# Fluoride exposure and reported learning disability diagnosis among Canadian children: Implications for community water fluoridation

Amanda M. Barberio, BHSc (hons), MSc,[1,2] Carlos Quiñonez, DMD, MSc, PhD, FRCD(C),[3] F. Shaun Hosein, MD, MSc,[4] Lindsay McLaren, PhD[2]

## ABSTRACT

**OBJECTIVES:** Recent studies have connected increased fluoride exposure with increased risk of neurodevelopmental-related outcomes, such as ADHD (attention deficit hyperactivity disorder) and lower IQ in children. Our primary objective was to examine the association between fluoride exposure and reported diagnosis of a learning disability among a population-based sample of Canadian children aged 3–12 years.

**METHODS:** We analyzed data from Cycles 2 and 3 of the Canadian Health Measures Survey. Four measures of fluoride exposure were available: 1) urinary fluoride ($\mu mol/L$), 2) creatinine-adjusted urinary fluoride ($\mu mol/mmol$), 3) specific gravity-adjusted urinary fluoride ($\mu mol/L$), and 4) fluoride concentration of tap water (mg/L) (Cycle 3 only). Diagnosis of a learning disability (yes/no) was based on parental- or self-report. Associations were examined using logistic regression (where possible), unadjusted and adjusted for covariates.

**RESULTS:** When Cycles 2 and 3 were examined separately, reported learning disability diagnosis was not significantly associated with any measure of fluoride exposure in unadjusted or adjusted models. When Cycles 2 and 3 were combined, a small but statistically significant effect was observed such that children with higher urinary fluoride had higher odds of having a reported learning disability in the adjusted model ($p = 0.03$). However, the association was not observed in models that used creatinine-adjusted urinary fluoride and specific gravity-adjusted urinary fluoride, which are believed to be more accurate measures due to their correction for urinary dilution.

**CONCLUSION:** Overall, there did not appear to be a robust association between fluoride exposure and parental- or self-reported diagnosis of a learning disability among Canadian children.

**KEY WORDS:** Population; fluoridation; cognition; learning disorders; surveys and questionnaires

Community water fluoridation (CWF) is the addition of a controlled quantity of fluoride to a public drinking water supply to prevent tooth decay. The weight of existing evidence suggests that CWF is an effective and equitable way to improve dental health, especially among children.[1–3] However, the methodological quality of existing research is modest and may not reflect contemporary circumstances.[4]

While there is no dispute that chronic ingestion of high concentrations of fluoride has negative effects, there is some debate regarding adverse health implications of concentrations deemed "optimal".[5] Canadian guidelines currently recommend a fluoride concentration of 0.7 parts per million (ppm), which is believed to achieve a balance between accruing dental benefits while minimizing risk of dental fluorosis.[3] Health Canada has identified a Maximum Acceptable Concentration of 1.5 ppm, which is based on the population (children aged 1–4 years) most vulnerable to developing dental fluorosis.[3]

Concerns regarding potential fluoride-related health problems, including carcinogenic, endocrine, neurological and skeletal effects, have been raised.[6] While several comprehensive reports have concluded that CWF is not associated with any of these adverse health effects at or below recommended concentrations,[1–3,7] some individuals remain concerned about the safety and efficacy of CWF.[8]

From among the potential harms associated with CWF, this paper focuses on cognitive-related concerns; in particular, learning disabilities. There are two main reasons for this focus. First, evidence from histological, chemical and molecular studies has established that the relationship between fluoride and impaired brain function is biologically plausible.[9] Second, clarifying the nature of this relationship is important and timely, because fluoride was

**Author Affiliations**

1. Department of Cancer Epidemiology and Prevention Research, Alberta Health Services, Edmonton, AB
2. Department of Community Health Sciences and O'Brien Institute for Public Health, University of Calgary, Calgary, AB
3. Dental Public Health, Faculty of Dentistry, University of Toronto, Toronto, ON
4. Faculty of Medicine, University of Queensland, St Lucia, QLD, Australia

**Correspondence:** Lindsay McLaren, PhD, Department of Community Health Sciences and O'Brien Institute for Public Health, University of Calgary, TRW3, 3280 Hospital Dr. NW Calgary, AB T2N 4Z6, Tel: 403-210-9424, E-mail: lmclaren@ucalgary.ca

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recently classified as one of six new neurodevelopmental toxins,[10] and recent studies have connected increased fluoride exposure with increased risk of neurodevelopmental-related outcomes, such as attention deficit hyperactivity disorder (ADHD) and lower intelligence quotient (IQ) in children.[11,12]

A highly-cited systematic review and meta-analysis by Choi et al. (2012)[12] explored the relationship between fluoride and children's IQ. A statistically significant standardized weighted mean difference in IQ score between children residing in areas with high vs. those in areas with low fluoride was found (−0.45, 95% CI: −0.56 to −0.34), which was robust to various sensitivity analyses.[12] However, most of the 27 cross-sectional studies were conducted in areas of rural China that have high levels of naturally occurring fluoride in the water ranging from 2 to 11 ppm, which is approximately 3–16 times higher than optimal fluoride concentrations in Canada.[12]

Not included in the aforementioned meta-analysis, eight additional cross-sectional studies performed in India ($n = 4$),[13–16] Iran ($n = 1$),[17] Mexico ($n = 1$)[18] and China ($n = 2$)[19,20] found that children classified as having "high" fluoride exposure (defined in various ways) scored lower on some or all components of metrics used to assess intelligence or cognition. In contrast, a prospective cohort study by Broadbent et al. found no significant differences in IQ scores between New Zealand children living in fluoridated versus those living in non-fluoridated communities, adjusting for several potential confounders.[21]

A recent ecological analysis by Malin and Till (2015) investigated the relationship between fluoridated drinking water and ADHD.[11] Data from the United States Centers for Disease Control and Prevention website were used to determine: 1) state-based fluoridation prevalence (i.e., % of state population receiving fluoridated water) at six time points between 1992 and 2008, and 2) ADHD prevalence based on parent-report collected during the National Survey of Children's Health in 2003, 2007 and 2011. Findings indicated a positive relationship between state CWF prevalence and state prevalence of parent-reported ADHD. Specifically, every 1% increase in fluoridation prevalence in 1992 corresponded to approximately 67 000, 93 000 and 131 000 additional ADHD diagnoses in 2003, 2007 and 2011 respectively, after controlling for 1992 state-level median household income.[11]

Overall, with the exception of Broadbent et al.,[21] the literature collectively suggests that high fluoride exposure negatively impacts a variety of outcomes related to cognitive functioning. However, these findings should be interpreted with caution due to: 1) substantial methodological limitations (e.g., ecological measurements of fluoride exposure), 2) most research being conducted outside the context of CWF, and 3) a lack of North American studies.

