



Community water fluoridation exposure and dental caries experience in newly enrolled members of the Canadian Armed Forces 2006–2017

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Abstract

Objectives This cross-sectional study examines the dental caries experience of new Canadian Armed Forces (CAF) members in relation to enrollment from municipalities with and without water fluoridation.

Methods The study population consisted of recruits who enrolled in the CAF between 2006 and 2017 with an enrollment address in municipalities with known fluoridation status ($n = 24,552$). Odontogram statistics from dental examinations were used to calculate the number of decayed, missing, and filled teeth (DMFT) and tooth surfaces (DMFS) for each recruit. The average difference between recruits from municipalities with and without fluoridation was determined using a linear regression model which adjusted for confounding by age and gender and allowed effect modification based on socio-economic status.

Results The average recruit was male, 24 years of age, with 5.6 DMFT and 11.6 DMFS. After adjusting for age and gender, recruits residing in municipalities with water fluoridation had lower DMFT by 0.67 (CI $-0.55, -0.79$) points and lower DMFS by 1.77 ($-1.46, -2.09$) points. When allowing for effect modification by median income quintile of the recruits' home census tract, the average reduction in DMFT and DMFS was similar in all income quintiles, with average reductions in DMFT ranging from 0.47 to 1.02 and average reductions in DMFS ranging from 1.33 to 2.70.

Conclusion Residence in a municipality with water fluoridation was associated with reduced caries experience in a national sample of newly enrolled CAF members. The benefits of water fluoridation were uniform across neighbourhood income and military rank classes.

Résumé

Objectifs Cette étude transversale examine l'importance du niveau de la carie dentaire des nouveaux membres des Forces armées canadiennes (FAC) par rapport à l'enrôlement provenant des municipalités avec et sans fluoruration de l'eau.

Méthodes La population étudiée était constituée de recrues qui se sont enrôlés dans les FAC entre 2006 et 2017 avec une adresse d'inscription dans les municipalités dont le statut de fluoruration est connu ($n = 24\ 552$). Les statistiques en provenance des odontogrammes des examens dentaires ont été utilisées pour calculer le nombre de dents et surfaces cariés, absents et obturés (CAOD & CAOOF) pour chaque recrue. La différence moyenne entre les recrues des municipalités avec ou sans fluoruration a été déterminée à l'aide d'un modèle de régression linéaire qui a été ajusté pour prendre en considération l'âge et le sexe et a permis une modification de l'effet en fonction du statut socioéconomique.

Résultats La recrue moyenne était un homme de 24 ans avec 5,6 CAOD et 11,6 CAOOF. Après ajustement en fonction de l'âge et du sexe, les recrues résidant dans les municipalités avec fluoruration de l'eau avaient un CAOD inférieur de 0,67 points (IC $-0,55, -0,79$) et un CAOOF inférieur de 1,77 points ($-1,46, -2,09$). En permettant la modification de l'effet par l'indice de revenu médian du secteur de recensement d'origine des recrues, la réduction moyenne du CAOD et du CAOOF était similaire dans tous les niveaux de revenu, avec des réductions moyennes du CAOD d'entre 0,47 et 1,02 et des réductions moyennes du CAOOF d'entre 1,33 et 2,70.

Conclusion La résidence dans une municipalité avec fluoruration de l'eau a été associée avec une réduction des caries dans un échantillonnage national de nouveaux membres enrôlés dans les FAC. Les avantages de la fluoruration de l'eau étaient uniformes dans l'ensemble des niveaux de revenu du quartier et des différentes classes de grade militaire.

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Mots-clés Fluoration · dentisterie de santé publique · caries dentaires · Index CAOD · personnel militaire

Introduction

Municipal water fluoridation is heralded as one of the most successful public health interventions of the previous century. Water fluoridation was first implemented in the 1940s after cross-sectional studies suggested that it could reduce the incidence of dental caries. At proper concentrations, water fluoridation is safe and effective; at higher concentrations, side effects include dental fluorosis, in which small spots become visible on the surface of the teeth (Clark et al. 2006). In 2012, more than 369 million people in 26 countries had access to drinking water that was optimally fluoridated to prevent dental caries (British Fluoridation Society 2012).

