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COMMENTARY

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Limitations of fluoridation effectiveness studies: Lessons from Alberta, Canada

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Abstract

A paper published in this journal, "Measuring the short-term impact of fluoridation cessation on dental caries in Grade 2 children using tooth surface indices," by McLaren et al had shortcomings in study design and interpretation of results, and did not include important pertinent data. Its pre–post cross-sectional design relied on comparison of decay rates in two cities: Calgary, which ceased fluoridation, and Edmonton, which maintained fluoridation. Dental health surveys conducted in both cities about 6.5 years prior to fluoridation cessation in Calgary provided the baseline. They were compared to decay rates determined about 2.5 years after cessation in a second set of surveys in both cities. A key shortcoming was the failure to use data from a Calgary dental health survey conducted about 1.5 years prior to cessation. When this third data set is considered, the rate of increase of decay in Calgary is found to be the same before and after cessation of fluoridation, thus contradicting the main conclusion of the paper that cessation was associated with an adverse effect on oral health. Furthermore, the study design is vulnerable to confounding by caries risk factors other than fluoridation: The two cities differed substantially in baseline decay rates, other health indicators, and demographic characteristics associated with caries risk, and these risk factors were not shown to shift in parallel in Edmonton and Calgary through time. An additional weakness was low participation rates in the dental surveys and lack of analysis to check whether this may have resulted in selection biases. Owing to these weaknesses, the study has limited ability to assess whether fluoridation cessation caused an increase in decay. The study's findings, when considered with the additional information from the third Calgary survey, more strongly support the conclusion that cessation of fluoridation had no effect on decay rate. Consideration of the limitations of this study can stimulate improvement in the quality of future fluoridation effectiveness studies.

KEYWORDS
caries, epidemiology, fluoridation, public health policy, study design

1 | INTRODUCTION

A recent paper in *Community Dentistry and Oral Epidemiology* (*CDOE*), titled "Measuring the short-term impact of fluoridation cessation on dental caries in Grade 2 children using tooth surface indices," by McLaren et al[1] argues that changes in decay rates over time in Calgary compared to Edmonton (Canada) support a conclusion that fluoridation cessation led to increases in decay. However, we believe

the study has serious shortcomings that raise concern for the validity of this conclusion. Most importantly, omitted data favor the opposite conclusion: cessation of fluoridation had no effect on decay rates. Other weaknesses, including lack of adequate control for confounding, further reduce confidence in the conclusion that fluoridation cessation increased decay.

This paper has attracted widespread media attention, with over 100 news stories in Canada and around the world.[2] It achieved the second highest Altmetric attention score of any article in *CDOE* and scored in the top 99th percentile for all Wiley journal articles.[3] The media reports and the lead author have said that this paper provides strong scientific evidence that should influence public policy. A careful evaluation of its strengths and weaknesses is therefore warranted. Such a discussion can also inform the important public health question of how to obtain high-quality scientific evidence to determine the effectiveness of water fluoridation. Accordingly, we first examine in detail the weaknesses of this study and then describe stronger study designs.

We limit our discussion to caries in primary teeth because there were too few permanent teeth in the 7-year-olds to provide reliable estimates of decay in the permanent dentition.

2 | UNUSED DATA

McLaren et al concluded "Trends observed for primary teeth were consistent with an adverse effect of fluoridation cessation on children's tooth decay, 2.5-3 years post-cessation." This conclusion is controverted by unused, but relevant, caries data, which suggest there was no effect, adverse or beneficial, of fluoridation cessation. The unused data, reported by the authors in a separate paper[4] in a different journal, were from a survey in Calgary in 2009/2010, shortly prior to fluoridation cessation in 2011.[5] The study reported in *CDOE* only used pre-cessation data from a 2004/2005 survey, which was 6-7 years prior to cessation. The 2009/2010 survey was conducted with similar methods to the 2004/2005 survey, on the same target population, and was intended to allow comparisons with the 2004/2005 survey. The omitted 2009/2010 data are important because they provide information temporally much closer to cessation. They also provide a third data point allowing Calgary pre-cessation trends to be compared to post-cessation trends (Figure 1). McLaren has stated that she excluded the Calgary 2009/2010 data because there were no corresponding data for Edmonton in 2009/2010.[a] However, adding the Calgary 2009/2010 data would have strengthened the study, not weakened it.

