### SCIENCE ADVANCES | RESEARCH ARTICLE

#### **PUBLIC HEALTH**

## Childhood fluoride exposure and cognition across the life course

John Robert Warren<sup>1</sup>\*, Gina Rumore<sup>1</sup>, Soobin Kim<sup>2</sup>, Eric Grodsky<sup>3</sup>, Chandra Muller<sup>4</sup>, Jennifer J. Manly<sup>5</sup>, Adam M. Brickman<sup>5</sup>

How are children's fluoride exposures associated with cognitive test performance in adolescence and midlife? Whereas most prior research has estimated effects of exposure to extremely high levels of fluoride, we consider exposure to levels of fluoride within the range typical in most places and of greatest relevance to policy debates about government water fluoridation. We use data from the nationally representative (United States) High School and Beyond cohort, characterize fluoride exposure from drinking water across adolescence, adjust for confounders, and observe cognitive test performance in both secondary school and at age ~60. We find that children exposed to recommended levels of fluoride in drinking water exhibit modestly better cognition in secondary school, an advantage that is smaller and no longer statistically significant at age ~60.

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#### INTRODUCTION

Overwhelming scientific evidence demonstrates that fluoride in drinking water lowers the risk of tooth decay in children and adults (1-4). Fluoridating drinking water is so effective in the United States that the US Centers for Disease Control recognized it as one of the "10 great public health interventions of the 20<sup>th</sup> century" (5). Despite clear evidence for improved oral health outcomes in children and adults exposed to fluoridated drinking water, the safety of fluoride in drinking water has been perennially debated for the eight decades since Grand Rapids, Michigan became the first city to fluoridate its water in 1945.

Current concern about fluoride in drinking water centers around its safety for fetuses and children, with a focus on whether fluoride reduces childhood IQ. A sizable body of scientific research addresses this question, much of which is summarized in two recent metaanalyses (6, 7).

First, Taylor et al. (6) meta-analyzed evidence from 74 articles and found a statistically significant inverse relationship between exposure to fluoride in drinking water and childhood IQ. However, nearly all of the studies considered by Taylor et al. (6) modeled the IQ consequences of exposure to fluoride levels much higher than those found in public drinking water in the United States; even the "low exposure" comparison groups in the studies they reviewed typically experienced fluoride levels considerably higher than those found almost anywhere in the United States (8). The levels of fluoride in many of the reviewed articles were so high that children showed evidence of fluoride toxicity—i.e., fluorosis. None of the studies considered by Taylor et al. (6) were conducted on children in the United States; none used nationally representative data; and most examined extremely poor, rural people in China (45 of the 74 studies), India (9), Mexico (4), or Iran (4).

While Taylor et al. (6) found a strong inverse relationship between fluoride exposure and children's IQ when fluoride concentrations in drinking water exceeded 1.5 mg/liter, their findings for concentrations below 1.5 mg/liter were null. Even this 1.5 mg/liter threshold is in the upper tail of the distribution of fluoride exposure experienced by people in the United States. A nationally representative study of Americans aged 6 to 19 years who were exposed to fluoride in their drinking water showed that only 4.3% were exposed to levels of fluoride in drinking water greater than 1.2 mg/liter (10). This is consistent with a 2023 survey of community water systems across the United States that estimated that 4.5% of all people in the United States are exposed to 1.5 mg/liter of fluoride or more (8). The currently recommended level of fluoride in drinking water in the United States is 0.7 mg/liter, lowered in 2015 from 0.7 to 1.2 mg/liter. Thus, essentially none of the studies included in Taylor et al. (6) are relevant to understanding the cognitive effects of children's exposure to fluoride in drinking water in the United States. Other studies of the effects of maternal fluoride exposure (at levels of exposure of relevance to policy debates) on children's cognition have come to mixed conclusions (9, 11, 12).

Second, Kumar et al.'s (7) meta-analysis included only studies conducted in areas with exposure to fluoride in drinking water equal to or less than 1.5 mg/liter; the eight articles in their analysis report effects of fluoride exposure on children's IQ in places in which fluoride levels are within ranges experienced by nearly all people living in the United States. The results of their meta-analysis "show that fluoride exposure relevant to community water fluoridation is not associated with lower IQ scores in children" (7:73). Like Taylor *et al.* (6), none of the studies considered by Kumar *et al.* (7) were conducted among children in the United States and none used nationally representative data.