In the current study, we analyze high-quality Canadian survey data that include individual-level estimates of fluoride exposure from urine and tap water samples and reported diagnosis of a learning disability. Our primary objective was to examine the association between fluoride exposure and reported learning disability diagnosis among a population-based sample of Canadian children aged 3–12 years. To explore implications for CWF, our secondary objective was to re-examine the association (as a sensitivity analysis) among a subset of children for whom we have some information on the source(s) of fluoride exposure, including drinking water.

## METHODS

### Data source
The data source was Cycles 2 (2009–2011) and 3 (2012–2013) of the Canadian Health Measures Survey (CHMS). Specifically, we analyzed data from children aged 3–12 years included in the environmental urine subsample (i.e., respondents who were randomly flagged to have environmental exposures measures, including fluoride, performed on their urine sample) for Cycle 2 ($n = 1120$) and the urine fluoride subsample for Cycle 3 ($n = 1101$). We analyzed Cycles separately and, when possible, combined.

Full survey details can be found online at www.statcan.gc.ca. Briefly, the CHMS is a cross-sectional survey of a nationally representative sample of Canadians that consists of a household interview followed by physical health measurements taken at mobile examination clinics. The target population is Canadians aged 3–79 years living in private households in the 10 provinces. Approximately 96% of the target population is represented, taking into account survey exclusions[22,23] Respondents were selected using complex random sampling. The overall response rates were 55.5% (Cycle 2) and 51.7% (Cycle 3). The environmental urine subsample (Cycle 2) and the urine fluoride subsample (Cycle 3) had combined response rates of 54.4% and 55.6% respectively.[22,23]

Health Canada and the Public Health Agency of Canada Research Ethics Board reviewed and approved all CHMS procedures. The data were analyzed at the Prairie Regional Research Data Centre (RDC) in Calgary, Alberta. Due to ethical standards in place at the time of data collection and the RDC integrity measures, this study was exempt from formal ethics approval.

### Variables
*Primary Exposure Variable: Fluoride*
First, estimates of urinary fluoride (μmol/L) from spot urine samples were available for a subsample of the respondents for Cycles 2 and 3 of the CHMS. Analysis was performed at the Human Toxicology Laboratory of the Institut national de santé publique du Québec (INSPQ) (accredited under ISO 17025) under standardized operating procedures,[22,23] using an Orion pH meter with ion selective electrode.[24] The selective electrode limit of detection was 20 μg/L for Cycle 2 and 10 μg/L for Cycle 3.[25]

Second, estimates of creatinine-adjusted urinary fluoride (μmol/mmol) were available for the same subsamples. Creatinine is formed by the breakdown of creatine, which is a key component of muscle metabolism. Since the production and excretion of urinary creatinine are fairly constant over a 24-hour period, creatinine can help to adjust for differences in urinary concentration, renal function, and lean body mass.[25]

Third, estimates of specific gravity-adjusted urinary fluoride (μmol/L) were available for the same subsamples. Similar to creatinine adjustment, adjustment for specific gravity helps to compensate for variations in urine output.[25]

Fourth, estimates of the fluoride concentration of tap water samples (mg/L) collected at respondents' homes were available, for Cycle 3 only. These samples reflect the fluoride concentration of the source of tap water supplied to the home (e.g., public water

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supply, private well). The tap water subsample was the same as the urine fluoride subsample.[23] Nearly all respondents (>99%) who provided a urine sample also provided a tap water sample. A basic anion exchange chromatography procedure was used to determine the level of fluoride in tap water with a limit of detection of 0.006 mg/L (Statistics Canada, personal communication, June 2016).

*Primary Outcome Variable: Reported Learning Disability Diagnosis*
Our primary outcome variable, diagnosis of a learning disability by a health professional, was based on a single item from the household survey asked to all respondents: "Do you have a learning disability?" (Yes/No/Don't know, Refused). For Cycle 2, those who indicated having a learning disability were also asked: "What kind of learning disability do you have?" (Attention Deficit Disorder, no hyperactivity [ADD]/Attention Deficit Hyperactivity Disorder [ADHD]/Dyslexia/Other). This follow-up question about the type of learning disability was omitted in Cycle 3.

As with all CHMS survey questions, parents or guardians answered all questions for children aged 3–11 years (coded as a proxy interview), while children aged 12 years and older answered questions themselves. Accordingly, for children aged 3–11 years, diagnosis of a learning disability was based on parent or guardian self-report whereas for children aged 12 years, diagnosis of a learning disability was based on the respondent's self-report.

*Other Variables*
We adjusted for the following potential confounders, collected at the household interview: sex, age (from 3 to 12 years), household education (two categories: less than a Bachelor's degree vs. Bachelor's degree or greater), and household income adequacy (a derived variable created by Statistics Canada based on total household income and household size; two categories: low and middle income adequacy vs. high income adequacy).

Finally, because fluoride estimates from urine reflect fluoride from any source, we also considered variables that permitted some discernment of source(s); namely, drinking water and dental products. For both Cycles 2 and 3, and following a procedure used elsewhere,[26] we classified each data collection site (i.e., the geographic location of the mobile examination clinic participants traveled to visit) as "fluoridated" or "not fluoridated" based on information from various public sources (see Supplementary Tables 1a and 1b in the ARTICLE TOOLS section on the journal site). The Office of the Chief Dental Officer, Public Health Agency of Canada, validated our classifications. We ascertained that, in general, mean urinary fluoride concentration and mean tap water fluoride concentration were higher among respondents who attended "fluoridated" sites compared to those who attended "non-fluoridated" sites (data not shown).

