. Regular search updates will be performed on databases that do not provide alert services. Studies identified in the alerts and meeting the selection criteria of the review may be incorporated into the analysis if they are identified prior to the completion of the stakeholder feedback period of the final report and offer new analytical insight.

Grey literature (literature that is not commercially published) will be identified by searching the *Grey Matters* checklist (https://www.cadth.ca/grey-matters), which includes the websites of HTA agencies, clinical guideline repositories, systematic review repositories, and professional associations. Google and other Internet search engines will be used to search for additional Web-based materials. These searches will be supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry.

Because of the emergent nature of our primary research question, the literature search will be an organic process involving multiple database searches, website searches, reference chaining, and expert guidance. By allowing the search strategy to remain broadly attuned to the "fuzziness" of our primary research question, we will be able to capture literature typically hidden within the margins of more formalized search strategies.

Literature Selection Criteria

Eligible papers include primary English- or French-language qualitative studies of any design as well as mixed-methods studies, surveys, or grey literature (e.g., policy briefs, position papers, manuscripts, municipal minutes) that explore CWF.

Rather than develop a list of a priori inclusion criteria (outside of the previously mentioned eligibility criteria), we will follow the lead of Moat et al.[71] by focusing on gathering "potentially relevant" literature through an explicit exclusion process. This will allow us to deliberately exclude any obviously irrelevant literature while simultaneously remaining honest to the ambiguity of our original research question. While further exclusion criteria will become apparent once we have begun our initial screening for potentially relevant literature, studies and grey literature will be initially be excluded according to the following:

- Literature addressing topics other than water fluoridation
- Literature on CWF with a sole focus on assessing clinical or cost effectiveness
- Literature available in abstract form only

Literature Screening and Selection

As data collection and analysis are co-constitutive within qualitative research, our analysis will begin with literature screening. Two reviewers experienced in qualitative research will use DistillerSR[55] to independently conduct title and abstract screening aligned with the aforementioned eligibility criteria. Once consensus has been achieved regarding which irrelevant literature should be excluded and a pool of potentially eligible literature has been established, we will begin developing a "schema"[71] for drawing out a purposive sample. While the development of this schema will rely on several preliminary title and abstract read-throughs by the primary qualitative researcher, broadly what we will be looking for is literature that contributes theoretical depth or breadth to our understanding of the primary research question, keeping the policy question in mind and the ultimate usefulness to decision-makers. With this in mind, we will meet as a team to have several in-depth discussions on what should qualify as our purposive sample based on this preliminary title and abstract screening. As CIS requires less focus on finding a homogenous sampling of literature and conversations, the resulting purposive sample will be heterogeneous and broad.

With our preliminary schema for identifying a purposive sample of the literature in hand, we will again screen through titles and abstracts in duplicate to identify that purposive sample. It

is important to note here that we will be in conversation with public health officials, municipal decision-makers, and members of the general public concerned about CWF (as detailed below) to ensure the review reflects what these individuals may consider to be important themes or literature for inclusion into this sample. Based on these conversations and the ensuing analysis, we may continue purposive sampling and conduct further directed literature searches to fill in any conceptual gaps or to tie various emerging analyses together.

Quality Assessment

In CIS, the goal is to include all literature capable of offering rich conceptual insight as opposed to literature that meets a threshold of quality based on the points on a methodological checklist. Therefore, we will assess the quality of included studies based on an evaluation of trustworthiness.

We will draw on Lincoln and Guba's[72] original model for this form of assessment and Krefting's[73] subsequent delineation of this model. For these authors, trustworthiness hinges on four primary points: credibility, confirmability, transferability, and dependability.

Credibility asks the basic question of whether the study authors were true to their interlocutors. This can be assessed by reviewing the forms of engagement with and observations of interlocutors. How were interpretations drawn from these engagements and observations reviewed: member checking, peer review, reflexive practices?

Confirmability attempts to trace the pathways leading to final interpretations of the data. As with credibility, our assessment of confirmability may draw on reflexive practices of the study authors and the ways in which they present their own assumptions (maybe even experiences) within the research. We will also follow the ways in which analyses are supported by their data and generally presented throughout the study.

Transferability is concerned with the ability of the results of the research to move around. While we consider qualitative research to draw out profoundly situated knowledges and experiences, it is also important to consider the possible relations between these varied knowledges and experiences. As such, our assessment of transferability will focus on the ways in which depth is built around the individuals and situations included in the literature. For example, are we presented with strong engagements, but not informed as to the contexts in which these engagements took place? If so, how can we know where the individuals in this study relate to individuals from another?

Dependability relates to the way in which consistency is established within researcher interpretations. As qualitative research explores the breadth of potentially idiosyncratic knowledge and experience, we are not interested in the exact reproducibility of interpretations were the study to be repeated. Instead, much like with confirmability, our assessment of dependability will examine the ways in which methods are described and used within each particular study and open the space up for particular interpretations.

Both researchers will independently conduct an appraisal on each of the included studies from our purposive sample, using Table 2 to collate the results. While we will provide a brief narrative summary of our appraisal in the final report, the bulk of our critique will be reserved for the analysis section, as subsequently detailed.

Table 2: Table of Quality Appraisal

First Author, Publication Year		Credibility	Dependability	Transferability	Confirmability
	Strengths				
	Limitations				
	Strengths				
	Limitations				
	Strengths				
	Limitations				

Data Analysis

CIS offers two primary analytical outcomes: a synthesizing argument and a refutational synthesis.

Synthesizing Arguments

As Dixon-Woods et al.'s[69] development of CIS is largely an adjustment of Noblit and Hare's[67] meta-ethnography methodology, in order to understand the term "synthesizing argument," it is important to quickly review meta-ethnography's use of line-of-argument (LOA) synthesis. As Dixon-Woods et al.[69] point out, LOA synthesis operates upon a series of ordered constructs in which "first-order" constructs represent understandings or conceptualizations of the subjects being studied within primary research, and "second-order" constructs represent the interpretations of the primary researchers themselves. Within meta-ethnography, "third-order" constructs are interpretations that build upon the original constructs and extend them while simultaneously maintaining consistency with them. This could be described as interpretations of interpretations.

As a synthesis of primary research surrounding a particular issue, synthesizing arguments within CIS closely parallel LOA synthesis, albeit with a few distinctions. One of the primary differences comes in the development of synthetic constructs rather than third-order constructs. While on the surface, this may seem to be little more than semantics, synthetic constructs find form as new interpretations of evidence in light of the whole body of evidence. Dixon-Woods et al. write that "synthetic constructs are grounded in the evidence, but result from an interpretation of the whole of that evidence, and allow the possibility of several disparate aspects of phenomenon being unified in a more useful and explanatory way."[69] Thus, the goal of synthesizing arguments within CIS is not merely to delineate congruency between primary study interpretations and "third-order" interpretations, but rather to potentially present new understandings of the primary research in light of the greater body of evidence.

For our study, the synthesizing argument will be developed through prolonged and intensive engagement with the included, purposive sampling of the literature. We will begin the analysis by dividing the included literature equally between both researchers and creating an annotated bibliography. Not only will this process help to continue our ongoing familiarization with the literature, it will also provide a quick point of reference as we move through the synthesis. From here, we will move into an iterative, inductive process of developing high-level categories and their interpretive synthetic constructs. To do this, we will use NVivo[74] to conduct independent, line-by-line coding of the first 10% of included literature chosen at

random. Once we have developed our codes, we will meet and discuss these codes and how they inform our research. At this point, if both researchers are in agreement on how to proceed with coding, the primary qualitative researcher will begin coding alone and constantly checking in with the secondary researcher for validation. As high-level categories begin to emerge, we will have in-depth discussions on how they relate to each other (or not), and these will form the basis for synthetic constructs to come to the fore. Much like Moat et al.,[71] we will utilize the constant comparative method to ensure that our constructs remain grounded in the available data.

Once we have begun developing these synthetic constructs, we will engage with public health officials, municipality decision-makers, and general members of the public (as detailed below) to identify conceptual gaps or constructs that may need further refining. Not only will this allow us to begin narrowing in on a specific end point, but it will force us to remain attuned to the real-life concerns and values of those involved in CWF. At this point, we may need to conduct further literature searches to fill out our purposive sample; but the goal is to use these conversations as a way of bounding our research and to ensure relevance and usefulness to decision-makers.

Following these conversations and any directed literature searches deemed necessary, we will work toward integrating the synthetic constructs into an overarching synthesizing argument as an interpretive theoretical model addressing our primary research and policy questions.

Refutational Synthesis

Again borrowing from meta-ethnography methodology, a refutational synthesis of the literature entails a critique of the existing evidence. Rather than accept wholesale the constructs or interpretations presented within the primary literature, a refutational synthesis intends to "reflect on the credibility of the evidence, to make critical judgments about how it contributes to the development of the synthesizing argument, and to root the synthesizing argument appropriately in critique of existing evidence."[69] Our critique will question how the literature under review constructs the issue of CWF (what is at stake?) and what underlying assumptions are guiding their analysis of CWF. By critiquing the literature included in our own purposive sample, we will be able to identify how the current literature informs the policy question and the possible strengths and weaknesses of this literature.

Our critique will be guided by the primary reviewer and discussed at length with the secondary reviewer.

Techniques to Strengthen Methodological Rigour

Aside from prolonged engagement with the literature and constant discussion between the two researchers, we will collaborate with CADTH's Patient Engagement and Knowledge Mobilization teams to engage with public health officials, municipality decision-makers, and members of the general public as a form of member checking. At various points throughout our review, we will work with these teams to conduct semi-structured conversations with the aforementioned individuals. While these conversations may initially serve as a way of orienting us toward the right questions to ask of our literature, they will also serve as points at which we can present our preliminary analyses for critique.

Implementation Issues

To help inform decisions regarding CWF programs, the following implementation questions will be addressed:

7. What are the main challenges, considerations, and enablers related to implementing or maintaining community water fluoridation programs in Canada?
8. What are the main challenges, considerations, and enablers related to the cessation of community water fluoridation programs in Canada?

Methods

To understand the implementation issues associated with the initiation, maintenance, or cessation of CWF programs in Canada, a multi-stage approach is planned. The protocol is sequentially designed such that the findings at each stage will inform the need and scope of the next stage of research. The three stages are telephone or email consultations, a review of the published literature, and a survey.