Historically, cross-sectional studies on water fluoridation and dental caries have been facilitated using the dental examination statistics of military recruits, who report to basic training from different jurisdictions with varying levels of fluoride in the water supply (Deatherage 1943). In recruit studies conducted since the 1980s, including studies in the British Armed Forces (Robinson et al. 1983) and the Australian Defence Force (Hopcraft and Morgan 2005; Mahoney et al. 2008), the benefit of water fluoridation has been less apparent. An increase in population dental awareness and alternative sources of fluoride, including fluoridated toothpaste, have led to a reduction in the protective benefits of municipal-level water fluoridation and have raised doubts as to the need and cost of maintaining the public health program. In recent years, some Canadian municipalities, including Calgary, Moncton, and Cornwall, have opted to discontinue community water fluoridation. Between 2007 and 2017, the number of Canadians who had access to fluoridated water decreased from 45.1% to 37% (Rabb-Waytowich 2009; Canadian Dental Association 2017).

Canada ranks highly among developed nations in terms of overall oral health of its citizens; however, challenges continue to exist for the more vulnerable segments of the population (Canadian Dental Association 2017). Since water fluoridation is an equitable population-based approach to caries prevention, concerns have been raised that cessation of water fluoridation will differentially affect people of lower socioeconomic status (SES). Recent Canadian publications have observed an increasing caries burden in school-age children in communities that have ceased fluoridation (McLaren et al. 2016). Globally, the burden of untreated caries appears to be shifting from children to adults as people are increasingly retaining their teeth and living longer (Kassebaum et al. 2015). This calls into question the merit of ceasing water fluoridation programs.

Public health planners and policy makers require current knowledge of population oral health trends in order to ensure that programs are achieving intended goals. Large-scale research studies on fluoridation cessation are limited due to methodological complexity and cost (Singhal et al. 2017). The CAF enrolls new members across Canada's geographic and economically diverse regions, enabling the evaluation of the oral health status of young adults from many different fluoridated and non-fluoridated jurisdictions. The aim of this study was to investigate the association between municipal water fluoridation and dental health in an extensive cohort of newly enrolled CAF members.

Methods

This paper follows the STROBE guidelines for reporting cross-sectional studies (von Elm et al. 2014).

Study design and population

This is a cross-sectional study of CAF recruits who enrolled between October 2006 and April 2017. All recruits who were between the ages of 16 and 45 on the date of their dental enrollment examination and resided in a location associated with a valid Canadian postal code in a tracted census agglomeration or census metropolitan area were included in the study population. Ethics approval for this study was received from the University of Manitoba's Research Ethics Board and from the Surgeon General's Health Research Board.

Data sources

This study combines demographic and dental data from the Canadian Forces Health Information System (CFHIS), residential postal codes, and publicly available census information from Statistics Canada, and fluoridation information obtained from cities and municipalities. CAF recruits receive a mandatory forensic dental enrollment examination, which includes a panoramic radiograph and an odontogram digital mapping of the dentition. These dental records are stored electronically in Adstra odontogram charting software component of the CFHIS in case they are required for the purpose of identification later in the recruits' military career. Clinical findings such as caries, root canals, and periodontal status as well as demographic information including age and gender are recorded at these examinations. Dental enrollment examinations are completed by the personnel at the military dental

clinic in Canadian Forces Base Saint-Jean during recruit Basic Military Qualification course at the Canadian Forces Leadership and Recruit School.

Exposure measurement

Municipal water fluoridation was the primary exposure in this study. The postal code provided by recruits at time of enrollment for their residence prior to joining the CAF allows the home census tract of the recruit to be obtained through use of the Canadian Postal Code Conversion File, which is maintained by Canada Post Corporation and provides the census tract (if available) for every postal code in Canada. This census tract was then linked to information on municipal water fluoridation status. A standardized list of the water fluoridation status of Canadian municipalities does not exist. Therefore, we assigned fluoridation status within Canadian census metropolitan area and tracted census agglomerations using information obtained via municipal websites, government reports, news articles, and personal correspondence. Canadian census metropolitan areas include all Canadian cities and surrounding areas with urban cores having a population of at least 100,000 people. Census agglomerations are smaller versions of census metropolitan areas, the urban cores of which have a population of at least 10,000. All census metropolitan areas and census agglomerations with urban-core populations greater than 50,000 are subdivided into census tracts with target populations of 2500 to 8000 people. The full list of cities with accompanying fluoridation status and sources is available in the supplementary material. Individuals were assigned fluoridation status based on that of their enrollment city on the date they enrolled. Only recruits from tracted census agglomerations and census metropolitan areas were assigned a municipality fluoridation status as fluoridated, non-fluoridated, or fluoridation ceased. The ceased-fluoridation status was assigned to recruits who enrolled from a municipality in the first calendar year and any year thereafter following the cessation of water fluoridation. Rural areas were not assigned water fluoridation status because of the high prevalence of alternative water sources, such as well water; recruits from rural areas are therefore considered to have missing fluoridation status.