For Cycle 2 only, in addition to identifying children who attended a fluoridated data collection site, we were also able to identify
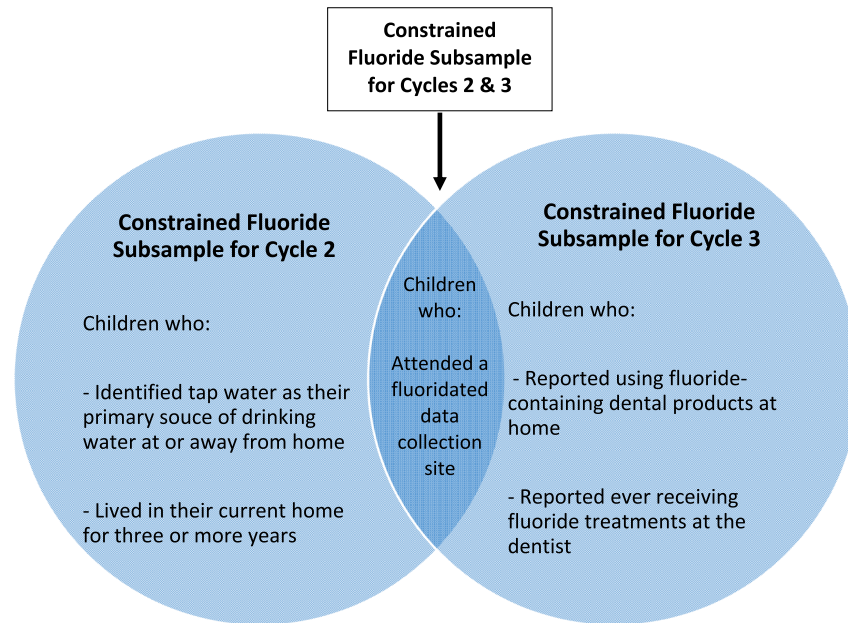


**Figure 1.** Venn diagram describing the constrained fluoride subsamples for Cycles 2 and 3, separately and combined
Note 1: For Cycle 2, the constrained fluoride subsample refers to children who: 1) attended a fluoridated data collection site, 2) identified tap water was their primary source of drinking water at home or away from home, and 3) lived in their current home for three or more years. For Cycle 3, the constrained fluoride subsample refers to children who: 1) attended a fluoridated data collection site, 2) reported using fluoride-containing dental products at home, and 3) reported ever having received fluoride treatments at the dentist. For Cycles 2 and 3 combined, the constrained fluoride subsample refers to children who: 1) attended a fluoridated data collection site.
Note 2: Due to differences in survey content between Cycles 2 and 3, fluoridation status of data collection site was the only variable related to the source of fluoride exposure that was comparable across the two cycles.
Note 3: For all CHMS survey questions, parents or guardians answered all questions for children aged 3–11 years (coded as a proxy interview), while children aged 12 years and older answered questions themselves.

**Table 1.**  Descriptive Statistics for Cycles 2 and 3 of the CHMS among children aged 3–12 years (weighted and bootstrapped)

| | Cycle 2 Full sample (N = 1844) | Cycle 2 Fluoride subsample (n = 1120) | Cycle 2 Constrained fluoride subsample* (n = 273) | Cycle 3 Full sample (N = 1726) | Cycle 3 Fluoride subsample (n = 1101) | Cycle 3 Constrained fluoride subsample† (n = 294) |
|---|---|---|---|---|---|---|
| **Predictors** | | | | | | |
| Urinary fluoride (μmol/L) | – | 32.06 (95% CI: 29.65–34.46) | 39.39 (95% CI: 35.63–43.16) | – | 26.17 (95% CI: 22.57–29.76) | 30.01 (95% CI: 24.77–35.25) |
| Creatinine-adjusted urinary fluoride (μmol/mmol) | – | 4.50 (95% CI: 4.09–4.91) | 5.12 (95% CI: 4.26–5.98) | – | 4.23 (95% CI: 3.50–4.97) | 4.87 (95% CI: 3.48–6.27) |
| Specific gravity-adjusted urinary fluoride (μmol/L) | – | 37.78 (95% CI: 34.78–40.79) | 43.46 (95% CI: 39.19–47.81) | – | 34.25 (95% CI: 29.00–39.50) | 40.71 (95% CI: 32.66–48.75) |
| Fluoride concentration of tap water (mg/L) | – | – | – | – | 0.23 (95% CI: 0.15–0.32) | 0.36 (95% CI: 0.23–0.49) |
| **Outcome** | | | | | | |
| Self-reported learning disability diagnosis (yes) | 8.41 (95% CI: 6.10–10.73) | 7.58 (95% CI: 4.80–10.37) | 7.02 (95% CI: 2.03–12.01) | 5.08 (95% CI: 2.64–7.53) | 3.78 (95% CI: 1.34–6.23) | 6.13 (95% CI: 0.73–11.52) |
| Attention deficit disorder (ADD), without hyperactivity (yes) | 1.60 (95% CI: 0.50–2.70) | 1.75 (95% CI: 0.58–2.92) | – | – | – | – |
| Attention deficit disorder, with hyperactivity (yes) | 3.17 (95% CI: 1.71–4.62) | 2.46 (95% CI: 0.50–4.41) | – | – | – | – |
| **Covariates** | | | | | | |
| Sex (males) | 52.08 (95% CI: 50.59–53.57) | 49.36 (95% CI: 46.45–52.26) | 58.39 (95% CI: 52.91–63.86) | 50.76 (95% CI: 49.24–52.28) | 51.75 (95% CI: 50.23–53.27) | 51.21 (95% CI: 45.33–57.10) |
| Age (years) | 7.61 (95% CI: 7.46–7.77) | 7.03 (95% CI: 6.84–7.21) | 7.15 (95% CI: 6.85–7.45) | 7.36 (95% CI: 7.17–7.54) | 6.80 (95% CI: 6.62–6.98) | 7.99 (95% CI: 7.70–8.28) |
| Household income adequacy (lower and middle income)‡ | 52.00 (95% CI: 43.57–60.41) | 51.45 (95% CI: 41.91–60.99) | 46.00 (95% CI: 30.61–61.39) | 54.48 (95% CI: 46.32–62.63) | 53.65 (95% CI: 45.50–61.80) | 57.94 (95% CI: 44.02–71.85) |
| Highest attained education in the household (less than bachelor's degree) | 60.38 (95% CI: 51.11–69.66) | 60.00 (95% CI: 50.37–69.55) | 59.33 (95% CI: 44.76–73.90) | 54.73 (95% CI: 47.01–62.45) | 54.16 (95% CI: 46.43–61.88) | 58.15 (95% CI: 47.06–69.25) |
| **Sources of fluoride exposure** | | | | | | |
| Respondent from a fluoridated collection site (yes) | 55.80 (95% CI: 40.76–70.85) | 53.92 (95% CI: 38.71–69.13) | – | 55.39 (95% CI: 27.89–82.89) | 57.49 (95% CI: 30.00–84.99) | – |
| Length of time in current home (≥3 years) | 69.11 (95% CI: 63.48–74.75) | 71.10 (95% CI: 66.69–75.51) | – | – | – | – |
| Primary source of drinking water (tap water) | 66.63 (95% CI: 60.18–73.09) | 68.89 (95% CI: 63.17–74.61) | – | – | – | – |
| Uses fluoride-containing dental products at home (yes) | – | – | – | 69.46 (95% CI: 64.53–74.40) | 70.89 (95% CI: 65.96–75.83) | – |
| Ever received fluoride treatments at the dentist (yes) | – | – | – | 78.57 (95% CI: 73.57–83.57) | 78.94 (95% CI: 73.95–83.94) | – |