Data Collection

Stage 1: Consultations

Consultations will be conducted with targeted experts and stakeholders identified through the clinician and professional networks managed by the Knowledge Mobilization team to provide a general overview of policy, practice, and issues related to CWF in Canada, as well as specific literature that may be important to incorporate. These stakeholders may include clinicians involved in public health dentistry, individuals involved in decision-making, and individuals who implement and carry out decisions regarding CWF in Canada. Individuals from multiple perspectives (e.g., different disciplines or different settings, such as rural or remote places) will be contacted in an effort to capture a range of issues relevant to CWF programs. An attempt will be made to contact more than one stakeholder from each relevant perspective to explore the issues related to CWF; however, this number might change depending on the availability of contacts, whether concept saturation is reached, and whether the information has been obtained or is still lacking.

To guide the consultations, a semi-structured interview guide will be developed. Interview questions related to implementation will be developed based on the research questions and the type of expert being consulted. Some example questions are: From your perspective, what are the barriers and supports for CWF in general, but also for specific groups of people or settings? How is the decision made to implement a CWF program, and how is this operationalized?

Consultations will be conducted by phone or email by a Knowledge Mobilization Officer; follow-up questions or clarifications will also be conducted by phone or email. In some cases (based on availability of this resource), phone conversations will be recorded with the consent and knowledge of all participants. Data from these consultations will be collected via detailed note-taking. Consent to publish comments and names will be sought.

Stage 2: Literature Search

The literature search will be performed by an information specialist using a peer-reviewed search strategy.

Implementation-related information will be identified by searching the following bibliographic databases: MEDLINE (1946–) with in-process records and daily updates; Embase (1974–) and ERIC (1965–) via Ovid; CINAHL (1981–) via EBSCO; PubMed; and Scopus. The search strategy will comprise both controlled vocabulary, such as the National Library of Medicine's MeSH, and keywords. The main search concepts will be fluoridation and fluoride in water.

Methodological filters will be applied to limit retrieval to studies relevant to implementation issues in the Canadian setting. No date limit will be applied. The search will be limited to English- or French-language publications.

Regular alerts will be established to update the searches until the publication of the final report. Regular search updates will be performed on databases that do not provide alert services. Studies identified in the alerts and meeting the selection criteria of the review will be incorporated into the analysis if they are identified prior to the completion of the stakeholder feedback period of the final report. Any studies that are identified after the stakeholder feedback period will be described in the discussion, with a focus on comparing the results of these new studies with the results of the analysis conducted for this report.

Grey literature (literature that is not commercially published) will be identified by searching the *Grey Matters* checklist (https://www.cadth.ca/grey-matters), which includes the websites of HTA agencies, clinical guideline repositories, systematic review repositories, economics-related resources, public perspective groups, and professional associations. Google and other Internet search engines will be used to search for additional Web-based materials. These searches will be supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry.

It is likely that an iterative strategy will be followed, such that as we begin to understand the important issues and strategies (which may arise as a result of expert consultations), more targeted searches will be conducted to identify more information on these new and currently unexpected issues. Canadian literature will be searched first; if insufficient information is found, the search will be expanded to include literature from other countries where community water is fluoridated (e.g., the US, Australia, and New Zealand).

Eligibility Criteria

We will include English- and French-language reports that describe implementation and context issues, including the barriers and facilitators associated with creating, maintaining, or discontinuing CWF programs.

Screening and Selecting Articles for Inclusion

Articles will be screened and selected for inclusion based on the eligibility criteria by one reviewer. First, titles and abstracts will be reviewed to identify potentially relevant papers; then, the full text of all potentially relevant reports will be retrieved for definitive determination of eligibility.

Data Extraction

Data extraction will be performed by one reviewer. The data extracted will include bibliographic details of included papers, reported implementation barriers and facilitators, and other key findings related to implementation and relevant context information. Contextual information and key issues will be coded for relevant concepts using the *Guidance for the Assessment of Context and Implementation in Health Technology Assessments (HTA) and Systematic Reviews of Complex Interventions: The Context and*

Implementation of Complex Interventions (CICI) Framework (INTEGRATE-HTA framework) as a guiding framework.[75] INTEGRATE-HTA defines eight domains of context (i.e., setting, geographical, epidemiological, socio-economic, sociocultural, political, legal, and ethical) and four domains of implementation (i.e., provider, organization and structure, funding, and policy), each contributing differently to how an intervention is implemented, who can access it, and ultimately, its effectiveness. If applicable (i.e., not all studies will have all domains), INTEGRATE-HTA domains of context and implementation will guide the coding of relevant results and context from the included studies.

Stage 3: Survey

A survey may be initiated to specifically address gaps in information regarding implementation issues related to CWF for specific stakeholders (such as those previously mentioned). The need for a survey will consider the likelihood of gaining additional information not captured through literature or expert consultations. Gaps will be identified through previous stages (i.e., consultation and literature search). For example, if a particular domain of INTEGRATE-HTA has little to no information from the consultations and literature review, any potential survey would aim to add to our knowledge of this domain. Specific questions will be developed and a survey will be delivered via email to appropriate respondents. Respondents will be identified using the networks of stakeholders engaged in the project and the professional and clinical networks of CADTH's liaison officers.

Data Analysis

The analysis of data collected from each section of this research study will be guided, as below.

Perspectives

When analyzing data, the items coded and summaries written will be those most relevant to those at the health services delivery level (e.g., dental professionals), decision-makers, and invested stakeholders (e.g., public health). The aim will be to provide information to policy-makers and decision-makers regarding the encouragement, initiation, maintenance, or cessation of CWF.

Descriptive Analysis

The data from the staged components of the review (i.e., expert consultations, literature review, or survey, if conducted) will be combined into a common data set in preparation for analysis. A narrative summary of the findings will be written by a Knowledge Mobilization (KM) Officer. As data become available, the summary will categorize findings based on the INTEGRATE-HTA framework.[75] Once all data have been coded by one reviewer, a second researcher will verify the coding assignments and coding framework. Literature and data from other sections of this report (e.g., ethical, clinical, health economics) may also inform this section of the HTA by adding contextual information relevant to the discussion of implementation issues.

Once all data have been read and coded, text coded within each domain will be summarized; if necessary, subcategories within each code will also be identified. For example, subcategories may be developed to account for issues relevant to special populations or those with the potential to be differentially affected by implementation or

cessation of a CWF program. The summary will include a description of the domain (and its subcategories where relevant) and how the factor relates to CWF programs. Once all summaries have been written, they will be read and compared with the original data by a second reviewer to ensure comprehensiveness and consistency within the accounts.

A list and description of factors that have the potential to facilitate or challenge successful implementation will be presented, as well as a summary of potential strategies that could be used to increase the uptake or aid in the cessation of CWF programs, if the decision is made to do so.

Additionally, a summary of how each factor influences implementation will be provided and, where possible, strategies will be identified that could be used to ensure these factors are taken into consideration or mitigated.

Given the emergent nature of this review and the open-ended data that will be collected, it is possible that adaptations to this planned analytic strategy will be required to accommodate the data obtained and the needs of stakeholders. The final report will detail the actual analytic methods used.

Knowledge Mobilization

The implementation issues identified will guide the development of knowledge mobilization activities, tools, and tactics to support the implementation of any resulting decisions or changes to the public health system or health service delivery. Activities and tools will be developed in consultation with CADTH Liaison Officers, stakeholders, and customers; the format of these activities and tools can be tailored to the context and needs of specific customers and jurisdictions.

Environmental Assessment

An environmental assessment will be conducted to answer the following question:

9. What are the potential environmental (toxicological) risks associated with community water fluoridation?

Study Design

To address the question of "what are the possible environmental (toxicological) risks associated with CWF," a narrative review of published literature and qualitative risk assessment will be conducted to support the environmental assessment. Environmental risk experts and information specialists will work together to develop a literature search strategy to obtain primary and grey literature on the possible ecosystem effects and risks associated with fluoridation in water. A plain-language narrative summary will be prepared. As well, the focus of the qualitative risk assessment will be a summary of findings from the primary and grey literature on the reported effects (or lack thereof) of CWF on ecosystems and a qualitative discussion of ecosystem risks from CWF.

Literature Search Strategy

The literature search will be performed by an information specialist using a peer-reviewed search strategy.

Environmental impact-related information will be identified by searching the following bibliographic databases: MEDLINE (1946–) with in-process records and daily updates; ERIC (1965–) and BIOSIS Previews (1989 to 2010) via Ovid; CINAHL (1981–) and GreenFILE via EBSCO; PubMed; Toxline; and Scopus. The search strategy will comprise both controlled vocabulary, such as the National Library of Medicine's MeSH, and keywords. The main search concepts will be fluoridation and fluoride in water.

In the absence of a globally accepted and suitable definition of the "environment," we refer to select keywords extracted from Environment and Climate Change Canada's mandate,[76] namely: natural environment, water, air, soil, flora, fauna, and renewable resources. Relevant synonyms will also be searched (e.g., wildlife for fauna). Key search terms will include, but will not be limited to, the following overarching themes: community water fluoridation, aquatic, terrestrial, water quality, animals (e.g., invertebrates, fish, birds, mammals, plants), effect(s), ecosystem(s), toxicology, and ecological risk assessment.

Methodological filters will be applied to limit retrieval to studies relevant to environmental impact on non-humans. No date limit will be applied. The search will be limited to English- or French-language publications. Conference abstracts will be excluded from all searches.

Regular alerts will be established to update the searches until the publication of the final report.

Grey literature (literature that is not commercially published) will be identified by searching the *Grey Matters* checklist (https://www.cadth.ca/grey-matters), which includes the websites of HTA agencies, clinical guideline repositories, systematic review repositories, economics-related resources, public perspective groups, and professional associations. Google and other Internet search engines will be used to search for additional Web-based materials.

These searches will be supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry.

Selection Criteria

As a first step in the review of the literature, titles of candidate articles will be reviewed and assessed for relevance in relation to the objective by one reviewer. Articles that provide insights into the potential environmental effects associated with CWF will be included.

Based on initial findings and review of the literature, further searches to identify additional information on the environmental effects of CWF may be conducted.

Data Extraction

From each relevant article, the bibliographic details (authors, year of publication, and country of origin) and issues related to the environmental effects will be captured by one reviewer. The environmental factors related to possible effects will be broken down into variables, such as:

- source media (e.g., air, water, soil)
- receptor-macro (e.g., flora, fauna)
- receptor-micro (e.g., fish, wildlife, vegetation)
- receptor-specific (e.g., organism)
- effect-macro (e.g., contamination, growth, reproduction, survival)
- effect-specific (e.g., specific change).