Outcome measurement

The number of decayed, missing, or filled teeth and/or surfaces (DMFT and DMFS) are commonly used measures of adult dental caries and were used as the outcome measures for this study (Fontana et al. 2010). Both DMFS and DMFT were calculated using 28 teeth (the wisdom teeth are excluded) and excluded congenitally missing teeth (e.g., missing maxillary lateral incisors) and teeth removed for cosmetic reasons (Rakhshan 2015). The DMFT score for a patient is the total

number of teeth that have any decay or fillings or that are missing and can range from 0 to 28. The DMFS score is the total number of surfaces with any decay or repair and ranges from 0 to 140. For the purposes of DMFS calculation, a missing tooth was counted as equivalent to five affected surfaces (Broadbent and Thomson 2005). Dental officers, who receive rigorous training and are held to a consistent set of standards, conduct intake forensic exams on new recruits and record the results in CFHIS. Using these data from CFHIS, which includes surface-level measures of tooth presence, decay, and repair, DMFT and DMFS scores were calculated for each recruit in the study population. These calculations were carried out after the fact using an extract of the CFHIS database in R version 3.6.2 (R Core Team 2019). Teeth and surfaces that had active carious lesions extending into the dentine or visible cavitation were considered “decayed.” These two scores were treated as continuous measures of the caries experience of recruits. Recruits without an odontogram were considered to have missing outcome status.

Covariates

Age, gender, and military rank (officer or non-commissioned member (NCM) status) are recorded at enrollment. Officers require higher levels of education and training as compared to NCMs (Park 2008); thus, we considered rank a proxy measure for education. Median income in each census tract was determined using the 2016 census to serve as a proxy for area-level SES. If the area of a recruit’s postal code intersected two or more census tract areas, a simple mean of the census tract incomes was assigned to the recruit. An income quintile for each recruit was assigned based on the median income in their home census tract relative to all other tracts within the same census metropolitan area or census agglomeration (Fuller and Winters 2017). All covariates were measured at the time of the dental enrollment examination. Recruits without these demographic data were excluded from the analysis.

Statistical analysis

Descriptive statistics were calculated, with means and standard deviations calculated for continuous variables and frequencies calculated for categorical variables.

Linear regression models were fit using ordinary least squares to model the effect of municipal water fluoridation on DMFT and DMFS scores. All models controlled for age and gender. Rank and area-level SES were investigated as effect modifiers. Since both of these variables are measurements of effect modification through the same pathway, they were considered in separate models. The treatment of SES as an effect modifier is consistent with previous guidelines (Singhal et al. 2017). In total, six linear regression models—

a main effects model for DMFT and for DMFS, plus models with effect modification by SES with two different measures of SES (community-level income and rank)—were fit to estimate the total effect of municipal water fluoridation on the dental health of the recruits. These models used a complete case analysis strategy for missing data. All analyses were conducted in R version 3.6.2 using the *dplyr* package for data processing and the *tableone* package for creation of tables (R Core Team 2019).

Sensitivity analysis

Measuring municipal water fluoridation at the time of enrollment may misclassify recruits if their recruitment address does not reflect their true exposure history. Models were tested in a subset of the population that had the same birth city and enrollment city to increase the likelihood of correctly assigning a recruit to a municipality with water fluoridation and without water fluoridation. It was hypothesized that this would result in reduced heterogeneity within exposure categories and a larger effect size for municipal water fluoridation. Birth and enrollment city matches were accomplished using text matching. To reduce the number of missed matches due to spelling errors, the Levenshtein distance between birth city and enrollment city names was calculated and manually checked for a match when the distance was lower than five (Soukoreff and MacKenzie 2001).