Note: The sample sizes presented at the top of the chart reflect the full available sample; however, in some cases, the sample sizes in the cells are lower due to age exclusions (primary reason) and missing data (<5% in all cases). We report urinary fluoride in units of micromoles per litre (μmol/L), creatinine-adjusted urinary fluoride in units of micromoles per millimole (μmol/mmol), and fluoride concentration in tap water in units of milligrams per litre (mg/L) to be consistent with how these variables are presented in Statistics Canada documentation. One can convert micromoles per litre of fluoride to milligrams per litre using the following formula: 1 μmol/L equals 0.019 mg/L.[9]
\* For Cycle 2, the constrained fluoride subsample refers to children who: 1) attended a fluoridated data collection site, 2) identified tap water was their primary source of drinking water at home or away from home, and 3) lived in their current home for three or more years.
† For Cycle 3, the constrained fluoride subsample refers to children who: 1) attended a fluoridated data collection site, 2) reported using fluoride-containing dental products at home, and 3) reported ever having received fluoride treatments at the dentist.
‡ Only 71% and 77% of respondents reported their total household income for Cycles 2 and 3 of the CHMS respectively. Accordingly, Statistics Canada developed a regression model to impute total household income for all respondents for both cycles.[22,23]

children: 1) for whom tap water (vs. bottled or other) was their primary source of drinking water at home or away from home and, 2) who had lived in his or her current home for three or more years (as a proxy for exposure to presence/absence of CWF). These children comprise the constrained fluoride subsample for Cycle 2 (*n* = 273).

Due to differences in survey content between Cycles, we had to define the constrained fluoride subsamples differently for Cycles 2 and 3 (see Figure 1). For Cycle 3 only, in addition to identifying children who attended a fluoridated data collection site, we were also able to identify children who reportedly: 1) used fluoride-containing products at home (e.g., toothpaste, mouthwash) and, 2) had ever (vs. never) received fluoride treatments at the dentist. These children comprise the constrained fluoride subsample for Cycle 3 (*n* = 294).

### Statistical analysis
First, using logistic regression, we regressed diagnosis of a learning disability (yes/no) on fluoride exposure using: 1) urinary fluoride, 2) creatinine-adjusted urinary fluoride, 3) specific gravity-adjusted urinary fluoride, and 4) fluoride from tap water (mg/L) (Cycle 3 only), separately by CHMS Cycle, unadjusted and adjusted for covariates. For Cycle 2, we also used logistic regression to examine the association between urinary fluoride concentration and type of learning disability (i.e., ADD [yes/no] and ADHD [yes/no]), unadjusted and adjusted for covariates.

Second, we had planned to rerun the logistic regression models that examined the association between fluoride exposure (from urine and tap water) and the diagnosis of a learning disability among a constrained sample of children for whom we had some information about the source(s) of fluoride exposure; however, Statistics Canada sample size requirements precluded these analyses. Instead, we performed simple mean comparisons to examine whether fluoride (from urine and tap water) differed between children with and without a learning disability, who were included in the constrained fluoride subsample for Cycles 2 and 3.

**Table 2a.** Results from logistic regression where parental- or self-reported diagnosis of a *learning disability among children aged 3–12 years* was regressed on urinary fluoride, creatinine-adjusted urinary fluoride, and specific gravity-adjusted urinary fluoride for Cycle 2 of the CHMS

| Predictor variable | Cycle 2 of CHMS | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| | Urinary fluoride | | Creatinine-adjusted urinary fluoride | | Specific gravity-adjusted urinary fluoride | |
| | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for fluoride subsample (OR, 95% CI) | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for fluoride subsample (OR, 95% CI) | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for fluoride subsample (OR, 95% CI) |
| Urinary fluoride (μmol/L) (cont[§]) | 1.01 (95% CI: 0.99–1.03) | 1.01 (95% CI: 0.99–1.04) | – | – | – | – |
| Creatinine-adjusted urinary fluoride (μmol/mmol) (cont) | – | – | 0.99 (95% CI: 0.87–1.13) | 1.04 (95% CI: 0.95–1.15) | – | – |
| Specific gravity-adjusted urinary fluoride (μmol/L) (cont) | – | – | – | – | 1.00 (95% CI: 0.99–1.02) | 1.01 (95% CI: 0.99–1.02) |
| Sex (ref: female) | – | 2.59** (95% CI: 1.17–5.77) | – | 2.73** (95% CI: 1.25–6.01) | – | 2.77** (95% CI: 1.26–6.08) |
| Age (cont) | – | 1.28*** (95% CI: 1.18–1.39) | – | 1.29*** (95% CI: 1.17–1.42) | – | 1.27*** (95% CI: 1.16–1.39) |
| Household income adequacy (ref: lower and middle income) | – | 0.94 (95% CI: 0.22–4.07) | – | 0.94 (95% CI: 0.20–4.38) | – | 0.95 (95% CI: 0.21–4.36) |
| Highest attained education in the household (ref: less than bachelor's degree) | – | 0.49* (95% CI: 0.20–1.16) | – | 0.46 (95% CI: 0.18–1.19) | – | 0.47* (95% CI: 0.19–1.17) |

Note: We report urinary fluoride and specific gravity-adjusted urinary fluoride in units of micromoles per litre (μmol/L), creatinine-adjusted urinary fluoride in units of micromoles per millimole (μmol/mmol), and fluoride concentration of tap water in units of milligrams per litre (mg/L) to be consistent with how these variables are presented in Statistics Canada documentation. One can convert micromoles per litre of fluoride to milligrams per litre using the following formula: 1 μmol/L equals 0.019 mg/L.[9]

***$p < 0.01$; **$p < 0.05$; *$p < 0.1$.

[†] Column contains bivariate associations between predictor variable and the outcome (parental- or self-reported diagnosis of a learning disability).