Analysis

The analysis will be conducted in two phases by one reviewer. First, once relevant literature has been obtained, it will be reviewed and summarized in a plain-language narrative summary. In this summary, general themes, findings, and conclusions will be presented. The information extracted from the articles will be reviewed, categorized, and organized into themes (if apparent) and summarized narratively.

The second phase is the qualitative risk assessment. All chemicals (from anthropogenic and natural sources) have the potential to cause toxicological effects. However, the level of effect depends on the ecological receptor (e.g., mammal, bird, fish, plant) being exposed, the route and duration of exposure (e.g., ingestion or dermal contact for chronic periods of time), and the hazard (i.e., inherent toxicity) of the chemical. If all three components are present (Figure 1), the possibility of a toxicological risk exists. If any one of these three is not present, potential ecological risks cannot be present. If, for example, a receptor and a chemical are present but there is no means of the receptor encountering the chemical (i.e., an exposure pathway is not present), there would be no potential health risk.

Figure 1: Risk Venn Diagram

Each component of the risk Venn diagram will be qualitatively assessed based on the data extracted during the literature review. Given the variety of ways in which fluoride can enter the environment from CWF, potential exposure pathways between fluoride and ecological receptors will be identified. This information will be summarized in an ecological conceptual site model, which will provide a visual depiction of the relevant pathways linking fluoride exposure in various environmental media and biota to the identified receptors.

The inherent toxicity of fluoride, based on laboratory and environmental studies (as available), will be reviewed and commented on in terms of ecological relevance to the identified ecological receptors.

The Canadian Council of Ministers of the Environment has environmental quality guidelines (EQGs) for fluoride in water that are meant to protect aquatic life and irrigation.[77] Based on the data extraction, environmental concentrations of fluoride in water associated with CWF will be compared with these EQGs to make qualitative or quantitative characterizations of environmental risk.

Ethical Considerations

The purpose of this analysis is to identify and reflect upon key ethical concerns that should be considered when comparing the relative merits and demerits of CWF versus no CWF for the prevention of dental caries in children and adults in Canada. Although other sections of this HTA implicitly touch upon broadly ethical concerns, the aim of this analysis is to make such issues explicit and to identify others that may be relevant to any decisions in this regard.

The issues raised in this section necessarily go beyond narrowly defined ethical concerns to encompass broader legal, social, and cultural considerations. It is common in the ethics literature, across a broad range of health-related issues, to refer to ethical, legal, and social issues (ELSIs) when addressing broader values-related considerations. While the primary emphasis here will be on ethical considerations, legal and social issues may also figure in the discussion.

There are two sets of questions to consider when comparing CWF:

10. What are the major ethical issues raised by the implementation of community water fluoridation?
11. What are the major ethical issues raised by the cessation of community water fluoridation?
12. What are the major ethical issues raised by the legal, social, and cultural considerations to consider for implementation and cessation?

Inquiry

Ethics analysis for questions 10 to 12 requires a two-step approach to identifying potential issues. The first is a review of the ethics, clinical, and public health literatures to identify existing ethical analyses of the technology. The second is a de novo ethical analysis based on gaps identified in the ethics literature and the results of concurrent reviews. This may require selective searches to provide the basis in theoretical ethics, in applied ethical analyses of similar technologies, and in evidence for the ethical analysis of emerging issues specific to CWF. Through this approach, we identify and assess the relative importance and strength of the identified concerns and proposed solutions, identify and assess issues that have not yet come to the attention of ethics researchers, and delineate ethical desiderata for possible solutions to the issues where such solutions have not yet been proposed.

Insofar as this process involves ethical concerns in applied ethics, typically the analysis will reflect on the specific details of community and patient perspectives, clinical effectiveness and safety, economic analysis, environmental impacts, and implementation considerations. As such, the ethical review involves an iterative process whereby the analysis is responsive to results emerging from clinical, implementation, public perspective, and economic reviews.

Review of the Bioethics Literature

A review of the empirical and normative bioethics literature will be conducted to identify literature relevant to the identification and analysis of the potential ELSI issues related to CWF. We will search for articles, studies, and reports that explicitly and specifically raise ELSI issues related to the central question of this HTA as well as literature not explicitly about ethical issues (for example, an empirical investigation of public attitudes about water

fluoridation) but which may point to potential ethical issues even if the participants and researchers did not formulate them as such.

Literature Search Strategy

The literature search will be performed by an information specialist using a peer-reviewed search strategy.

Ethics-related information will be identified by searching the following bibliographic databases: MEDLINE (1946–) via Ovid; PsycINFO (1967–) via Ovid; CINAHL (1981–) via EBSCO; and PubMed. The search strategy will comprise both controlled vocabulary, such as the National Library of Medicine's MeSH, and keywords. The main search concepts will be fluoridation and fluoride in water.

Methodological filters will be applied to limit retrieval to studies related to ELSIs. No date limit will be applied. The search will also be limited to English- or French-language publications. Conference abstracts will be excluded from all searches.

Regular alerts will be established to update the searches until the final report is published. Regular search updates will be performed on databases that do not provide alert services. Studies identified in the alerts and meeting the selection criteria of the review will be incorporated into the analysis if they are identified prior to the completion of the stakeholder feedback period of the final report. Any studies that are identified after the stakeholder feedback period will be described in the discussion, with a focus on comparing the results of these new studies to the results of the analysis conducted for this report.

Grey literature (literature that is not commercially published) will be identified by searching the *Grey Matters* checklist (https://www.cadth.ca/grey-matters), which includes the websites of HTA agencies, clinical guideline repositories, systematic review repositories, and professional associations. Google and other Internet search engines will be used to search for additional Web-based materials. These searches will be supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts and industry.

Literature Screening and Selection

The selection of relevant literature will proceed in two stages. In the first stage, the title and abstracts of citations will be screened for relevance by a single reviewer. Articles will be categorized as "retrieve" or "do not retrieve" according to the following criteria:

- Provides normative analysis of an ethical issue arising in the use (or not) of CWF;
- Presents empirical research directly addressing an ethical issue arising in the use (or not) of CWF;
- Explicitly identifies but does not analyze or investigate empirically an ethical issue arising in the use (or not) of CWF.

The goal of this review of bioethics literature is to canvass what arises as an ethical issue from a broad range of relevant perspectives. As such, the quality of normative analysis does not figure in the article selection criteria: any identification of an issue by the public, dental care providers, researchers, or policy-makers is of interest whether presented through rigorous ethical argumentation or not. For example, academic ethicists may focus on certain issues because they relate to theoretical trends in their discipline, while an opinion piece by a clinical leader, policy leader, or member of the public may bring to the fore ethical

questions that are neglected by academic ethicists but are highly pertinent to the assessment of the technology in the relevant context. Despite the different standards of normative argumentation for each kind of report, the importance of the issues raised cannot be assessed solely by these standards; therefore, literature cannot be excluded based on methodological standards.

In the second stage, the full-text reports will be reviewed by two reviewers. Reports meeting the abovementioned criteria will be included in the analysis; reports that do not will be excluded.

Data Extraction and Abstraction Strategy

The bibliographic details for each report (e.g., author, publication date, journal), the potential ethical issues raised, and the report's conclusions (issues identified, values at stake identified through normative analysis, and solutions proposed, and their normative justification if presented) will be summarized in a table.

Analysis

The ethical issues identified, values described, and solutions proposed in the literature will at this stage be evaluated using the methods of ethical (applied philosophical) analysis, which include applying standards of logical consistency and rigour in argumentation, particularly where specific implications are identified and specific solutions advocated; responsiveness to important values of health care and health care policy in the field in which the technology is proposed for implementation; adequacy to the context for which the technology is being considered; and the representation of perspectives from diverse relevant communities, particularly attending to the possibility of the neglect of marginalized and vulnerable populations.

The proposed analysis will employ an axiological questions-based approach[78] to explore the issues identified, values described, and solutions proposed in the systematic review to further clarify and uncover ethical issues raised in the technology under review that are relevant to policy-makers. The aim of this approach is to uncover considerations that are likely to be important to decisions in the context within which they are made. This method is distinct from, and advantageous over, other approaches to ethics analysis as it is not limited to a particular theoretical ethical framing. Instead, it uncovers ethics considerations using a range of ethical perspectives including deontology, utilitarianism, principlism, casuistry, and virtue ethics. Identified issues that are not addressed by the axiological approach will be highlighted, and supplementary searches will be pursued in case there are axiological questions that were not addressed by any of the identified issues in the initial search.

This axiological approach applies 33 questions to highlight overt and covert values issues with regard to health technology. These questions are designed to explore a comprehensive set of values. In the area of population or systems-level ethics, important values include justice (equity in access and outcomes, resource allocation in relation to community needs, and social justice concerns about voice and control); the (feasible) minimization of harms and maximization of benefits in the implementation of technology, and the acceptability of residual harms given realistically anticipated benefits; responsibility, accountability, and the trustworthiness of health care providers, health care systems, and those responsible for public safety; the tension as it appears in public health between individual autonomy and pursuit of a public good (in this case, reduced dental disease and improved overall oral

health); and cultural, social, and religious values and mores that may be engaged by a public health program.

Summarizing and Presenting Results

Ethical issues are multi-dimensional. Their reporting can be organized procedurally (through a patient or clinical care continuum); structurally (through the levels of the health care system at which they emerge, as micro, meso, and macro level issues); according to the key values standardly identified in the public health ethics literature; or according to the specific issues and concerns identified in the review and in communication with other review processes. The review will be organized according to the framework among these four that best suits the results of the review and facilitates its use by decision-makers.

Ethical analysis assists in social and policy decision-making, but is not itself the site of legitimate social decision-making, which requires consultation and deliberation by relevant stakeholders in a given context. Decisions will also be sensitive to emerging empirical evidence. Furthermore, the ethical implications of a health technology are often determined by the nature of the local context. For example, the implications of values of fair access and consistency of service within the population are determined by facts about how health care services are arranged and provided.

Given these features of ethical decision-making, results of the ethics review will be presented in a way that helps decision-makers better understand the ethical implications of the decisions and recommendations they come to. For example, a number of contextualizing questions will be developed based on the identified issues so that decision-makers can assess localized impact; proposed solutions will be analyzed to indicate the relevant ethical trade-offs at stake and the mitigation strategies that could be employed to manage them.

Protocol Amendments

If amendments to the protocol are required at any time during the study, reasons for the changes will be recorded and reported in the final report.