Beyond the limitations in the research meta-analyzed by Taylor et al. (6), Kumar et al. (7), and others, two other common shortcomings of the extant research are notable. First, given recent evidence that cognitive skills in adolescence play an important role in determining later-life cognitive functioning (13), a broader weakness of the extant research is its inattention to the effects of childhood fluoride exposure on cognitive outcomes over the life course. Although many factors across the life course may mitigate negative effects of fluoride exposure in adolescence, given the importance of early life

<sup>&</sup>lt;sup>1</sup>Institute for Social Research and Data Innovation, University of Minnesota, Minneapolis, MN, USA. <sup>2</sup>Center for Demography of Health and Aging, University of Wisconsin-Madison, Madison, WI, USA. <sup>3</sup>Department of Sociology, University of Wisconsin-Madison, Madison, WI, USA. <sup>4</sup>Department of Sociology, University of Texas at Austin, Austin, TX, USA. <sup>5</sup>Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Department of Neurology — Vagelos College of Physicians and Surgeons, Columbia University, New York, NY, USA. \*Corresponding author. Email: warre046@umn.edu

academic achievement for long-term cognitive functioning (13), it is important to investigate the long-term effects of exposure on cognition. Second, much of the extant research fails to account for spatial and other contextual factors that may confound associations between levels of fluoride exposure and IQ or other cognitive outcomes. In the United States, for example, there are urban-rural inequalities in adolescents' cognitive performance; it is also true that American children in rural areas are less likely to be exposed to the US Public Health Service's recommended level of fluoride (0.7 mg/liter). These shortcomings in extant research are largely driven by a lack of prospective, nationally representative, longitudinal data that characterize childhood fluoride exposures, adolescent cognition, late life cognition, and relevant potential confounders.

We investigate the association between children's levels of fluoride exposure from drinking water and cognitive outcomes in adolescence and later adulthood. Our analysis innovates by (i) using data from a nationally representative sample of children in the United States; (ii) considering the effects of fluoride exposure in drinking water within ranges commonly observed and of relevance to debates about community water fluoridation policy in the United States; (iii) adjusting for potential confounders; and (iv) considering both adolescent and adult cognitive outcomes.

#### **RESULTS**

Table 1 describes the distribution of all measures, separately by fluoride exposure category. Students who were always exposed to sufficient levels of fluoride through 12th grade were disproportionately from urban areas and from the southern and midwestern United States; because of these spatial patterns, they are also somewhat more likely to be Black and to have modestly lower scores on measures of adolescent and adult cognition. Figure 1 maps each High School and Beyond cohort (HS&B:80) high school (with spatial perturbation to protect confidentiality) and indicates each school's fluoride treatment category. Both Table 1 and Fig. 1 highlight the spatial patterning of fluoride exposure—which is correlated with students' demographic and socioeconomic attributes.

In table S1 we, report results of a multinomial logistic regression model predicting fluoride exposure category as a function of spatial, demographic, and socioeconomic factors. These results demonstrate that spatial factors drive exposure; net of region and urbanicity, few student- or school-level factors are associated with fluoride exposure category.

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Figure 2 depicts coefficient estimates (and 95% confidence intervals) for fluoride exposure's conditional associations with adolescent cognitive performance and with cognitive functioning at age ~60. Detailed model results appear in table S2. The model for each outcome conditions on family socioeconomic background, demographic attributes, urbanicity, and region.

For each measure of adolescent cognitive performance, students performed better if they were exposed to sufficient levels of fluoride—either throughout childhood, or during part of childhood. The estimated effects are modest—about 7% of a SD in magnitude—but they are consistently positive and distinguishable from zero. All else equal, fluoride exposure is not statistically significantly associated

with cognitive functioning at age ~60; however, the point estimates in that model are also positive.

#### **Robustness checks**

To assess the robustness of our results, we performed two sets of supplementary analyses; full details and results appear in the Supplementary Materials. First, because we characterize childhood fluoride exposure on the basis of the location of students' secondary schools, we risk mischaracterizing the exposure of students who lived in different communities before attending secondary school. To assess the robustness of our findings to this issue, we repeated our analyses after restricting the analytic sample to students who had not changed schools because they or their families had changed residence since the start of fifth grade. In general, and as shown in table S3, we derive very similar substantive results as in the analyses that include all students.

Second, we attempt to distinguish between the effects of (i) the biological processes resulting from ingesting sufficient levels of fluoride and (ii) the social, political, cultural, economic, and other dynamics that may have influenced municipalities to adopt water fluoridation. Municipalities that fluoridate their water may also be places that make other investments—in education, housing, healthcare, etc.—that lead to better cognitive outcomes. To address this threat to inference, we follow Elwert and Pfeffer (14) and others in using a "future treatment" to parse these effects—adding a category to our exposure variable that indicates whether schools were in locations that began municipal water fluoridation shortly after adolescent achievement tests were completed. This approach accounts for any time invariant attributes of communities associated with the adoption of water fluoridation practices that may also contribute to cognitive skills. The results, shown in fig. S1, suggest that it is likely not the area-level social, economic, political, or other dynamics that are driving the results depicted in Fig. 2; this lends credibility to the idea that it is the ingestion of fluoride into their bodies that is associated with improved adolescent cognitive performance.