[‡] Column contains associations from single model containing all predictor variables (age, sex, household income adequacy, and highest attained education in the household).

[§] cont = continuous.

**Table 2b.** Results from logistic regression where parental- or self-reported diagnosis of a *learning disability among children aged 3–12 years* was regressed on urinary fluoride, creatinine-adjusted urinary fluoride, specific gravity-adjusted urinary fluoride, and fluoride concentration of tap water for Cycle 3 of the CHMS

| Predictor variable | Cycle 3 of CHMS | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Urinary fluoride | | Creatinine-adjusted urinary fluoride | | Specific gravity-adjusted urinary fluoride | | Fluoride concentration of tap water | |
| | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[†] estimates for fluoride subsample (OR, 95% CI) | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for fluoride subsample (OR, 95% CI) | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[†] estimates for fluoride subsample (OR, 95% CI) | Unadjusted[†] estimates for fluoride tap water subsample (OR, 95% CI) | Adjusted[‡] estimates for fluoride tap water subsample (OR, 95% CI) |
| Urinary fluoride (μmol/L) (cont) | 1.01 (95% CI: 0.996–1.03) | 1.02 (95% CI: 0.99–1.04) | – | – | – | – | – | – |
| Creatinine-adjusted urinary fluoride (μmol/mmol) (cont) | – | – | 1.01 (95% CI: 0.77–1.34) | 1.03 (95% CI: 0.86–1.23) | – | – | – | – |
| Specific gravity-adjusted urinary fluoride (μmol/L) (cont) | – | – | – | – | 1.01 (95% CI: 0.99–1.02) | 1.01 (95% CI: 0.99–1.03) | – | – |
| Fluoride concentration of tap water (mg/L) | – | – | – | – | – | – | 1.41 (95% CI: 0.14–14.41) | 0.88 (95% CI: 0.068–11.33) |
| Sex (ref: female) | – | 1.23 (95% CI: 0.41–3.70) | – | 1.29 (95% CI: 0.43–3.85) | – | 1.32 (95% CI: 0.43–4.03) | – | 1.24 (95% CI: 0.42–3.64) |
| Age (cont) | – | 1.36** (95% CI: 1.09–1.70) | – | 1.35** (95% CI: 1.04–1.76) | – | 1.35 (95% CI: 1.06–1.71) | – | 1.33** (95% CI: 1.04–1.69) |
| Household income adequacy (ref: lower and middle income) | – | 0.69 (95% CI: 0.18–2.66) | – | 0.68 (95% CI: 0.18–2.61) | – | 0.69 (95% CI: 0.18–2.65) | – | 0.66 (95% CI: 0.17–2.57) |
| Highest attained education in the household (ref: less than bachelor's degree) | – | 0.30 (95% CI: 0.06–1.51) | – | 0.33 (95% CI: 0.07–1.53) | – | 0.33 (95% CI: 0.07–1.54) | – | 0.32 (95% CI: 0.069–1.50) |

Note: We report urinary fluoride and specific gravity-adjusted urinary fluoride in units of micromoles per litre (μmol/L), creatinine-adjusted urinary fluoride in units of micromoles per millimole (μmol/mmol), and fluoride concentration of tap water in units of milligrams per litre (mg/L) to be consistent with how these variables are presented in Statistics Canada documentation. One can convert micromoles per litre of fluoride to milligrams per litre using the following formula: 1 μmol/L equals 0.019 mg/L.[9]
***$p < 0.01$; **$p < 0.05$; *$p < 0.1$.
[†] Column contains bivariate associations between predictor variable and the outcome (parental- or self-reported diagnosis of a learning disability).
[‡] Column contains associations from single model containing all predictor variables (age, sex, household income adequacy, and highest attained education in the household).

**Table 3a.** Results from logistic regression where parental- or self-reported diagnosis of *ADHD among children aged 3–12 years* was regressed on urinary fluoride for Cycle 2 of the CHMS

| | Cycle 2 of CHMS | |
| --- | --- | --- |
| | Unadjusted[†] estimates for the fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for the fluoride subsample (OR, 95% CI) |
| Urinary fluoride (µmol/L) (cont) | 1.02 (95% CI: 0.97–1.08) | 1.02 (95% CI: 0.97–1.09) |
| Creatinine-adjusted urinary fluoride (µmol/mmol) (cont) | 0.97 (95% CI: 0.71–1.32) | 1.01 (95% CI: 0.85–1.21) |
| Specific gravity-adjusted urinary fluoride (µmol/L) (cont) | 1.01 (95% CI: 0.97–1.05) | 1.01 (95% CI: 0.96–1.06) |

Notes: One or more parameters could not be estimated in 37 bootstrap replicates. We report urinary fluoride and specific gravity-adjusted urinary fluoride in units of micromoles per litre (µmol/L), creatinine-adjusted urinary fluoride in units of micromoles per millimole (µmol/mmol), and fluoride concentration of tap water in units of milligrams per litre (mg/L) to be consistent with how these variables are presented in Statistics Canada documentation. One can convert micromoles per litre of fluoride to milligrams per litre using the following formula: 1 µmol/L equals 0.019 mg/L.[9] Based on Statistics Canada sample size requirements, the only types of learning disabilities that we considered were ADD and ADHD.
[†] Column contains bivariate associations between predictor variable and the outcome (parental- or self-reported diagnosis of ADHD).
[‡] Column contains associations from single model containing all predictor variables (age, sex, household income adequacy, and highest attained education in the household).