References

1. Water fluoridation: questions & answers [Internet]. Toronto (ON): University of Toronto, Faculty of Dentistry, Dental Public Health program; 2012 Apr. [cited 2017 Sep 20]. Available from: http://www.caphd.ca/sites/default/files/WaterFluoridationQA.pdf
2. Health Canada. Guidelines for Canadian drinking water quality: guideline technical document -- fluoride [Internet]. Ottawa (ON): Health Canada, Healthy Environments and Consumer Safety Branch, Water, Air and Climate Change Bureau; 2010 Dec. [cited 2017 Oct 31]. Available from: https://www.canada.ca/content/dam/canada/health-canada/migration/healthy-canadians/publications/healthy-living-vie-saine/water-fluoride-fluorure-eau/alt/water-fluoride-fluorure-eau-eng.pdf
3. Bellemare M, Simard P, Trahan L. [Summary on fluoridation of drinking water (1979)]. J Dent Que. 1979 Oct;16:13-20. French.
4. Smith GE. Fluoride and fluoridation. Soc Sci Med. 1988;26(4):451-62.
5. Cutress TW, Suckling GW. Differential diagnosis of dental fluorosis. J Dent Res. 1990 Feb;69 Spec No:714-20.
6. Fejerskov O, Manji F, Baelum V. The nature and mechanisms of dental fluorosis in man. J Dent Res. 1990 Feb;69 Spec No:692-700.
7. Burt BA. The changing patterns of systemic fluoride intake. J Dent Res. 1992 May;71(5):1228-37.
8. Hutton WL, Linscott BW, Williams DB. The Brantford fluorine experiment. Interim report after five years of water fluoridation. Can J Public Health. 1951 Mar;42(3):81-7.
9. Connor RA. Editorial. Twenty-fifth anniversary of fluoridation. A public health success story. Can J Public Health. 1970 Jul;61(4):283-4.
10. Dunton EA. Two fluoridation health surveys in Ontario. Can J Public Health. 1967 Jul;58(7):319-23.
11. Smith AG. The Brantford fluorine experiment. J Can Dent Assoc (Tor). 1946 Jan;12:11-4.
12. The state of oral health in Canada [Internet].Canadian Dental Association; 2017 Mar. [cited 2017 Oct 18]. Available from: https://www.cda-adc.ca/stateoforalhealth/_files/TheStateofOralHealthinCanada.pdf
13. Whitford GM. The metabolism and toxicity of fluoride. Basel (CH): S.Karger; 1996 May 30. (Monographs in oral science, vol. 16 (book 16)).
14. Whitford GM. Fluoride metabolism and excretion in children. J Public Health Dent. 1999;59(4):224-8.
15. Fluoride. In: Nutrient reference values for Australia and New Zealand. Version 1.1. Canberra (AU): Australian Government, National Health and Medical Research Council; 2017.
16. Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary reference intakes for calcium, phosphorus, magnesium, vitamin D and fluoride [Internet]. Washington (DC): National Academy Press; 1997. [cited 2017 Nov 9]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK109825/pdf/Bookshelf_NBK109825.pdf
17. Behrman RE, Kliegman RM, Arvin AM, editors. Nelson textbook of pediatrics. 15th ed. Philadelphia (PA): W.B. Saunders Co.; 1996.
18. Report on the findings of the oral health component of the Canadian Health Measures Survey 2007-2009 [Internet]. Ottawa: Health Canada; 2010. [cited 2017 Oct 31]. Available from: http://publications.gc.ca/collections/collection_2010/sc-hc/H34-221-2010-eng.pdf
19. Ripa LW. A half-century of community water fluoridation in the United States: review and commentary. J Public Health Dent. 1993;53(1):17-44.
20. Locker D, Matear D. Oral disorders, systemic health, well-being and the quality of life: a summary of recent research evidence. Toronto: University of Toronto; 2000.
21. Low W, Tan S, Schwartz S. The effect of severe caries on the quality of life in young children. Pediatr Dent. 1999 Sep;21(6):325-6.
22. Ayhan H, Suskan E, Yildirim S. The effect of nursing or rampant caries on height, body weight and head circumference. J Clin Pediatr Dent. 1996;20(3):209-12.
23. Jackson SL, Vann WF, Jr., Kotch JB, Pahel BT, Lee JY. Impact of poor oral health on children's school attendance and performance. Am J Public Health [Internet]. 2011 Oct [cited 2017 Nov 9];101(10):1900-6. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3222359
24. Gift HC, Reisine ST, Larach DC. The social impact of dental problems and visits. Am J Public Health [Internet]. 1992 Dec [cited 2017 Nov 9];82(12):1663-8. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1694558
25. Clarke M, Locker D, Berall G, Pencharz P, Kenny DJ, Judd P. Malnourishment in a population of young children with severe early childhood caries. Pediatr Dent. 2006 May;28(3):254-9.
26. Offenbacher S, Katz V, Fertik G, Collins J, Boyd D, Maynor G, et al. Periodontal infection as a possible risk factor for preterm low birth weight. J Periodontol. 1996 Oct;67(10 Suppl):1103-13.
27. Dasanayake AP. Poor periodontal health of the pregnant woman as a risk factor for low birth weight. Ann Periodontol. 1998 Jul;3(1):206-12.
28. National health expenditure trends, 1975-2011 [Internet]. Ottawa: Canadian Institute for Health Information; 2011. [cited 2017 Oct 18]. Available from: https://secure.cihi.ca/free_products/nhex_trends_report_2011_en.pdf
29. Featherstone JD. Prevention and reversal of dental caries: role of low level fluoride. Community Dent Oral Epidemiol. 1999 Feb;27(1):31-40.

30. Singh KA, Spencer AJ, Armfield JM. Relative effects of pre- and posteruption water fluoride on caries experience of permanent first molars. J Public Health Dent. 2003;63(1):11-9.

31. Singh KA, Spencer AJ. Relative effects of pre- and post-eruption water fluoride on caries experience by surface type of permanent first molars. Community Dent Oral Epidemiol. 2004 Dec;32(6):435-46.

32. Singh KA, Spencer AJ, Brennan DS. Effects of water fluoride exposure at crown completion and maturation on caries of permanent first molars. Caries Res. 2007;41(1):34-42.

33. Newbrun E, editor. Fluorides and dental caries. Springfield (IL): Charles C. Thomas; 1986.

34. Groeneveld A, Van Eck AA, Backer DO. Fluoride in caries prevention: is the effect pre- or post-eruptive? J Dent Res. 1990 Feb;69 Spec No:751-5.

35. Hamilton IR. Biochemical effects of fluoride on oral bacteria. J Dent Res. 1990 Feb;69 Spec No:660-7.

36. Lambrou D, Larsen MJ, Fejerskov O, Tachos B. The effect of fluoride in saliva on remineralization of dental enamel in humans. Caries Res. 1981;15(5):341-5.

37. Quinonez CR, Locker D. Public opinions on community water fluoridation. Can J Public Health. 2009 Mar;100(2):96-100.

38. Knox MC, Garner A, Dyason A, Pearson T, Pit SW. Qualitative investigation of the reasons behind opposition to water fluoridation in regional NSW, Australia. Public Heath Res Pract [Internet]. 2017 Feb 15 [cited 2017 Nov 22];27(1):e2711705. Available from: http://www.phrp.com.au/wp-content/uploads/2017/02/PHRP2711705.pdf

39. Horowitz AM, Kleinman DV, Child W, Maybury C. Perspectives of Maryland adults regarding caries prevention. Am J Public Health [Internet]. 2015 May [cited 2017 Aug 21];105(5):e58-e64. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4386533/pdf/AJPH.2015.302565.pdf

40. Pollick HF. Water fluoridation and the environment: current perspective in the United States. Int J Occup Environ Health. 2004 Jul;10(3):343-50.

41. Crocombe LA, Goldberg LR, Bell E, Seidel B. A comparative analysis of policies addressing rural oral health in eight English-speaking OECD countries. Rural remote health [Internet]. 2017 Jul [cited 2017 Dec 8];17(3). Available from: http://www.rrh.org.au/publishedarticles/article_print_3809.pdf

42. McLaren L, Singhal S. Does cessation of community water fluoridation lead to an increase in tooth decay? A systematic review of published studies. J Epidemiol Community Health [Internet]. 2016 Sep [cited 2017 Sep 21];70(9):934-40. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5013153

43. Moncton to debate return of fluoride in drinking water [Internet]. Moncton (NB): CBC News; 2016 Dec 16. [cited 2017 Sep 20]. Available from: http://www.cbc.ca/news/canada/new-brunswick/moncton-fluoride-water-meeting-1.3900235

44. Cromwell A. Saint John councillor says province should pay for water fluoridation [Internet]. Saint John: Global News; 2016 Oct 3. [cited 2017 Sep 20]. Available from: https://globalnews.ca/news/2980007/saint-john-councillor-says-province-should-pay-for-water-fluoridation/

45. National Health and Medical Research Council. A systematic review of the efficacy and safety of fluoridation. Part A: review of methodology and results. Canberra (AU): Australian Government; 2007.

46. Iheozor-Ejiofor Z, Worthington HV, Walsh T, O'Malley L, Clarkson JE, Macey R, et al. Water fluoridation for the prevention of dental caries. Cochrane Database Syst Rev. 2015 Jun 18;(6):CD010856.

47. Fluoride in drinking water: a scientific review of EPA's standards. Washington (DC): The National Academies Press; 2006.

48. McDonagh M, Whiting P, Bradley M, Cooper J, Sutton A, Chestnutt I. A systemic review of public water fluoridation. York (GB): University of York; 2000 Sep.

49. Griffin SO, Regnier E, Griffin PM, Huntley V. Effectiveness of fluoride in preventing caries in adults. J Dent Res. 2007 May;86(5):410-5.

50. Rugg-Gunn AJ, Do L. Effectiveness of water fluoridation in caries prevention. Community Dent Oral Epidemiol. 2012 Oct;40 Suppl 2:55-64.

51. Robinson KA, Chou R, Berkman ND, Newberry SJ, Fu R, Hartling L, et al. Integrating bodies of evidence: existing systematic reviews and primary studies. In: Methods guide for effectiveness and comparative effectiveness reviews [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2015 Feb 26 [cited 2018 Jan 15]. Available from: https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0077778/pdf/PubMedHealth_PMH0077778.pdf

52. Jack B, Ayson M, Lewis S, Irving A, Agresta B, Ko H. Health effects of water fluoridation: evidence evaluation report. Sydney (AU): The University of Sydney; 2016 Aug 24.

53. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev [Internet]. 2015 Jan 1 [cited 2017 Sep 21];4:1. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4320440

54. Higgins PT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. London: The Cochrane Collaboration; 2011 Mar. [cited 2017 Nov 10]. (Version 5.1.0). Available from: http://handbook-5-1.cochrane.org/

55. DistillerSR [software]. Ottawa: Systematic Review and Literature Review Software from Evidence Partners; 2017. [cited 2017 Oct 11]. Available from: https://www.evidencepartners.com/products/distillersr-systematic-review-software/ Subscription required.

56. Methods for the development of NICE public health guidance (third edition) [Internet]. London: National Institute for Health and Care Excellence (NICE); 2012 Sep. [cited 2017 Sep 20]. (Process and methods; no. 4). Available from: https://www.nice.org.uk/process/pmg4/chapter/about-this-document

57. Moimaz SAS, Saliba O, Marques LB, Garbin CAS, Saliba NA. Dental fluorosis and its influence on children. Braz Oral Res [Internet]. 2015 [cited 2017 Dec 5];29(1):1-7. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1806-83242015000100214&lng=en&nrm=iso&tlng=en

58. Ran T, Chattopadhyay SK, Community Preventive Services Task Force. Economic evaluation of community water fluoridation: a community guide systematic review. Am J Prev Med. 2016 Jun;50(6):790-6.

59. Sullivan SD, Mauskopf JA, Augustovski F, Jaime CJ, Lee KM, Minchin M, et al. Budget impact analysis-principles of good practice: report of the ISPOR 2012 Budget Impact Analysis Good Practice II Task Force. Value Health [Internet]. 2014 Jan [cited 2017 Oct 5];17(1):5-14. Available from: https://www.ispor.org/budget-impact-health-study-guideline.pdf

60. Jacobs P, Budden A, Lee KM. Guidance document for the costing of health care resources in the Canadian setting [Internet]. 2nd ed. Ottawa (ON): CADTH; 2016 Mar. [cited 2017 Oct 5]. Available from: https://www.cadth.ca/sites/default/files/pdf/CP0009_CADTHCostingGuidance.pdf

61. Lai G, Budziakowski J, Edmonds T, Patrick J, Ministry of the Environment Drinking Water Technical Working Group. Design guidelines for drinking-water systems [Internet]. Toronto (ON): Ontario Ministry of the Environment; 2017. [cited 2017 Oct 5]. Available from: https://www.ontario.ca/document/design-guidelines-drinking-water-systems-0

62. Building community resilience through asset management [Internet]. Edmonton (AB): Alberta Government; 2015. [cited 2017 Oct 6]. Available from: http://www.municipalaffairs.alberta.ca/documents/ms/2015-11-17_Handbook_-_FINAL.pdf

63. Asset managment for sustainable service delivery: A BC framework [Internet]. Victoria (BC): Asset Management BC; 2015. [cited 2017 Oct 6]. Available from: https://www.civicinfo.bc.ca/Library/Asset_Management/Tools_and_Resources/Asset_Management_for_Sustainable_Service_Delivery_-_A_BC_Framework--Asset_Management_BC--September_16_2015.pdf

64. Building together - guide for municipal asset management plans [Internet]. Toronto (ON): Government of Ontario; 2016. [cited 2017 Oct 6]. Available from: https://www.ontario.ca/page/building-together-guide-municipal-asset-management-plans

65. Water and wastewater policy and level of services standards (corporate manual system). Volume 1 - capital facilities and maintenance - potable water and wastewater systems [Internet]. Ottawa: Indigenous and Northern Affairs Canada; 2011. [cited 2017 Oct 19]. Available from: http://www.aadnc-aandc.gc.ca/eng/1312228309105/1312228630065

66. Rittel HWJ, Webber MM. Dilemmas in a general theory of planning. Policy Science. 1973;4:155-69.

67. Noblit GW, Hare RD. Meta-ethnography: synthesizing qualitative studies. Newbury Park (CA): SAGE Publications; 1988. 88 p.

68. Flemming K. Synthesis of qualitative research and evidence-based nursing. Br J Nurs. 2007 May 24;16(10):616-20.

69. Dixon-Woods M, Cavers D, Agarwal S, Annandale E, Arthur A, Harvey J, et al. Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. BMC Med Res Methodol. 2006 Jul 26 [cited 2017 Oct 11];6:35. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1559637

70. Eakin JM, Mykhalovskiy E. Reframing the evaluation of qualitative health research: reflections on a review of appraisal guidelines in the health sciences. J Eval Clin Pract. 2003 May;9(2):187-94.

71. Moat KA, Lavis JN, Abelson J. How contexts and issues influence the use of policy-relevant research syntheses: a critical interpretive synthesis. Milbank Q. 2013 Sep [cited 2017 Oct 23];91(3):604-48. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3790526

72. Lincoln YS, Guba EG. Naturalistic inquiry. Beverly Hills (CA): SAGE Publications; 1985. 416 p.

73. Krefting L. Rigor in qualitative research: the assessment of trustworthiness. Am J Occup Ther. 1991 Mar;45(3):214-22.

74. NVivo qualitative data analysis [software]. Version 11. Doncaster (Australia): QSR International Pty Ltd; 2015. [cited 2017 Oct 11].

75. Pfadenhauer L, Pohwer A, Burns J, Both A, Lysdahl LB, Hofmann B. Guidance for the assessment of context and implementation in health technology assessments (HTA) and systematic reviews of complex interventions: the Context and implementation of Complex Interventions (CICI) framework [Internet]. Bremen (DE): Integrate-HTA; 2016 Feb 1. [cited 2016 Apr 4]. Available from: http://www.integrate-hta.eu/wp-content/uploads/2016/02/Guidance-for-the-Assessment-of-Context-and-Implementation-in-HTA-and-Systematic-Reviews-of-Complex-Interventions-The-Co.pdf

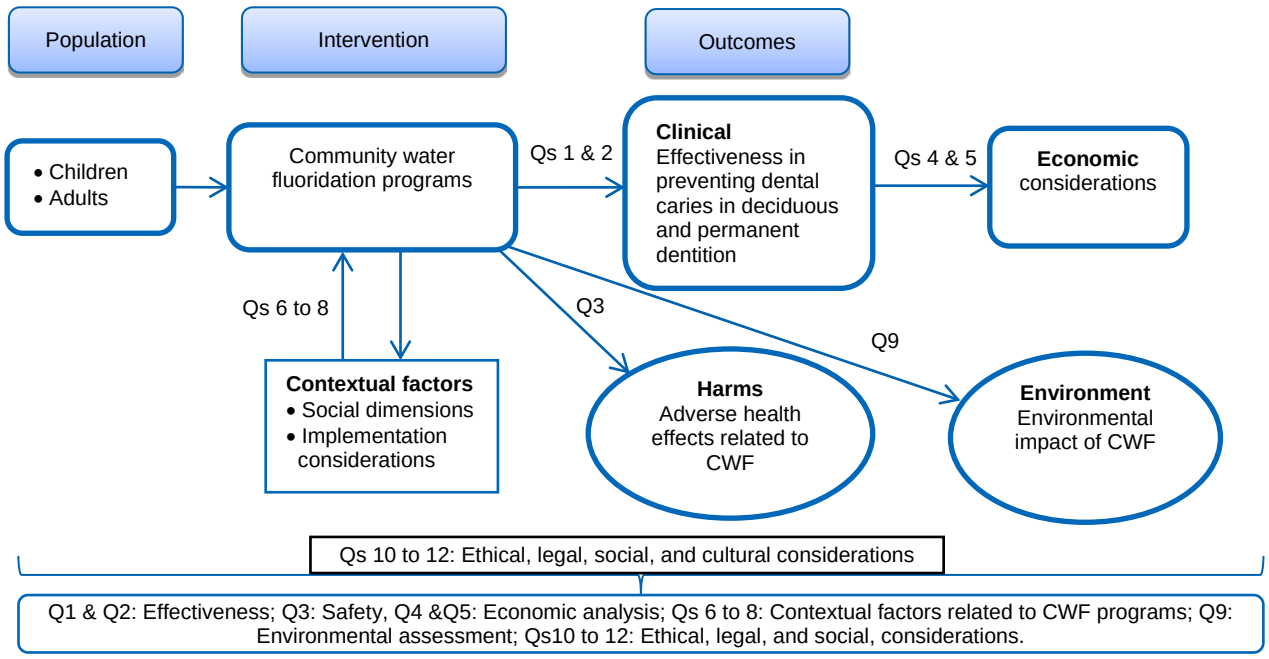
76. About Environment and Climate Change Canada [Internet]. Ottawa: Environment and Climate Change Canada; 2016. [cited 2018 Jan 17]. Available from: http://www.ec.gc.ca/default.asp?lang=En&n=BD3CE17D-1

77. Canadian Environmental Quality Guidelines [Internet]. Winnipeg: Canadian Council of Ministers of the Environment; 2007. [cited 2017 Nov 10]. Available from: http://ceqg-rcqe.ccme.ca/en/index.html#void

78. Hofmann B, Droste S, Oortwijn W, Cleemput I, Sacchini D. Harmonization of ethics in health technology assessment: a revision of the Socratic approach. Int J Technol Assess Health Care. 2014 Jan;30(1):3-9.

Appendix 1: Analytic Framework

Figure 2: Policy Question: Should community water fluoridation be encouraged and maintained in Canada?



CWF = community water fluoridation; Q = question.