Results

Of the 41,786 recruits who joined the military during the time period of the study, 28,929 were located in Canadian census metropolitan areas or tracted census agglomerations. We were able to determine municipality fluoridation status for 24,975 of these recruits. Those who were excluded were from rural areas which were close enough to be included in census metropolitan areas, but not close enough to be supplied with municipal water. The final study population, comprised of recruits who had complete information for all covariates of interest, included 24,552 recruits: 13,166 were from fluoridated municipalities, 1651 were from municipalities that had ceased fluoridation, and 9735 were from non-fluoridated municipalities.

Demographic information about the study population is presented in Table 1. The average age of the population at enrollment was 24 years. Eighty-six percent of the recruits were male. The most common province of residence at enrollment was Ontario. In this sample population, the average DMFT score was 5.6 and the average DMFS score was 11.6. No difference in age at enrollment was observed between fluoridated municipalities, non-fluoridated municipalities, and municipalities where water fluoridation was ceased

($p = 0.38$). Recruits who enrolled from communities with fluoridated water were more likely to be male and were more likely to be officers ($p < 0.001$). Recruits who enrolled from higher income communities were also more likely to have fluoridated water ($p < 0.001$).

Municipal water fluoridation was associated with significantly lower DMFT and DMFS scores after adjusting for age and gender (Table 2). Recruits from communities with water fluoridation had an average DMFT score 0.67 teeth lower (95% CI $-0.79, -0.55$) than that of recruits from communities without water fluoridation. Similarly, recruits from communities with water fluoridation had an average DMFS score 1.77 surfaces lower (95% CI $-2.09, -1.46$) compared with that of recruits from communities without water fluoridation. The effect of water fluoridation did not vary significantly by median community income or between recruits who enrolled as officers or non-commissioned members (Table 3).

The sensitivity analysis consisted of 6664 recruits who reported the same city of birth and city of enrollment in the CAF. In this subgroup, the observed difference in DMFT and DMFS between recruits from communities with and without water fluoridation was larger than in the entire population. The average difference after adjusting for age and gender was 0.88 teeth ($-0.66, -1.10$) for DMFT and 2.38 surfaces ($-1.81, -2.95$) for DMFS.

Discussion

The analysis of dental records from a census of CAF recruits presents a unique and inexpensive opportunity to study the effect of municipal water fluoridation on oral health in a geographically diverse segment of the Canadian population. We observed that CAF recruits who resided in a fluoridated municipality at the time of enrollment had achieved a better state of oral health than recruits who enrolled from a non-fluoridated municipality. We did not find evidence to suggest the effectiveness of water fluoridation differed according to income or education in this population.

Previous studies have estimated that fluoridated water exposure results in a 25–30% reduction of dental caries in adult populations (Griffin et al. 2007; Australian Government 2017). Our overall study observations are consistent with the international literature and support the hypothesis that fluoridation has benefits beyond when permanent teeth have finished developing (Burt and Eklund 2005). We also documented a larger benefit of water fluoridation in the subgroup of recruits who likely had the least residential mobility and the greatest exposure to municipal water fluoridation. This finding supports the evidence suggesting an inverse dose response relationship between lifetime exposure to fluoridated drinking water and DMFT (Mahoney et al. 2008).

Table 1 Characteristics of Canadian Armed Forces recruits (*n* = 24,552) stratified by their enrollment community municipal water fluoridation status