**Table 3b.** Results from logistic regression where parental- or self-reported diagnosis of *ADD (no hyperactivity) among children aged 3–12 years* was regressed on urinary fluoride for Cycle 2 of the CHMS

| Predictor | Cycle 2 of CHMS | |
| --- | --- | --- |
| | Unadjusted[†] estimates for the fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for the fluoride subsample (OR, 95% CI) |
| Urinary fluoride (µmol/L) (cont) | 0.98 (95% CI: 0.93–1.04) | 0.99 (95% CI: 0.93–1.05) |
| Creatinine-adjusted urinary fluoride (µmol/mmol) (cont) | 0.62*** (95% CI: 0.47–0.83) | 0.79 (95% CI: 0.59–1.06) |
| Specific gravity-adjusted urinary fluoride (µmol/L) (cont) | 0.97 (95% CI: 0.92–1.03) | 0.98 (95% CI: 0.94–1.03) |

Note: One or more parameters could not be estimated in 30 bootstrap replicate. We report urinary fluoride and specific gravity-adjusted urinary fluoride in units of micromoles per litre (µmol/L), creatinine-adjusted urinary fluoride in units of micromoles per millimole (µmol/mmol), and fluoride concentration of tap water in units of milligrams per litre (mg/L) to be consistent with how these variables are presented in Statistics Canada documentation. One can convert micromoles per litre of fluoride to milligrams per litre using the following formula: 1 µmol/L equals 0.019 mg/L.[9] Based on Statistics Canada sample size requirements, the only types of learning disabilities that we considered were ADD and ADHD.
***$p < 0.01$; **$p < 0.05$; *$p < 0.1$.
[†] Column contains bivariate associations between predictor variable and the outcome (parental- or self-reported diagnosis of ADD).
[‡] Column contains associations from single model containing all predictor variables (age, sex, household income adequacy, and highest attained education in the household).

Finally, we reran analyses (as possible) using pooled Cycles 2 and 3 data. Specifically, we used logistic regression to examine the association between urinary fluoride exposure and reported learning disability diagnosis, among the full sample of children aged 3–12 years, and among a constrained sample of those who visited a fluoridated collection site. Please recall that due to differences in survey content between Cycles 2 and 3, fluoridation status of data collection site was the only variable related to the source of fluoride exposure that was comparable across the two cycles (see Figure 1).

To generate estimates that were representative of the underlying target population, survey weights were applied to all models as directed by Statistics Canada. Bootstrap weights were also applied to ensure the proper computation of variance estimates.

## RESULTS

Table 1 presents descriptive statistics. In all analyses, missing data were <5%, which is considered inconsequential.[27] The amount of missing data was higher for household income (reported by 71% and 77% of respondents in Cycles 2 and 3 respectively); however, Statistics Canada provided imputed estimates for all participants.[22,23]

Results from the logistic regression analyses with reported learning disability diagnosis (yes/no) regressed on measures of fluoride exposure are presented in Table 2a for Cycle 2 (first three rows) and Table 2b for Cycle 3 (first four rows), unadjusted and

adjusted for covariates. Reported learning disability diagnosis was not significantly associated with urinary fluoride, creatinine-adjusted urinary fluoride, specific gravity-adjusted urinary fluoride (Cycles 2 and 3), or fluoride concentration of tap water (Cycle 3) in unadjusted or adjusted models.

Tables 3a and 3b show the results from the logistic regression analyses examining the association between fluoride concentration in urine and the type of learning disability (Cycle 2 only), unadjusted and adjusted for covariates (fluoride concentration of tap water was not available for this analysis). Reported diagnosis of ADHD (Table 3a) was not significantly associated with any measure of fluoride exposure. Reported diagnosis of ADD (Table 3b) was not significantly associated with urinary fluoride (first row) or specific gravity-adjusted urinary fluoride (third row). However, reported diagnosis of ADD was significantly associated with creatinine-adjusted urinary fluoride (second row) in the unadjusted model (first column), such that those with higher creatinine-adjusted urinary fluoride had lower odds of reporting ADD ($p = 0.003$). This association was reduced to non-significance ($p = 0.107$) in the adjusted model (second column). These results should be interpreted with caution due to small sample sizes and the fact that some bootstrap weights (37 out of 500) dropped out of the models.

Table 4 shows the mean comparisons of fluoride exposure (from urine and tap water) for those with and without a reported learning disability diagnosis among the constrained fluoride subsamples for

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**Table 4.** Mean comparisons of urinary fluoride (Cycles 2 and 3) and fluoride from tap water (Cycle 3 only) between those with and without a parental- or self-reported diagnosis of a learning disability among the constrained fluoride subsamples (weighted and bootstrapped)

| | Cycle 2 of CHMS | | | Cycle 3 of CHMS | | | |
|---|---|---|---|---|---|---|---|
| | Mean urinary fluoride (μmol/L) for the constrained fluoride subsample† | Creatinine-adjusted mean urinary fluoride (μmol/mmol) for the constrained fluoride subsample† | Specific gravity-adjusted mean urinary fluoride (μmol/L) for the constrained fluoride subsample† | Mean urinary fluoride (μmol/L) for the constrained fluoride subsample‡ | Creatinine-adjusted mean urinary fluoride (μmol/mmol) for the constrained fluoride subsample‡ | Specific gravity-adjusted mean urinary fluoride (μmol/L) for the constrained fluoride subsample‡ | Mean fluoride concentration of tap water (mg/L) for the constrained fluoride subsample‡ |
| Has not been diagnosed with a learning disability | 39.33 (95% CI: 35.55–43.11) | 5.33 (95% CI: 4.46–6.20) | 43.47 (95% CI: 39.25–47.69) | 29.66 (95% CI: 24.26–35.06) | 4.77 (95% CI: 3.28–6.26) | 39.76 (95% CI: 31.20–48.33) | 0.36 (95% CI: 0.23–0.49) |
| Has been diagnosed with a learning disability | 41.91 (95% CI: 30.35–53.47) | 5.28 (95% CI: 2.97–7.59) | 44.46 (95% CI: 32.24–56.68) | 28.26 (95% CI: 17.60–38.92) | 4.24 (95% CI: 2.66–5.81) | 39.73 (95% CI: 28.94–50.51) | 0.38 (95% CI: 0.21–0.56) |

Note: We report urinary fluoride and specific gravity-adjusted urinary fluoride in units of micromoles per litre (μmol/L), creatinine-adjusted urinary fluoride in units of micromoles per millimole (μmol/mmol), and fluoride concentration of tap water in units of milligrams per litre (mg/L) to be consistent with how these variables are presented in Statistics Canada documentation. One can convert micromoles per litre of fluoride to milligrams per litre using the following formula: 1 μmol/L equals 0.019 mg/L.[9]
† For Cycle 2, the constrained fluoride subsample refers to children who: 1) attended a fluoridated data collection site, 2) identified tap water was their primary source of drinking water at home or away from home, and 3) lived in their current home for three or more years.
‡ For Cycle 3, the constrained fluoride subsample refers to children who: 1) attended a fluoridated data collection site, 2) reported using fluoride-containing dental products at home, and 3) reported ever having received fluoride treatments at the dentist.