When data from all three Calgary surveys are used in a time-trend analysis, it can be seen that more of Calgary's increase in decay occurred during the years before fluoridation ceased, and importantly, that there is no detectable difference between the annual average increase in decay before and after fluoridation cessation (Figure 1B). In both time periods, the increase was +0.12 deft (sum of decayed, extracted due to caries, and filled teeth) per year (Table 1). Therefore, the better-supported conclusion is that fluoridation cessation did not lead to an increase in caries rates. This is consistent with several previous studies of fluoridation cessation conducted over the past 20 years in Canada, Finland, East Germany, and Cuba.[6-10]

Results of the time-trend analysis strongly suggest factors other than fluoridation cessation played the dominant role in increasing the decay rate in Calgary. Further evidence is provided by the Edmonton data, which showed a substantial increase in decay over the entire study period of 2004-2014 despite continuous fluoridation (Figure 1A). Similar secular increases in deciduous tooth decay have been reported in developed countries, especially in North America, over the last 10-20 years.[11-17]

McLaren et al[1] argue that the tooth surface level decay measure (defs, sum of decayed, extracted due to caries, and filled tooth surfaces), which was only available for the 2004/2005 and 2013/2014 surveys, is "more sensitive" than the tooth level measure deft, and therefore preferable. There is indeed a difference in effect size between the two measures (Figure 1 and Supplement Figure S1 available in online Supplement). The slopes, which reflect time-trend effect sizes, were steeper with the defs measure, but the data points maintained the same relationships with each other. The precision of the estimates was similar using either measure, as seen in the 95% confidence intervals. The lesser sensitivity of deft is compensated for by the added inferential power of having three time points with deft data, rather than just two with defs data.

3 | INADEQUATE CONSIDERATION OF CONFOUNDING

The authors claim that factors besides fluoridation, such as socio-demographic characteristics of the samples and less dental treatment and preventive programming, had been considered and ruled out as the cause of the increase in decay.[1] Similarly, the lead author is quoted in a media story[18]:

> *McLaren said the study is clear about the cause and effect at play.*
> *"We designed the study so we could be as sure as possible that [the increased tooth decay] was due to [fluoride] cessation rather than due to other factors," she told the CBC. "We systematically considered a number of other factors . . . and in the end, everything pointed to fluoridation cessation being the most important factor."* (edits in square brackets in original media story)

However, the *CDOE* paper itself did not consider or measure any potential confounders. Therefore, it could not rule out any other factors that might contribute to the differences in decay.

A related paper in the *International Journal for Equity in Health* (*IJEH*) likewise fails to support the claims that potential confounding

[a]McLaren L. Email from Lindsay McLaren to Hamidah Meghani, Halton Region (Canada) Minister of Health, March 7, 2016.