	Community water fluoridation status			<i>p</i> value
	Not fluoridated (<i>n</i> = 9735)	Fluoridation ceased (<i>n</i> = 1651)	Fluoridated (<i>n</i> = 13,166)	
Age (mean (SD))	23.95 (4.97)	23.78 (4.83)	23.96 (4.81)	0.38
Male	8341 (85.7)	1398 (84.7)	11,475 (86.9)	0.004
Median community income		326 (19.8)	2398 (18.2)	< 0.001
Lowest	2020 (20.8)	299 (18.1)	2210 (16.8)	
Low	1866 (19.2)	334 (20.3)	2534 (19.2)	
Medium	1859 (19.1)	397 (24.1)	2918 (22.2)	
High	1967 (20.2)	293 (17.8)	3106 (23.6)	
Highest	2015 (20.7)			
Province of residence				< 0.001
Alberta	74 (0.8)	293 (17.7)	1160 (8.8)	
British Columbia	2386 (24.5)	19 (1.2)	52 (0.4)	
Manitoba	0 (0.0)	0 (0.0)	763 (5.8)	
New Brunswick	289 (3.0)	128 (7.8)	385 (2.9)	
Newfoundland and Labrador	163 (1.7)	0 (0.0)	0 (0.0)	
Nova Scotia	0 (0.0)	0 (0.0)	1850 (14.0)	
Ontario	2447 (25.1)	99 (6.0)	7970 (60.4)	
Prince Edward Island	0 (0.0)	0 (0.0)	0 (0.0)	
Quebec	4245 (43.6)	1112 (67.4)	859 (6.5)	
Saskatchewan	129 (1.3)	0 (0.0)	160 (1.2)	
Recruitment type				< 0.001
Officer	2090 (21.5)	283 (17.1)	3032 (23.0)	
Non-commissioned member	7645 (78.5)	1368 (82.9)	10,134 (77.0)	
Environment				< 0.001
Air Force	2125 (21.8)	309 (18.7)	2834 (21.5)	
Army	6119 (62.9)	1190 (72.1)	7835 (59.3)	
Navy	1491 (15.3)	152 (9.2)	2533 (19.2)	

Our study observations do not support the hypothesis that municipal water fluoridation is most effective for individuals with lower income or education. McLaren et al. found that the effectiveness of water fluoridation was particularly higher in lower education household and higher income adequacy socio-economic groups (McLaren and Emery 2012). Recent analysis of national data suggested a greater effect in caries reduction in the most deprived communities in England (Public Health England 2014), and an attenuation of income-related inequality in dental caries among children

and adolescents in the United States (Sanders et al. 2019). Our results may not be consistent with the literature, given that our measure of income is at the community rather than individual level and that we did not have enough variation in the spectrum of SES in a military-connected population.

Research studies on caries outcomes following water fluoridation cessation are limited, highly diverse, and variable in methodological structure; however, the bulk of the evidence indicates an increase in dental caries following cessation (McLaren et al. 2016). The longer span of data in this study,

Table 2 Effect estimates of the association between community water fluoridation status and DMFT and DMFS score, adjusted for age and gender

	Mean DMFT	Adjusted difference (95% CI)	Mean DMFS	Adjusted difference (95% CI)
Community fluoridation status				
Not fluoridated	5.97	Reference	12.5	Reference
Fluoridation ceased	5.61	- 0.31 (- 0.55, - 0.06)	11.6	- 0.81 (- 1.44, - 0.19)
Fluoridated	5.33	- 0.67 (- 0.79, - 0.55)	10.9	- 1.77 (- 2.09, - 1.46)

Table 3 Estimates of the community water fluoridation effect on DMFT and DMFS scores stratified by community income and by pre-recruitment education status (reference category = community water not fluoridated)

Effect modifier	DMFT*		DMFS**	
	Fluoridation ceased	Fluoridated	Fluoridation ceased	Fluoridated
Median community income				
Lowest	-0.26 (-0.80, 0.29)	-0.47 (-0.75, -0.19)	-0.91 (-2.31, 0.49)	-1.33 (-2.04, -0.62)
Low	0.00 (-0.57, 0.57)	-1.02 (-1.30, -0.73)	-0.12 (-1.58, 1.34)	-2.70 (-3.44, -1.97)
Middle	-0.42 (-0.96, 0.13)	-0.56 (-0.84, -0.28)	-1.24 (-2.64, 0.15)	-1.65 (-2.37, -0.93)
High	-0.47 (-0.97, 0.04)	-0.58 (-0.85, -0.31)	-0.84 (-2.13, 0.45)	-1.41 (-2.10, -0.73)
Highest	-0.34 (-0.91, 0.23)	-0.65 (-0.92, -0.39)	-0.86 (-2.32, 0.61)	-1.66 (-2.33, -0.99)
Officer status				
Officer	0.12 (-0.45, 0.70)	-0.62 (-0.88, -0.36)	-0.01 (-1.49, 1.48)	-1.55 (-2.22, -0.89)
Non-commissioned member	-0.46 (-0.72, -0.19)	-0.66 (-0.80, -0.52)	-1.11 (-1.80, -0.43)	-1.78 (-2.14, -1.43)

Results displayed in the table are the estimate of the effect of water fluoridation (partial or complete, as compared to no water fluoridation) within the strata generated using a linear regression model. All estimates control for confounding by age and gender

*Count of decayed, missing, or filled teeth

**Count of decayed, missing, or filled tooth surfaces

from 2006 to 2017, made it possible to investigate differences in DMFT and DMFS between members who enrolled from municipalities that changed water fluoridation status, enabling the investigation of this mostly unreported and growing segment in the fluoridation debate. Our findings support the idea that the benefit in caries reduction diminished in the years following the cessation of water fluoridation.