Cycles 2 and 3. As noted, logistic regression was not feasible due to minimum sample size requirements. For Cycle 2, children with and without a reported learning disability diagnosis did not differ on any measure of fluoride exposure, based on substantially overlapping 95% confidence intervals (CIs). Similarly, for Cycle 3, children with and without a reported learning disability diagnosis did not differ on any measure of fluoride exposure, based on substantially overlapping 95% CIs.

Table 5 shows results from analysis of pooled data from Cycles 2 and 3. A small but statistically significant effect was observed (first row) such that children with higher urinary fluoride had higher odds of having a reported learning disability diagnosis among both the fluoride subsample ($p = 0.03$) and the constrained fluoride subsample ($p = 0.04$), in adjusted models. However, when these models were run using creatinine-adjusted urinary fluoride as the outcome (second row), and specific gravity-adjusted urinary fluoride as the outcome (third row), no statistically significant associations were observed among either the fluoride subsample or the constrained fluoride subsample, in unadjusted or adjusted models.

## DISCUSSION

We found no association between fluoride exposure (from urine and tap water) and parental or self-reported diagnosis of a learning disability among a national population-based sample of Canadian children aged 3–12 years when we examined Cycles 2 and 3 of the CHMS separately. The one exception is the inverse relationship observed (higher creatinine-adjusted urinary fluoride associated with lower reported ADD diagnosis) in the unadjusted model, but this finding disappeared in the adjusted model.

When we examined the association between urinary fluoride and reported learning disability diagnosis among the pooled sample (i.e., Cycles 2 and 3 combined), we detected a small but statistically significant association such that for every one unit increase in urinary fluoride (μmol/L), the odds of having a reported learning disability diagnosis increased by 1.02 in the adjusted models, among the fluoride subsample and the constrained fluoride subsample. These significant findings were not observed with creatinine-adjusted urinary fluoride or specific gravity-adjusted urinary fluoride, which are thought to be more accurate because they help to correct for the effect of urinary dilution, which can vary between individuals and different points in time. Accordingly, these adjusted measures help to offset some of the limitations associated with spot urine samples. The finding that the effect was reduced to non-significance when creatinine-adjusted and specific gravity-adjusted urinary fluoride were used, suggests that the association between urinary fluoride and reported learning disability diagnosis may not be robust.

Because we were interested in implications for CWF, we examined associations for the subset of children for whom we had some information on source of fluoride exposure, using the pooled Cycle 2 and 3 samples. Theoretically, if CWF was playing a key role, we would have observed a stronger effect among the constrained fluoride subsample. Although we observed a small effect where the odds of a reported learning disability diagnosis increased with urinary fluoride concentration in this constrained subsample, that effect was not robust to creatinine and specific gravity adjustment. However, we acknowledge that by

**Table 5.** Results from logistic regression where self-reported diagnosis of a *learning disability among children aged 3–12 years* was regressed on urinary fluoride, creatinine-adjusted urinary fluoride, and specific gravity-adjusted urinary fluoride among the fluoride subsample and the constrained fluoride subsample using pooled data from Cycles 2 and 3 of the CHMS

| Predictor variable | Cycles 2 and 3 of CHMS | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Urinary fluoride | | Creatinine-adjusted urinary fluoride | | Specific gravity-adjusted urinary fluoride | | Urinary fluoride | | Creatinine-adjusted urinary fluoride | | Specific gravity-adjusted urinary fluoride | |
| | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for fluoride subsample (OR, 95% CI) | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for fluoride subsample (OR, 95% CI) | Unadjusted[†] estimates for fluoride subsample (OR, 95% CI) | Adjusted[‡] estimates for fluoride subsample (OR, 95% CI) | Unadjusted[†] estimates for constrained fluoride subsample[§] (OR, 95% CI) | Adjusted[‡] estimates for constrained fluoride subsample[§] (OR, 95% CI) | Unadjusted[†] estimates for constrained fluoride subsample[§] (OR, 95% CI) | Adjusted[‡] estimates for constrained fluoride subsample[§] (OR, 95% CI) | Unadjusted[†] estimates for constrained fluoride subsample[§] (OR, 95% CI) | Adjusted[‡] estimates for constrained fluoride subsample[§] (OR, 95% CI) |
| Urinary fluoride (µmol/L) (cont) | 1.01* (95% CI: 1.00–1.03) | 1.02** (95% CI: 1.00–1.03) | – | – | – | – | 1.02* (95% CI: 1.00–1.04) | 1.02** (95% CI: 1.00–1.04) | – | – | – | – |
| Creatinine-adjusted urinary fluoride (µmol/mmol) (cont) | – | – | 1.00 (95% CI: 0.91–1.10) | 1.04 (95% CI: 0.98–1.10) | – | – | – | – | 1.02 (95% CI: 0.92–1.13) | 1.04 (95% CI: 0.97–1.12) | – | – |
| Specific gravity-adjusted urinary fluoride (µmol/L) (cont) | – | – | – | – | 1.01 (95% CI: 1.00–1.02) | 1.01 (95% CI: 1.00–1.02) | – | – | – | – | 1.01 (95% CI: 1.00–1.02) | 1.01 (95% CI: 1.00–1.02) |
| Sex (ref: female) | – | 1.90** (95% CI: 1.11–3.26) | – | 2.02** (95% CI: 1.17–3.50) | – | 2.04** (95% CI: 1.17–3.54) | – | 1.82 (95% CI: 0.80–4.13) | – | 1.99 (95% CI: 0.85–4.64) | – | 2.04 (95% CI: 0.86–4.80) |
| Age (cont) | – | 1.31*** (95% CI: 1.21–1.43) | – | 1.31*** (95% CI: 1.19–1.46) | – | 1.31*** (95% CI: 1.19–1.43) | – | 1.29*** (95% CI: 1.13–1.47) | – | 1.29*** (95% CI: 1.11–1.51) | – | 1.28*** (95% CI: 1.11–1.47) |
| Household income adequacy (ref: lower and middle income) | – | 0.88 (95% CI: 0.33–2.38) | – | 0.88 (95% CI: 0.32–2.45) | – | 0.89 (95% CI: 0.32–2.48) | – | 1.19 (95% CI: 0.36–3.98) | – | 1.19 (95% CI: 0.33–4.28) | – | 1.21 (95% CI: 0.36–4.34) |
| Highest attained education in the household (ref: less than bachelor's degree) | – | 0.41** (95% CI: 0.21–0.80) | – | 0.41** (95% CI: 0.21–0.81) | – | 0.42** (95% CI: 0.21–0.81) | – | 0.31** (95% CI: 0.12–0.81) | – | 0.32** (95% CI: 0.12–0.88) | – | 0.32** (95% CI: 0.12–0.85) |