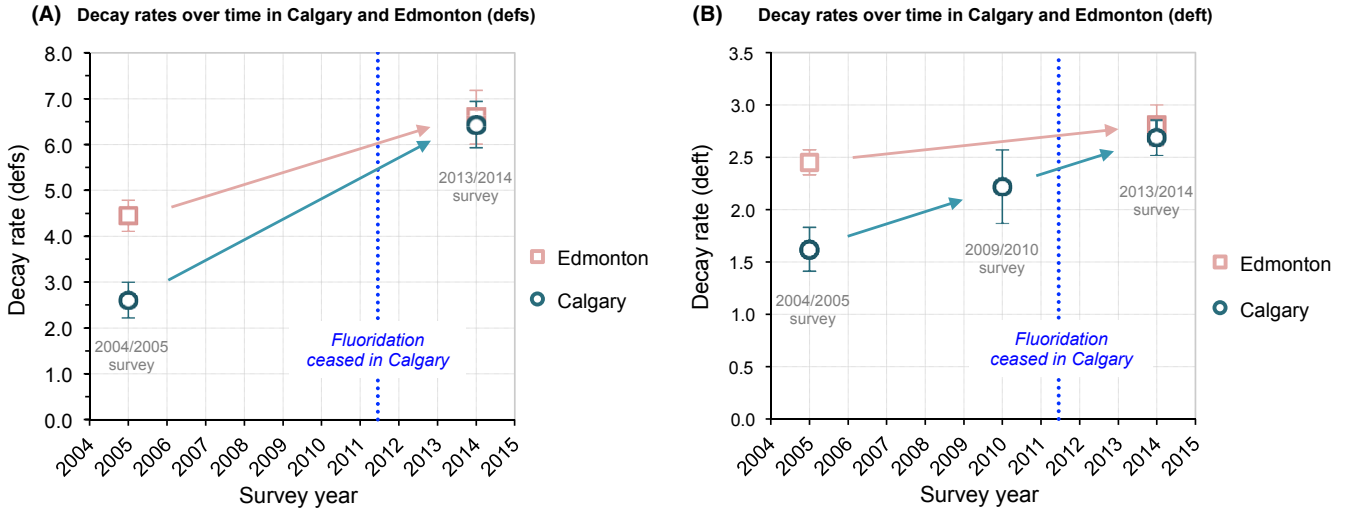

FIGURE 1 Dental decay rates by two measures: (A) defs, (B) deft. All data, including Calgary 2009/2010 data, provided by study author (personal communication, McLaren, February 25, 2016). Weighted values. Error bars indicate 95% CIs. Arrows rather than continuous lines are used to connect points to emphasize they are not regression lines. No data are available for any times other than the survey dates

TABLE 1 Annualized decay trends (deft/y) for the two time periods between the three Calgary dental surveys

Survey years	2004/2005	2009/2010	2013/2014
Mean deft, weighted	1.62	2.22	2.69
Midpoint of survey	January 1, 2005	January 1, 2010	January 1, 2014
Period between surveys	**Pre-cessation**		**Mostly Post-cessation**
Years between surveys	5.0		4.0
Change in deft between surveys	+0.60		+0.47
Time-trend (deft/y)	+0.12		+0.12

The two periods approximate the pre-cessation and post-cessation periods. The deft rates were supplied by the lead study author (personal communication, McLaren, February 25, 2016).

was adequately addressed.[4] The *IJEH* paper controlled for just two alternative factors that might account for its findings: presence/absence of dental insurance and a deprivation index of socioeconomic status. The authors acknowledged the two variables were "crude" or "limited" and concluded, "further research is needed to … explore possible alternative reasons for the findings." A more recent related paper in *Public Health* (*PH*) did not adjust for any confounders.[19]

None of the three papers (*CDOE*, *IJEH*, *PH*) controlled for many factors that may affect decay rates.[20-22] Such factors include ethnicity/genetics; diet/nutritional status; health status; sugar consumption; vitamin D/sunlight; oral hygiene; fluoridated toothpaste; fluoride varnishes; sealants; access to dental services; dental care practices; public health dental policies; public health dental expenditures; blood lead; enamel hypoplasia; and cariogenic oral bacteria. The increasing rate and large differences in caries, when both cities were fluoridated, show that factors besides fluoridation were involved. Data on several of the potentially confounding factors (eg ethnicity, health status, sealants) are publicly available but were not considered.[5,23-26] A recent Cochrane review judged fluoridation studies that controlled for fewer than four confounding variables to be at high risk of bias.[27] Thus, none of the three papers (*CDOE*, *IJEH*, *PH*) adequately addressed alternative explanations for differences or increases in decay.

4 | UNSUITABLE COMPARISON CITY

The authors elected to control for confounding by choosing Edmonton as a control city rather than measuring and adjusting for confounding factors. They mentioned only two similarities between Edmonton and Calgary: They are the two largest cities in Alberta, and both are urban centers with diverse demographic profiles.[1] Size and diverse demographics say little about factors that influence decay rates. A government report on the health of Albertans in 2006 found many differences between the cities.[25] For most health measures, Edmonton was worse than Calgary. It had significantly higher rates of diabetes, arthritis, and injuries, and twice the "aboriginal" percentage.[28,29] The authors have not demonstrated that Edmonton is sufficiently similar on factors that may affect caries to be considered "well matched" to Calgary. The defs rate was about 73% higher in Edmonton than Calgary in 2004/2005 when both cities were fluoridated. This large difference in decay rate remains unexplained, and any comparisons between the two cities are of limited validity.