Table 3: Research Questions and Methods

Research Questions	Methods
Q1. What is the effectiveness of community water fluoridation compared with non-fluoridated drinking water in the prevention of dental caries in children and adults?	Update of two published systematic reviews
Q2. What are the effects of community water fluoridation cessation on dental caries in children and adults compared with continued community water fluoridation, the period before cessation of water fluoridation, or non-fluoridated communities?	
Q3. What are the negative effects of community water fluoridation (at a given fluoride level) compared with non-fluoridated drinking water (fluoride level < 0.4 ppm) or fluoridation at different levels on human health outcomes?	
Q4. From a societal perspective, what is the budget impact of introducing water fluoridation in a Canadian municipality without an existing community water fluoridation program?	Budget impact analyses
Q5. From a societal perspective, what is the budget impact of ceasing water fluoridation in a Canadian municipality that currently has a community water fluoridation program?	
Q6. How is community water fluoridation conceptualized, communicated, and enacted by public health practitioners, municipal decision-makers, and members of the general public who may be affected by its implementation or cessation?	Critical interpretative synthesis of qualitative studies and mixed-methods studies, surveys, questionnaires
Q7. What are the main challenges, considerations, and enablers related to implementing or maintaining community water fluoridation programs in Canada?	Consultations with targeted experts and stakeholders

Research Questions	Methods
Q8. What are the main challenges, considerations, and enablers related to the cessation of community water fluoridation programs in Canada?	Narrative summary of the published and grey literature Survey on implementation issues related to CWF
Q9. What are the potential environmental (toxicological) risks associated with community water fluoridation?	Narrative summary of the published and grey literature Qualitative risk assessment
Q10. What are the major ethical issues raised by the implementation of community water fluoridation?	Review of the bioethics literature and analysis of ethical issues raised by reports answering questions 1 to 9
Q11. What are the major ethical issues raised by the cessation of community water fluoridation?	
Q12. What are the major ethical issues raised by the legal, social, and cultural considerations to consider for implementation and cessation?	

CWF = community water fluoridation.

CADTH

Appendix 2: Literature Search Strategies

Clinical Database Search

OVERVIEW	
Interface:	Ovid
Databases:	EBM Reviews - Cochrane Central Register of Controlled Trials August 2017 EBM Reviews - Cochrane Database of Systematic Reviews 2005 to September 26, 2017 Embase 1974 to 2017 October 02 Ovid MEDLINE(R) ALL 1946 to October 02, 2017 **Note:** Subject headings have been customized for each database. Duplicates between databases were removed in Ovid.
Date of Search:	October 18, 2017
Alerts:	Bi-weekly search updates until project completion
Study Types:	No filter
Limits:	Publication years 2014-current Humans

SYNTAX GUIDE	
/	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
adj#	Adjacency within # number of words (in any order)
.ti	Title
.ab	Abstract
.kf	Author keyword heading word (MEDLINE)
.kw	Keyword heading (MEDLINE)
.kw	Author keyword (Embase)
medall	Ovid database code; MEDLINE ALL
cctr	Ovid database code; Cochrane Central Register of Controlled Trials
coch	Ovid database code; Cochrane Database of Systematic Reviews
oemezd	Ovid database cose; Embase 1974 to present

MULTI-DATABASE STRATEGY	
#	**Searches**
	Water Fluoridation Concept (MEDLINE & The Cochrane Library)
1	Fluoridation/
2	(antifluorid* or defluorid* or defluorin* or deflurin* or deflurid* or fluoridation* or nonfluorid* or nonfluorin* or nonflurin* or nonflurid*).ti,ab,kf,kw.
3	or/1-2

MULTI-DATABASE STRATEGY	
#	**Searches**
4	exp Fluorides/
5	(fluorid* or fluorin* or flurin* or flurid*).ti,ab,kf,kw.
6	or/4-5
7	exp Water supply/
8	Drinking Water/
9	Water Quality/
10	(water* or groundwater* or ground-water*).ti,ab,kf,kw.
11	or/7-10
12	3 or (6 and 11)
13	exp animals/
14	exp animal experimentation/ or exp animal experiment/
15	exp models animal/
16	nonhuman/
17	exp vertebrate/ or exp vertebrates/
18	or/13-17
19	exp humans/
20	exp human experimentation/ or exp human experiment/
21	or/19-20
22	18 not 21
23	12 not 22
24	23 use medall
25	limit 24 to yr="2014 -Current"
26	(201408* or 201409* or 20141* or 2015* or 2016* or 2017* or 2018*).dc,ed,ep.
27	24 and 26
28	25 or 27
29	limit 12 to yr="2014 -Current"
30	29 use cctr
31	29 use coch
32	**Water Fluoridation Concept (Embase)** Fluoridation/
33	(antifluorid* or defluorid* or defluorin* or deflurin* or deflurid* or fluoridation* or nonfluorid* or nonfluorin* or nonflurin* or nonflurid*).ti,ab,kw.
34	or/32-33
35	Fluoride/
36	(fluorid* or fluorin* or flurin* or flurid*).ti,ab,kw.
37	or/35-36
38	Water supply/
39	Drinking Water/
40	Water Quality/
41	(water* or groundwater* or ground-water*).ti,ab,kw.
42	or/38-41

MULTI-DATABASE STRATEGY	
#	**Searches**
43	34 or (37 and 42)
44	43 not 22
45	44 use oemezd
46	(201408* or 201409* or 20141* or 2015* or 2016* or 2017* or 2018*).dd.
47	limit 45 to yr="2014 -Current"
48	45 and 46
49	or/47-48
50	49 not conference abstract.pt.
51	**All Clinical Results (Duplicates removed)** 28 or 30 or 31 or 50
52	remove duplicates from 51

OTHER DATABASES		
PubMed	A limited PubMed search was performed to capture records not found in MEDLINE. Same MeSH, keywords, limits, and study types used as per MEDLINE search, with appropriate syntax used.	
CINAHL (EBSCO interface)	Same keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for EBSCO platform.	
Scopus (Elsevier)	Same keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Scopus platform.	

Social Dimensions Database Search

OVERVIEW	
Interface:	Ovid
Databases:	BIOSIS Previews 1989 to 2010 ERIC 1965 to August 2017 Ovid MEDLINE(R) ALL 1946 to October 16, 2017 **Note:** Subject headings have been customized for each database. Duplicates between databases were removed in Ovid.
Date of Search:	October 17, 2017
Alerts:	Bi-weekly search updates until project completion
Study Types:	Qualitative, survey/questionnaire, and patient perspectives filters
Limits:	No date limit English or French languages

SYNTAX GUIDE	
/	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
exp	Explode a subject heading
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
adj#	Adjacency within # number of words (in any order)
.ti	Title

SYNTAX GUIDE

.ab	Abstract
.kf	Author keyword heading word (MEDLINE)
.kw	Keyword heading (MEDLINE)

MULTI-DATABASE STRATEGY

#	Searches
1	**Water Fluoridation Concept** Fluoridation/
3	or/1-2
4	exp Fluorides/
5	(fluorid* or fluorin* or flurin* or flurid*).ti,ab,kf,kw.
6	or/4-5
7	exp Water Supply/
8	Drinking Water/
9	Water Quality/
10	(water* or groundwater* or ground-water*).ti,ab,kf,kw.
11	or/7-10
12	3 or (6 and 11)
	Study Type Filters
13	exp Patient Acceptance of Health Care/
14	((citizen? or individual? or societ* or survivor* or public*) and (preference* or preferred or input or experience or experiences or value or values or perspective* or perception* or perceive or perceived or expectation* or choice* or choose* or choosing or "day-to-day" or lives or participat* or acceptance or acceptability or acceptable or accept or accepted or adheren* or adhere or nonadheren* or complian* or noncomplian* or willingness or convenience or convenient or challenges or concerns or limitations or quality of life or satisfaction or satisfied or dissatisfaction or dissatisfied or burden or attitude* or knowledge or belief* or opinion* or understanding or lessons or reaction* or motivation* or motivated or intention* or involvement or engag* or consult* or interact* or dialog* or conversation* or decision* or decide* or deciding or empower* or barrier* or facilitator* or survey* or questionnaire* or Likert)).ti.
15	((citizen? or individual? or societ* or survivor* or public*) adj2 (preference* or preferred or input or experience or experiences or value or values or perspective* or perception* or perceive or perceived or expectation* or choice* or choose* or choosing or "day-to-day" or lives or participat* or acceptance or acceptability or acceptable or accept or accepted or adheren* or adhere or nonadheren* or complian* or noncomplian* or willingness or convenience or convenient or challenges or concerns or limitations or quality of life or satisfaction or satisfied or dissatisfaction or dissatisfied or burden or attitude* or knowledge or belief* or opinion* or understanding or lessons or reaction* or motivation* or motivated or intention* or involvement or engag* or consult* or interact* or dialog* or conversation* or decision* or decide* or deciding or empower* or barrier* or facilitator* or survey* or questionnaire* or Likert)).ab,kf.
16	((citizen? or individual? or societ* or survivor* or public*) adj7 (preference* or preferred or input or experience or experiences or value or values or perspective* or perception* or perceive or perceived or expectation* or choice* or choose* or choosing or "day-to-day" or lives or participat* or acceptance or acceptability or acceptable or accept or accepted or adheren* or adhere or nonadheren* or complian* or noncomplian* or willingness or convenience or convenient or challenges or concern or limitations or quality of life or satisfaction or satisfied or dissatisfaction or dissatisfied or burden or attitude* or knowledge or belief* or opinion* or understanding or lessons or reaction* or motivation* or motivated or intention* or involvement or engag* or consult* or interact* or dialog* or conversation* or decision* or decide* or deciding or empower* or barrier* or facilitator* or survey* or questionnaire* or Likert)).ab. /freq=2
17	((personal or spous* or partner or partners or couples or users or participant* or people or child* or teenager* or adolescent* or youth or girls or boys or adults or elderly or females or males or women* or men or men's or mother* or father* or parents or parent or parental or maternal or paternal) adj2 (preference* or preferred or input or experience or experiences or value or values or perspective* or perception* or perceive or perceived or expectation* or choice* or choose* or choosing or "day-to-day" or lives or participat* or acceptance or acceptability or acceptable or accept or accepted or adheren* or adhere or