Note: We report urinary fluoride and specific gravity-adjusted urinary fluoride in units of micromoles per litre (µmol/L), creatinine-adjusted urinary fluoride in units of micromoles per millimole (µmol/mmol), and fluoride concentration of tap water in units of milligrams per litre (mg/L) to be consistent with how these variables are presented in Statistics Canada documentation. One can convert micromoles per litre of fluoride to milligrams per litre using the following formula: 1 µmol/L equals 0.019 mg/L.[9]
***$p < 0.01$; **$p < 0.05$; *$p < 0.1$.
[†] Column contains bivariate associations between predictor variable and the outcome (diagnosis of a learning disability).
[‡] Column contains associations from single model containing all predictor variables (age, sex, household income adequacy, and highest attained education in the household).
[§] For Cycles 2 and 3 combined, the constrained fluoride subsample refers to children who attended a fluoridated data collection site.

constraining our sample, we had a smaller sample size and reduced power to detect an effect. Overall, there does not appear to be a robust association between fluoride exposure and reported learning disability diagnosis, regardless of whether or not the sample was constrained to children who visited a fluoridated data collection site.

Compared with the only other population-based study of fluoride and ADHD,[11] our findings have some similarities and some differences. There are several possible explanations for the different findings. First, Malin and Till (2015) use an ecological measure of fluoride exposure whereas we used an individual-level measure that reflects fluoride from all sources, including CWF. Second, our lack of an association could reflect small sample sizes, which we identify as reasons for interpreting our results with caution in Tables 3a and 3b. Third, Malin and Till examine reported ADHD prevalence among American children and adolescents aged 4–17 years whereas we focused on Canadian children aged 3–12 years. There are differences between the two countries in terms of fluoridation policy and coverage, with Canada having lower coverage and, until recently, a lower recommended optimal concentration.[3,28–30] A finding that is somewhat similar between the two studies is our finding, based on the pooled sample, of a significant association between higher urinary fluoride and reported learning disability diagnosis among both the fluoride subsample and the constrained fluoride subsample in adjusted models. However, as we argued above, that effect may not be robust because it did not appear in models that used creatinine-adjusted or specific gravity-adjusted urinary fluoride.

There are limitations related to how learning disabilities were captured in the CHMS. First, the reported nature of that variable makes it subject to reporting bias. Second, Cycle 2 only inquired about the type of learning disability (including ADHD) if a positive response was obtained for the previous question ("Do you have a learning disability?"); however, ADHD is not formally classified as a learning disability.[31] Accordingly, in analyses related to ADHD, our sample may have only captured children who have a comorbid diagnosis of a learning disability and ADHD. Third, the learning disability variable was a simple yes/no classification and thus, the severity of the disorder is unknown. While it is desirable to use more objective assessments of cognitive and academic functioning that can describe the severity of the disorder and are not sensitive to self-report (e.g., IQ or memory testing), it is likely only feasible to collect such measures in smaller-scale studies. In the context of large population-based studies, a trade-off exists between the breadth of knowledge generated (i.e., nationally representative estimates) and the depth of data collection. When examining potential harms related to CWF, smaller-scale clinical studies, basic science studies, and larger-scale population studies all have important contributions to make.

Other limitations reflect the study design and the time frame captured by the variables. First, spot urine samples used to measure urinary fluoride are vulnerable to fluctuations.[3] Second, reported learning disability diagnosis could have preceded measured fluoride exposure. Upcoming cycles of the CHMS should consider collecting biomarkers such as hair and/or fingernails, which estimate fluoride intake over a longer time frame and can be collected non-invasively.[32] Finally, we are not able to discern causality due to the cross-sectional nature of the survey data.

Our study has several strengths, including: a large representative sample of Canadian children aged 3–12 years with high response rates, multiple quality-control measures implemented throughout the data collection process, and individual estimates of fluoride exposure and reported learning disability diagnosis.

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## RÉSUMÉ

**OBJECTIFS :** Des études récentes ont révélé que la croissance de l'exposition au fluorure augmente le risque de maladies reliées au développement des neurones telles que, TDAH (trouble déficitaire de l'attention, avec ou sans hyperactivité) et de QI moins élevés chez les enfants. Notre objectif principal est d'examiner le lien entre l'exposition au fluorure et les diagnostics publiés sur les troubles d'apprentissage selon un échantillon de la population d'enfants âgés de 3 à 12 ans.

**MÉTHODES :** Nous avons analysé les données des cycles 2 et 3 de l'Enquête canadienne sur les mesures de la santé. Quatre mesures de fluorure étaient disponibles : 1) fluorure urinaire (µmol/L), 2) fluorure urinaire normalisée par la créatinine (µmol/mmol), 3) fluorure urinaire spécifique normalisée pour la gravité (µmol/L), et 4) concentration de fluorure de l'eau du robinet (mg/L) (Cycle 3 seulement). Le diagnostic des troubles d'apprentissage (oui ou non) était fondé sur les rapports parentaux ou sur l'auto-évaluation. Les liens ont été examinés en utilisant la régression logistique (là où c'était possible), données non corrigées et corrigées pour les covariables.

**RÉSULTATS :** Lorsque les cycles 2 et 3 ont été examinés séparément, le diagnostic sur les troubles d'apprentissage ne présentait aucun lien significatif avec les mesures d'exposition au fluorure, dans les modèles corrigés ou non corrigés. Lorsque les cycles 2 et 3 ont été regroupés, un léger effet, mais dont la signification statistique a été observée comme quoi les enfants ayant démontré un taux de fluorure urinaire plus élevé avaient plus de chances d'avoir des troubles d'apprentissage selon le modèle corrigé ($p = 0.03$). Cependant, ce lien n'a pas été observé dans les modèles qui utilisaient des taux de fluorure urinaire corrigés pour la créatinine et corrigés pour la gravité spécifique, lesquels sont censés être plus précis en raison de la correction pour la dilution urinaire.

**CONCLUSION :** En général, nous n'avons trouvé aucun lien solide entre l'exposition au fluorure et les diagnostics des parents ou des auto-évaluations parmi les enfants canadiens quant aux troubles d'apprentissages.

**MOTS CLÉS :** population; fluorisation; cognition; troubles d'apprentissage; sondages et questionnaires