The authors' pre–post cross-sectional design in itself cannot eliminate confounding. Factors influencing caries can change over time in either city, and there is no assurance that such temporal changes

will occur in parallel so as to cause the same degree of confounding in both cities at both times. Studies by Künzel et al[9,10] of four cities at 15 sequential time points over more than 35 years illustrate how decay rates can change rapidly even when fluoridation status is not changing. Both the York Review of fluoridation[30] and the follow-up Cochrane Review[27] required that in studies of pre–post type, the baseline rates for the comparison cities be similar. The McLaren et al study does not meet this criterion.

5 | LOW SURVEY PARTICIPATION RATES, POSSIBLE SELECTION BIASES

The overall participation rates in the 2013/2014 surveys were only about 25%, which raises concern for selection bias.[1] No information was provided on characteristics of nonparticipants versus participants, or on why schools and individual students declined to participate. Bias is also a concern in the 2004/2005 surveys. Student-level participation rates were higher (Calgary 60%, Edmonton 89%), but school-level participation rates were not reported, and no information was given on characteristics of nonparticipants versus participants. An example of a possible selection bias occurs in the 2009/2010 Calgary survey because children in Catholic schools appear to have been substantially over-represented.[5,31] If children in religious-affiliated schools have different decay rates than those in other schools, selection bias could impair the validity of results.

The paper claims that "... because of the rigorous sampling methods and development and application of sampling weights, we believe the 2004/2005 estimates to be an accurate reflection of the caries experience at that time," but no weighting details were given.[1] Stratified sampling by urban/rural and neighborhood household income was used in the Calgary 2004/2005 survey,[32] but urban/rural was irrelevant to the McLaren et al study, because it was restricted to urban schools. It is unclear whether weighting by income was applied. In neither the McLaren et al study nor the final report of the Calgary 2004/2005 survey was there any suggestion that weighting took place on other potential risk factors for caries, such as age, gender, ethnicity, or Catholic versus non-Catholic school. Only age and gender were even measured in the 2004/2005 survey.

6 | SUBGROUP ANALYSES: EQUALLY SUBJECT TO CONFOUNDING

McLaren et al argue that subgroup analyses are more sensitive to the effect of fluoridation on decay. Their main analysis is of the defs rate differences for all tooth surfaces of all children while their two subgroup analyses are as follows: (i) for the subset of tooth surfaces that are smooth, by excluding those tooth surfaces that have pits and fissures; and (ii) for the subset of children with any decay (defs>0). The authors state that they expect the smooth surface subgroup to be more sensitive to effects of fluoridation. They do not explicitly state that the subset with defs>0 will also be more sensitive, although this can be inferred.

McLaren et al found larger differences in decay rates between Calgary and Edmonton and over time in both subset analyses, but the relative percent differences in the defs>0 subgroup were smaller than in their full group analysis (see Supplement Figures S1a and S2). The defs>0 subgroup analysis therefore lends little support to the claim that fluoridation cessation causes an increase in decay. Furthermore, the confounding that occurs in the main analysis would have equal or greater chance of distorting relationships in both subgroup analyses. Many factors besides fluoridation could have larger effects in higher-risk children, and some factors, like flossing, would be expected to influence decay rates on smooth surfaces more than on pitted surfaces.

To see whether a time-trend subgroup analysis might produce a different result than we showed for the full group of all children (Figure 1 and Supplement Figure S1; Table 1), we conducted an analysis using the three Calgary survey points for the subset of children with defs>0 (Figure 2 and Supplement Figure S2). It shows that this subset demonstrates a *deceleration* in rate of increase in the period after the 2009/2010 survey, not an acceleration, suggesting that ceasing fluoridation is associated with a decrease in dental caries, the opposite conclusion of McLaren et al. Data on smooth surface decay in 2009/2010 were not available to us, so we could not conduct a similar time-trend analysis for this subgroup.