MULTI-DATABASE STRATEGY	
#	**Searches**
	nonadheren* or complian* or noncomplian* or willingness or convenience or convenient or challenges or concerns or limitations or quality of life or satisfaction or satisfied or dissatisfaction or dissatisfied or burden or attitude* or knowledge or belief* or opinion* or understanding or lessons or reaction* or motivation* or motivated or intention* or involvement or engag* or consult* or interact* or dialog* or conversation* or decision* or decide* or deciding or empower* or barrier* or facilitator* or survey* or questionnaire* or Likert)).ab. /freq=2
18	(patient adj (reported or centered* or centred* or focused)).ti,ab,kf.
19	(treatment* adj2 (satisf* or refus*)).ti,ab,kf.
20	or/13-19
21	exp Empirical Research/ or Interview/ or Interviews as Topic/ or Personal Narratives/ or Focus Groups/ or Narration/ or Nursing Methodology Research/
22	Interview/
23	interview*.ti,ab,kf.
24	qualitative.ti,ab,kf,jw.
25	(theme* or thematic).ti,ab,kf.
26	ethnograph*.ti,ab,kf.
27	ethnomedicine.ti,ab,kf.
28	ethnonursing.ti,ab,kf.
29	anthropolog*.ti,ab,kf.
30	phenomenol*.ti,ab,kf.
31	(grounded adj (theor* or study or studies or research or analys?s)).ti,ab,kf.
32	((lived or life) adj (experience* or stor*)).ti,ab,kf.
33	(emic or etic or hermeneutic* or heuristic* or semiotic*).ti,ab,kf.
34	((data or theor*) adj1 saturat*).ti,ab,kf.
35	participant observ*.ti,ab,kf.
36	(social construct* or postmodern* or post-structural* or post structural* or poststructural* or post modern* or post-modern* or feminis*).ti,ab,kf.
37	Actor Network Theory.ti,ab,kf.
38	(action research or cooperative inquir* or co-operative inquir*).ti,ab,kf.
39	(humanistic or existential or experiential or paradigm*).ti,ab,kf.
40	(field adj (study or studies or research or work)).ti,ab,kf.
41	(human science or social science).ti,ab,kf.
42	biographical method.ti,ab,kf.
43	theoretical sampl*.ti,ab,kf.
44	((purpos* adj4 sampl*) or (focus adj group*)).ti,ab,kf.
45	(open-ended or narrative* or textual or texts or semi-structured).ti,ab,kf.
46	(life world* or life-world* or personal experience*).ti,ab,kf.
47	cluster sampl*.ti,ab,kf.
48	content analysis.ti,ab,kf.
49	conversation analys?s.ti,ab,kf.
50	(constant adj (comparative or comparison)).ti,ab,kf.
51	((discourse* or discurs*) adj3 analys?s).ti,ab,kf.
52	narrative analys?s.ti,ab,kf.
53	(heidegger* or colaizzi* or spiegelberg* or merleau* or husserl* or foucault* or ricoeur or glaser*).ti,ab,kf.
54	(van adj manen*).ti,ab,kf.

MULTI-DATABASE STRATEGY	
#	**Searches**
55	(van adj kaam*).ti,ab,kf.
56	(corbin* adj2 strauss*).ti,ab,kf.
57	case study.ti,ab,kf.
58	(Yin or Stake).ti,ab,kf.
59	(reflexive or reflexivity).ti,ab,kf.
60	(perspective or experience).ti,ab,kf.
61	or/21-60
62	"Surveys and Questionnaires"/
63	Health Care Surveys/
64	Self Report/
65	questionnaire*.ti,ab,kf.
66	survey*.ti,ab,kf.
67	or/62-66
68	20 or 61 or 67
69	12 and 68
70	limit 69 to (english or french)

OTHER DATABASES		
PubMed	A limited PubMed search was performed to capture records not found in MEDLINE. Same MeSH, keywords, limits, and study types used as per MEDLINE search, with appropriate syntax used.	
CINAHL (EBSCO interface)	Same keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for EBSCO platform.	
Scopus (Elsevier)	Same keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Scopus platform.	

Grey Literature

Dates for Search:	Nov-Dec 2017
Keywords:	Included terms for fluoridation or fluoride in water
Limits:	English or French language

Relevant websites from the following sections of the CADTH grey literature checklist *Grey Matters: a practical tool for searching health-related grey literature* (https://www.cadth.ca/grey-matters) were searched:

- Health Technology Assessment Agencies
- Health Economics
- Clinical Practice Guidelines
- Databases (free)
- Internet Search
- Open Access Journals

CADTH

Appendix 3: Clinical Studies Full-Text Screening Checklists

Full-Text Screening Checklist Q1

Reviewer: _____ Date: _____

Ref ID: **Author:** **Publication Year:**			
Did the study include:	**Yes (Include)**	**Unclear[a]**	**No (Exclude)**
1) Population: • Humans of any age living in any community with or without fluoridated water (artificially or naturally)	☐	☐	☐
2) Intervention: • Fluoridated water (fluoride level 0.4 ppm to 1.5 ppm)	☐	☐	☐
3) Comparators: • Non-fluoridated water (fluoride level < 0.4 ppm); before introduction of water fluoridation	☐	☐	☐
4) Outcomes: • Any measure of dental caries	☐	☐	☐
5) Study design: • Primary studies of any design with controls	☐	☐	☐
Decision for including the study:[b]	Yes ☐		No ☐
Reason(s) for exclusion:	☐ Ineligible study population ☐ Irrelevant intervention ☐ No or irrelevant comparator ☐ Irrelevant outcome(s) ☐ Ineligible study design ☐ Insufficient duration of study follow-up ☐ Ineligible publication format ☐ Other:		

[a] This will be discussed with a second reviewer.
[b] If the answers to all items abovementioned are “Yes” or ”Unclear,” then the study will be included.

Full-Text Screening Checklist Q2

Reviewer: _____ Date: _____

Ref ID: **Author:** **Publication Year:**			
Did the study include:	**Yes (Include)**	**Unclear[a]**	**No (Exclude)**
1. Population: • Humans of any age living in any community with or without fluoridated water (artificially or naturally)	☐	☐	☐
2. Intervention: • Water fluoridation cessation	☐	☐	☐
3. Comparators: • Fluoridated water (fluoride level 0.4 ppm to 1.5 ppm); non-fluoridated water; before water fluoridation cessation	☐	☐	☐
4. Outcomes: • Any measure of dental caries	☐	☐	☐
5. Study designs: • Primary studies of any design with controls	☐	☐	☐
Decision for including the study:[b]	Yes ☐		No ☐
Reason(s) for exclusion:	☐ Ineligible study population ☐ Irrelevant intervention ☐ No or irrelevant comparator ☐ Irrelevant outcome(s) ☐ Ineligible study design ☐ Ineligible publication format ☐ Other:		

[a] This will be discussed with a second reviewer.
[b] If the answers to all items abovementioned are “Yes” or ”Unclear,” then the study will be included.

Full-Text Screening Checklist Q3

Reviewer: _____ Date: _____

Ref ID: **Author:** **Publication Year:**			
Did the study include:	**Yes (Include)**	**Unclear[a]**	**No (Exclude)**
1. Population: • Humans of any age living in any community with or without fluoridated water (artificially or naturally)	☐	☐	☐
2. Intervention: • Fluoridated water (any fluoride level)	☐	☐	☐
3. Comparators: • Non-fluoridated water (fluoride level < 0.4 ppm) or water of different fluoride levels	☐	☐	☐
4. Outcomes: • Any measure of adverse health outcomes other than dental caries	☐	☐	☐
5. Study designs: • Primary studies of any design with controls	☐	☐	☐
Decision for including the study:[b]	Yes ☐		No ☐
Reason(s) for exclusion:	☐ Ineligible study population ☐ Irrelevant intervention ☐ No/irrelevant comparator ☐ Irrelevant outcome(s) ☐ Ineligible study design ☐ Ineligible publication format ☐ Other:		

[a] This will be discussed with a second reviewer.
[b] If the answers to all items abovementioned are “Yes” or ”Unclear,” then the study will be included.

CADTH

Appendix 4: Clinical Studies Data Extraction Forms

Proposed Data Extraction Form for Included Studies

Researcher: _____ Date: _____

GENERAL INFORMATION	
Ref ID	
Title	
Author(s)	
Publication year	
Country (where the study was conducted)	
Funding sources	
Reported conflict of interest	□ Yes □ No

STUDY CHARACTERISTICS	
Objectives	
Study design	
Study location	
Study duration	
Exposure duration	
Fluoride levels or exposures:	
• Intervention	
• Comparator	
Setting	
Source of population	
Inclusion/exclusion criteria	
Recruitment or sampling procedure	
Applicability to Canadian context (based on conditions such as fluoridation level, health and dental care system, and socio-economic factors [income and education levels])	□ High □ Partial □ Low

PARTICIPANT CHARACTERISTICS			
	Total	**Intervention**	**Comparator**
Number of participants enrolled			
Age			
Sex			
(Other characteristics)			
Subgroups reported			

REPORTED OUTCOMES	
Definition (with units) and method of measurement	
Number of participants analyzed	
Number of participants excluded or missing (with reasons)	
Imputing of missing data	
Statistical method of analysis	
Results	

CONCLUSION	
Authors' conclusion	
Reviewer's note	

CADTH

Appendix 5: Clinical Studies Quality Assessment Forms

Proposed Quality Assessment Form for Quantitative Intervention Studies

Researcher: _____ Date: _____

Item	Question	Rating	Comment
Section 1: Population			
1.1	Is the source population or source area well described? • Were the country (e.g., developed or non-developed, type of health care system), setting (primary schools, community centres, etc.), location (urban, rural), population demographics, etc. adequately described?		
1.2	Is the eligible population or area representative of the source population or area? • Was the recruitment of individuals, clusters, or areas well defined (e.g., advertisement, birth register)? • Was the eligible population representative of the source? Were important groups under-represented?		
1.3	Do the selected participants or areas represent the eligible population or area? • Was the method of selecting participants from the eligible population well described? • What % of selected individuals or clusters agreed to participate? Were there any sources of bias? • Were the inclusion or exclusion criteria explicit and appropriate?		
Section 2: Method of allocation to intervention (or comparison)			
2.1	How was selection bias minimized? • Was allocation to exposure and comparison randomized? Was it truly random ++ or pseudo-randomized + (e.g., consecutive admissions)? • If not randomized, was significant confounding likely (–) or not (+)? • If a crossover, was order of intervention randomized?		
2.2	Were interventions (and comparisons) well described and appropriate? • Were interventions and comparisons described in sufficient detail (i.e., enough for study to be replicated)? • Was comparisons appropriate (e.g., usual practice rather than no intervention)?		
2.3	Was the allocation concealed? • Could the person(s) determining the allocation of participants or clusters to intervention or comparison groups have influenced the allocation? • Adequate allocation concealment (++) would include centralized allocation or computerized allocation systems.		
2.4	Were participants or investigators blind to exposure and comparison? • Were participants and investigators — i.e., those delivering or assessing the intervention — kept blind to intervention allocation? (Triple or double blinding score ++) • If lack of blinding is likely to cause important bias, score –.		