In a 24-year-old recruit, a 15% reduction in DMFT or a 20% reduction in DMFS is clinically and financially significant. Over the course of a lifetime, restored surfaces can require replacement several times. More importantly, dental operative interventions elevate the risk for the requirement of more extensive treatment to alleviate endodontic pain and/or tooth fracture in the future. A missing tooth may require prosthodontic replacement. Replacement via fixed and removable prosthesis or implants comes with risks of further complications and may not serve as a permanent solution over an individual's lifetime (Giannobile and Lang 2016). In Ontario, the cost of a one-surface restoration is over \$150, whereas a restored implant will cost more than \$4000 (Ontario Dental Association 2019). A recent economic assessment in the province of Quebec concluded that if the incidence of dental caries is reduced by 20%, each \$1 invested in water fluoridation produces a saving of approximately \$49 to \$57 in dental care costs (Tchouaket et al. 2013). Moreover, the budget impact analysis report from the Canadian Agency for Drugs and Technologies in Health determined that introducing or continuing a municipal water fluoridation program contributes to cost savings under a broad societal perspective (Canadian Agency for Drugs and Technologies in Health 2017). However, individual municipalities incur the cost of operating municipal water fluoridation programs while the direct

beneficiaries include the federal and provincial governments, private insurance companies, and citizens. This disconnect has contributed negatively to the longevity of municipal water fluoridation programming in the country.

Our study used data from CAF recruit dental examinations to measure DMFT and DMFS. These routine dental screenings are standardized via consistent training programs and rigorous standards, and data are systematically collected with fewer dentists completing the assessments than within the civilian public sector. These examinations used panoramic radiographs, which have been shown to have lower sensitivity than the gold standard bitewing radiographs (Kamburoglu et al. 2012), which may have introduced a bias toward the null in our effect size estimation. The military recruit population used in this study was younger, likely healthier, and predominately male. The homogeneity of the recruit population contributes to the internal validity of the study and the findings. Nevertheless, the lack of representativeness of a random cross-section of the general population may have reduced the ability to detect effect modification by income and education and could reduce the generalizability of the findings to females or older and younger Canadians. Our measure of municipal water fluoridation exposure using a single address and point in time and publicly available municipal records was not validated and may have resulted in misclassification. We do not anticipate that this misclassification would have systematically placed individuals in fluoridated or non-fluoridated exposure categories and would likely bias our results toward the null. In addition, we did not have access to data on alternative sources of fluoride exposure. It is likely that this would bias the results toward the null, underestimating the effect of municipal-level fluoridation on dental health. We addressed

possible misclassification by completing the sensitivity analysis restricted to those recruits who appeared to have greater residential stability to estimate exposure more accurately. Finally, dental caries was only captured in our data source if the teeth had active carious lesions extending into the dentine or visible cavitation, which represents late-stage caries. This improves the reliability of the measurement across dentists but may cause more mild cases of caries to be missed. It may be that some number of the cases of caries that we have assumed were prevented were in fact simply reduced in severity below the threshold that was set for caries. This under-counting of dental caries would also result in an underestimation of the true protective effect of fluoridation if fluoridation prevents early-stage caries.

Conclusion

Municipal water fluoridation appears to have retained its effectiveness for reduction of dental caries in this contemporary national population. Given the significant statistical and clinical differences in caries experience observed between fluoridated municipalities as compared with non-fluoridated municipalities and ceased-fluoridation municipalities, Canadian cities should carefully consider the health and economic benefits obtained through water fluoridation and the downstream costs associated with the discontinuation of water fluoridation programs. Future work in this area can support this decision-making process by more accurately estimating the cost savings and secondary health benefits of fluoridation. Water fluoridation remains an equitable public health intervention with the potential for large population-level dental health benefits for Canadians.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.



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