An unavoidable limitation in our time-trend analysis for the subset defs>0 is that data for 2009/2010 were only available as deft, not defs. Therefore, we used the ratio of defs to deft in the 2013/2014 survey to make the conversion, the values coming from the *CDOE* and *IJEH* articles, respectively, as well as from the lead author.[b] Support for the validity of this conversion factor comes from the 2013/2014 and 2009/2010 surveys being relatively close in time, done in the same city, and using very similar methods. Furthermore, when we applied this conversion to the 2004/2005 Calgary survey, where both deft and defs are known, the calculated defs was very close to the known defs.

7 | LOW FLUORIDE BOTTLED WATER CONSUMPTION UNLIKELY TO EXPLAIN INCREASES IN DECAY

McLaren et al state that an increasing use of bottled water (generally low in fluoride) over the study period may explain the increases in decay in both Calgary and Edmonton. The reasoning is circular because it assumes that fluoridated water reduces decay, which is the main hypothesis being tested. Nevertheless, to explore this claim, we used bottled water consumption data from McLaren et al, noting the limitation that it is for all of Canada, rather than specific to Calgary and Edmonton. The information on bottled water intake per household leads to a per capita daily consumption of 0.11 L in

[b]McLaren, personal communication, February 26, 2016.

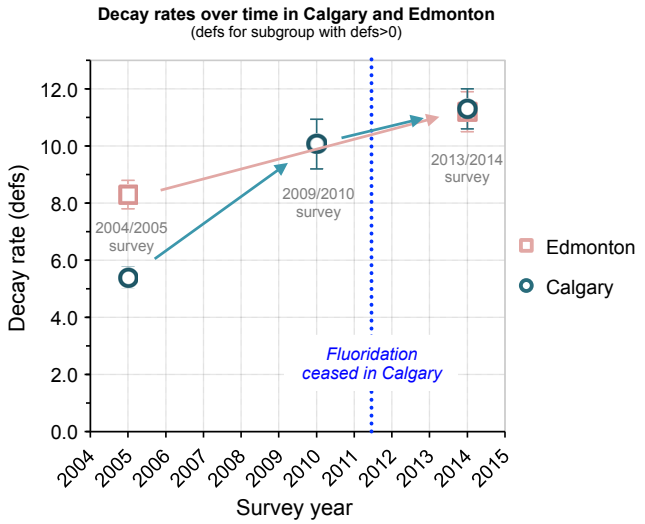

FIGURE 2 Dental decay rates for subgroup of those children with at least one defs (defs>0). Data for 2004/2005 and 2013/2014 from *CDOE* paper. Data for 2009/2010 from *IJEH* paper, but converted from deft to defs using conversion method described in text. Error bars indicate 95% CIs

2004, rising to 0.18 L in 2014 based on 2.5 people per household.[33] As adults consume about 1 L/d of drinking water,[34] the majority of consumed water would still be from fluoridated tap water: 89% in 2004 decreasing to 82% in 2014. It is implausible that such a small decrease in fluoridated water intake could account for a 45% increase in defs in always-fluoridated Edmonton and a 110% increase in decay while Calgary was fluoridated (Figure 1A).

8 | STRONGER STUDY DESIGNS TO ASSESS FLUORIDATION EFFECTIVENESS

We have shown that the McLaren et al study design gives only a weak test of whether fluoride cessation caused an increase in tooth decay, or whether confounding factors, both through time and between cities, were the true cause. The authors say cross-sectional studies that look at a single point in time (post-cessation) are weak, yet their pre–post cross-sectional study that examines two points in time is only slightly less weak. It is compromised by the unsuitability of Edmonton as comparison city, lack of adjustment for confounding, and the use of presurvey data collected 6-7 years prior to cessation. Both the York Review of fluoridation[30] and the Cochrane Review update[27] required that pre–post design studies have baseline data collected within 3 years of the change in fluoridation status because rapid changes in caries rates can occur unrelated to fluoridation. The McLaren et al study was also limited by ecological (group-level) measures of exposure with no information on individual-level exposures.