Item	Question	Rating	Comment
2.5	Was the exposure to the intervention and comparison adequate? • Is reduced exposure to intervention or control related to the intervention (e.g., adverse effects leading to reduced compliance) or fidelity of implementation (e.g., reduced adherence to protocol)? • Was lack of exposure sufficient to cause important bias?		
2.6	Was contamination acceptably low? • Did any in the comparison group receive the intervention or vice versa? • If so, was it sufficient to cause important bias? • If a crossover trial, was there a sufficient washout period between interventions?		
2.7	Were other interventions similar in both groups? • Did either group receive additional interventions or have services provided in a different manner? • Were the groups treated equally by researchers or other professionals? • Was this sufficient to cause important bias?		
2.8	Were all participants accounted for at study conclusion? • Were those lost to follow-up (i.e., dropped or lost pre-, mid-, or post-intervention) acceptably low (i.e., typically < 20%)? • Did the proportion dropped differ by group? For example, were drop-outs related to the adverse effects of the intervention?		
2.9	Did the setting reflect usual Canadian practice? • Did the setting in which the intervention or comparison was delivered differ significantly from usual practice in Canada? For example, did participants receive the intervention (or comparison) in a hospital rather than a community-based setting?		
2.10	Did the intervention or control comparison reflect usual Canadian practice? • Did the intervention or comparison differ significantly from usual Canadian practice? For example, did participants receive intervention (or comparison) delivered by specialists rather than GPs? Were participants monitored more closely?		
Section 3: Outcomes			
3.1	Were outcome measures reliable? • Were outcome measures subjective or objective (e.g., biochemically validated nicotine levels ++ versus self-reported smoking –)? • How reliable were outcome measures (e.g., inter- or intra-rater reliability scores)? • Was there any indication that measures had been validated (e.g., against a gold standard measure) or assessed for content validity?		
3.2	Were all outcome measurements complete? • Were all or most study participants who met the defined study outcome definitions likely to have been identified?		
3.3	Were all important outcomes assessed? • Were all important benefits and harms assessed? • Was it possible to determine the overall balance of benefits and harms of the intervention versus comparison?		

Item	Question	Rating	Comment
3.4	Were outcomes relevant? • Where surrogate outcome measures were used, did they measure what they set out to measure? (E.g., a study to assess impact on physical activity assesses gym membership — a potentially objective outcome measure — but is it a reliable predictor of physical activity?)		
3.5	Were there similar follow-up times in exposure and comparison groups? • If groups are followed for different lengths of time, then more events are likely to occur in the group followed-up for longer, distorting the comparison. • Analyses can be adjusted to allow for differences in length of follow-up (e.g., using person-years).		
3.6	Was follow-up time meaningful? • Was follow-up long enough to assess long-term benefits or harms? • Was it too long, e.g., were participants lost to follow-up?		
Section 4: Analyses			
4.1	Were exposure and comparison groups similar at baseline? If not, were these adjusted? • Were there any differences between groups in important confounders at baseline? • If so, were these adjusted for in the analyses (e.g., multivariate analyses or stratification)? • Were there likely to be any residual differences of relevance?		
4.2	Was intention-to-treat analysis conducted? • Were all participants (including those who dropped out or did not fully complete the intervention course) analyzed in the groups (i.e., intervention or comparison) to which they were originally allocated?		
4.3	Was the study sufficiently powered to detect an intervention effect (if one exists)? • A power of 0.8 (meaning it is likely the study will show the effect of a given size, if one exists, 80% of the time) is the conventionally accepted standard. • Is a power calculation presented? If not, what is the expected effect size? Is the sample size adequate?		
4.4	Were the estimates of effect size given or calculable? • Were effect estimates (e.g., relative risks, absolute risks) given or possible to calculate?		
4.5	Were the analytical methods appropriate? • Were important differences in follow-up time and likely confounders adjusted for? • If a cluster design, were analyses of sample size (and power) and effect size performed on clusters (and not individuals)? • Were subgroup analyses pre-specified?		
4.6	Was the precision of intervention effects given or calculable? Were they meaningful? • Were confidence intervals or P values for effect estimates given or possible to calculate? • Were confidence intervals wide or were they sufficiently precise to aid decision-making? If precision were lacking, was the study under-powered?		

Item	Question	Rating	Comment
Section 5: Summary			
5.1	Are the study results internally valid (i.e., unbiased)? • How well did the study minimize sources of bias (i.e., adjusting for potential confounders)? • Were there significant flaws in the study design?		
5.2	Are the findings generalizable to the Canadian population (i.e., externally valid)? • Are there sufficient details given about the study to determine if the findings are generalizable to the source population? Consider: participants, interventions and comparisons, outcomes, and resource and policy implications.		
Overall quality rating			

Question in sections 1 to 4 will be rated as "++," "+," "–," "Not Reported (NR),"or "Not Applicable (NA)."

"++" Indicates that for that particular aspect of study design, the study has been designed or conducted in so as to minimize the risk of bias.

"+" Indicates that either the answer to the checklist question is not clear the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

"–" Should be reserved for those aspects of the study design in which significant sources of bias may persist.

"NR" Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

"NA" Should be reserved for those study design aspects that are not applicable given the study design under review (for example, allocation concealment would not be applicable for case-control studies).

In section 5, the overall study quality for internal validity (5.1) and external validity (5.2) will be rated as "++," "+," or "–."

"++" All or most of the checklist criteria have been fulfilled; where they have not been fulfilled, the conclusions are very unlikely to change.

"+" Some of the checklist criteria have been fulfilled; where they have not been fulfilled, or have not adequately been described, the conclusions are unlikely to change.

"–" Few or no checklist criteria have been fulfilled. The conclusions are likely or very likely to change.

An overall quality rating will be assigned based on the scoring in section 5 as "High (++,++)," "Acceptable (++,+; +,++)," or "Low (+,+; +,–; –,+ or –, –)."

Proposed Quality Assessment Form for Quantitative Studies Reporting Correlations and Associations

Researcher: _____ Date: _____

Item	Question	Rating	Comment
Section 1: Population			
1.1	Is the source population or source area well described? • Was the country (e.g., developed or non-developed, type of health care system), setting (primary schools, community centres, etc.), location (urban, rural), population demographics, etc. adequately described?		
1.2	Is the eligible population or area representative of the source population or area? • Was the recruitment of individuals, clusters, or areas well defined (e.g., advertisement, birth register)? • Was the eligible population representative of the source? Were important groups under-represented?		
1.3	Do the selected participants or areas represent the eligible population or area? • Was the method of selecting participants from the eligible population well described? • What % of selected individuals or clusters agreed to participate? Were there any sources of bias? • Were the inclusion or exclusion criteria explicit and appropriate?		
Section 2: Method of selection of exposure (or comparison) group			
2.1	Selection of exposure (and comparison) group. How was selection bias minimized?		
2.2	Did the selection of explanatory variables have a sound theoretical basis? • How sound was the theoretical basis for selecting the explanatory variables?		
2.3	Was contamination acceptably low? • Did any in the comparison group receive the exposure? • If so, was it sufficient to cause important bias?		
2.4	How well were likely confounding factors identified and controlled? • Were there likely to be other confounding factors not considered or appropriately adjusted for? • Was this sufficient to cause important bias?		
2.5	Is the setting applicable to Canada? • Did the setting differ significantly from Canada?		
Section 3: Outcomes			
3.1	Were outcome measures reliable? • Were outcome measures subjective or objective (e.g., biochemically validated nicotine levels ++ versus self-reported smoking –)?		

Item	Question	Rating	Comment
	• How reliable were outcome measures (e.g., inter- or intra-rater reliability scores)? • Was there any indication that measures had been validated (e.g., against a gold standard measure) or assessed for content validity?		
3.2	Were all outcome measurements complete? • Were all or most study participants who met the defined study outcome definitions likely to have been identified?		
3.3	Were all important outcomes assessed? • Were all important benefits and harms assessed? • Was it possible to determine the overall balance of benefits and harms of the intervention versus comparison?		
3.4	Was there a similar follow-up time in exposure and comparison groups? • If groups are followed for different lengths of time, then more events are likely to occur in the group followed-up for longer, distorting the comparison. • Analyses can be adjusted to allow for differences in length of follow-up (e.g., using person-years).		
3.5	Was follow-up time meaningful? • Was follow-up long enough to assess long-term benefits and harms? • Was it too long, e.g., were participants lost to follow-up?		
Section 4: Analyses			
4.1	Was the study sufficiently powered to detect an intervention effect (if one exists)? • A power of 0.8 (meaning it is likely the study will show the effect of a given size if one exists, 80% of the time) is the conventionally accepted standard. • Is a power calculation presented? If not, what is the expected effect size? Is the sample size adequate?		
4.2	Were multiple explanatory variables considered in the analyses? • Were sufficient explanatory variables considered in the analysis?		
4.3	Were the analytical methods appropriate? • Were important differences in follow-up time and likely confounders adjusted for?		
4.4	Was the precision of association given or calculable? Is association meaningful? • Were confidence intervals or P values for effect estimates given or possible to calculate? • Were confidence intervals wide or were they sufficiently precise to aid decision-making? If precision is lacking, is this because the study is under-powered?		
Section 5: Summary			
5.1	Are the study results internally valid (i.e., unbiased)? • How well did the study minimize sources of bias (i.e., adjusting for potential confounders)? • Were there significant flaws in the study design?		

Item	Question	Rating	Comment
5.2	Are the findings generalizable to the Canadian population (i.e., externally valid)? • Are there sufficient details given about the study to determine if the findings are generalizable to the source population? Consider: participants, interventions and comparisons, outcomes, and resource and policy implications.		
Overall quality rating			

Question in sections 1 to 4 will be rated as "++," "+," "–," "Not Reported (NR)," or "Not Applicable (NA)."

"++" Indicates that for that particular aspect of study design, the study has been designed or conducted so as to minimize the risk of bias.

"+" Indicates that either the answer to the checklist question is not clear the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design.

"–" Should be reserved for those aspects of the study design in which significant sources of bias may persist.

"NR" Should be reserved for those aspects in which the study under review fails to report how they have (or might have) been considered.

"NA" Should be reserved for those study design aspects that are not applicable given the study design under review (for example, allocation concealment would not be applicable for case-control studies).

In section 5, the overall study quality for internal validity (5.1) and for external validity (5.2) will be rated as "++," "+," or "–."

"++" All or most of the checklist criteria have been fulfilled; where they have not been fulfilled, the conclusions are very unlikely to change.

"+" Some of the checklist criteria have been fulfilled; where they have not been fulfilled, or have not adequately been described, the conclusions are unlikely to change.

"–" Few or no checklist criteria have been fulfilled. The conclusions are likely or very likely to change.

An overall quality rating will be classified based on the scoring in section 5 as "High (++,++)," "Acceptable (++,+; +,++)," or "Low (+,+; +,–; –,+ or –, –)."