The highest quality, gold standard, study design is a randomized controlled trial (RCT). This is the only study design that can avoid most risk of confounding. For assessing fluoridated water effectiveness, a suitable RCT design would randomly assign individuals to receive either fluoridated or unfluoridated bottled water. RCTs could also be cluster-randomized by household so that the bottled water could be shared for family food preparation.

Some might argue an RCT would be impractical because the benefits of fluoridation are relatively small, thus requiring a large sample and long observation period to see an effect. However, statistical power calculations, based on a study population with a background decay rate typical for many developed countries (mean DMFT of 2 with SD of 3 in 12-15-year-olds),[11] show that a study duration of 2 years with a sample size of 2500 would be sufficient to have an 80% probability of detecting a 15% decrease in decay increment, or just over 0.3 DMFT.[35]

Another weakness of the McLaren et al study and most other observational studies of fluoridation effectiveness is lack of blinding. Even when participants are examined at a location that hides fluoridation status, dental fluorosis could reveal fluoride exposure to an examiner. Blinding may require dental radiographs assessed by persons blind to fluoridation status and fluorosis. RCT studies, however, could avoid radiographs because the fluoridated water need only be given when subjects are beyond the age of susceptibility to dental fluorosis.

Since 2003 when the authors of the York Review of fluoridation urged that higher-quality studies were necessary to provide a quantitative estimate of the effect of water fluoridation,[36] their recommendation has been largely ignored. The 2015 Cochrane Review confirmed that no RCT of fluoridated water has been conducted, but claimed, without explanation, that they are "unfeasible".[27] Presumably, they used a narrow definition of fluoridation that assumes the unit of randomization to be entire communities of relatively large size. Such a trial would indeed be difficult, but we have described how randomization at the individual or small cluster level would be feasible. Methods to allow generalizing an individual-level RCT to community-level are available.[37]

The study design that is next in order of quality, after RCTs, is the longitudinal study with individual-level information on the same subjects over time. This could be a cohort study, or for rare outcomes, a case-control study. Prospective cohort studies usually have less risk of recall bias than retrospective case-control studies, but for rare outcomes, such as extractions under general anesthesia in hospitals, the greater efficiency of case-control design studies can outweigh this limitation. Control of confounders is more easily achieved with longitudinal designs than with cross-sectional studies because many important confounding factors will remain relatively constant for individuals over time (such as oral hygiene practices, aboriginal). It will still be important to have diverse exposures to fluoride, rather than drawing a sample from just one fluoridated and one unfluoridated city. Otherwise, exposure will be completely correlated with location, causing any other risk factors that differ between those two locations to become confounders. Rothman describes how even RCTs suffer when there are only two study groups: "In the extreme case in which only one subject is included in each group (as in the community fluoridation trials with one

community in each group), randomization is completely ineffective in preventing confounding."[38]

The committee that oversaw the York Review issued a statement warning that the review had been frequently misinterpreted, that no high-quality evidence existed in any fluoridation literature, and that only rigorous studies could fill the gaps in knowledge about all aspects of fluoridation.[36] The chairperson of that committee assessed the *CDOE* and *IJEH* studies and concluded they do not "provide a valid assessment of the effect of fluoridation cessation on the levels or distribution of caries in these populations".[39] He cited many of the same shortcomings we have outlined, and also noted that the dramatic increase in tooth decay during periods of constant fluoridation in both Edmonton and Calgary indicates that fluoridation does not reduce tooth decay sufficiently to prevent poor oral health. McLaren et al acknowledge that the York Review and the Cochrane Review have both voiced concern for the dearth of higher-quality studies, but their study would score too low on quality criteria to be included in either of these authoritative reviews.

9 | CONCLUSIONS

In summary, due to the omission of key data that contradict the authors' conclusion, inadequate control of confounding factors, and limitations in the design of the study that were largely unacknowledged, we believe that claims by McLaren et al that their study supports the hypothesis that fluoridation cessation causes an increase in decay is unjustified. Recognition of the limitations of this study can point toward stronger designs in future studies.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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