#### **DISCUSSION**

Recent evidence about the negative effects on adolescent IQ of exposure to very high levels of fluoride—levels far exceeding those experienced by almost everyone in the United States—has been cited in efforts to curtail water fluoridation practices in many states and municipalities. Citing this evidence—virtually none of which comes from the United States and most of which does not account for other confounding exposures—critics of water fluoridation policies argue that the downsides to water fluoridation outweigh its benefits for oral health.

Using data from a nationally representative and prospectively observed cohort of people in the United States, we ask how adolescent and adult cognition vary as a function of level of exposure to fluoride throughout childhood. We find robust evidence that young people who are exposed to typical, recommended levels of fluoride in drinking water perform better on tests of mathematics, reading, and vocabulary achievement in secondary school than their peers who were never exposed to sufficient levels of fluoride. People who were exposed to typical, recommended levels of fluoride in adolescence may perform better on assessments of cognitive functioning at age ~60, but results of those models are inconclusive. Our future

**Table 1. Descriptive statistics by fluoride exposure category.** These analyses exclude a very small number of cases ( $n = \sim 110$ ) for whom we lack information about the year in which municipalities began to fluoridate their water. The analyses also exclude students ( $n = \sim 200$ ) in the small number of schools in Alaska and Hawaii. See the Supplementary Materials for full details. Source: High School and Beyond, 1980. Sample sizes have been rounded to the nearest 10.

Outcome measures	Full sample		Sufficient fluoride in all of childhood		Sufficient fluoride in part of childhood		Sufficient fluoride in none of childhood	
	Mean/%	(s.d.)	Mean/%	(s.d.)	Mean/%	(s.d.)	Mean/%	(s.d.)
Math achievement (Gr. 12)	0.00	(1.00)	-0.03	(1.01)	0.08	(1.01)	-0.02	(0.98)
Reading achievement (Gr. 12)	0.00	(1.00)	-0.03	(1.01)	0.07	(1.00)	-0.02	(0.98)
Vocab. achievement (Gr. 12)	0.00	(1.00)	-0.04	(1.01)	0.07	(1.02)	-0.01	(0.98)
Global cognition (Age ~ 60)	0.00	(1.00)	-0.04	(1.02)	0.06	(1.02)	0.01	(0.96)
Sex		•	•	•	•			•
Female	51.2%	•	51.8%	•	51.5%		50.5%	•
Male	48.8%		48.2%	•	48.5%		49.5%	•
Race		•	•	•		•		•
White	73.9%	•	70.9%	•	75.1%	•	76.1%	•••••
Black	11.7%	•••••	14.2%	***************************************	11.6%	•	9.2%	•••••
Hispanic	10.3%	•••••	10.7%	•	9.0%	•	10.7%	•••••
Other	4.1%	•	4.1%	•	4.2%		4.1%	•••••
Parental education		•	•	•	•			• • • • • • • • • • • • • • • • • • • •
High school or less	48.9%	•	49.2%	•	47.6%		49.6%	• • • • • • • • • • • • • • • • • • • •
Some college	26.9%	•	26.9%	•	25.7%	•	27.7%	• • • • • • • • • • • • • • • • • • • •
College graduate	12.8%		12.5%	•	13.5%		12.5%	• • • • • • • • • • • • • • • • • • • •
Graduate school	11.4%	•	11.4%	•	13.1%	•	10.2%	• • • • • • • • • • • • • • • • • • • •
Family income in 1980	20,728	(10,729)	20,719	(10,778)	21,163	(10,857)	20,433	(10,577)
High school region		•	••••	•	•••••	•		•
Northeast	22.9%	•	14.9%	•	28.0%		27.5%	•
South	31.7%		39.5%	•	25.7%		27.7%	•
Midwest	28.1%	•	32.9%	•	37.0%	•	16.9%	•
West	17.4%	•	12.7%	•	9.4%	•	27.9%	•••••
High school urbanicity		•	•	•		•		•
Urban	21.7%	•	27.5%	***************************************	25.5%	•	13.1%	•••••
Suburban	48.3%	•	47.4%	•	48.8%	•	48.9%	•••••
Rural	30.0%	•	25.1%	•	25.7%		38.0%	•••••
High school type		•		• • • • • • • • • • • • • • • • • • • •				•
Public	90.3%	•	88.6%	• • • • • • • • • • • • • • • • • • • •	89.3%		92.8%	• • • • • • • • • • • • • • • • • • • •
Catholic	6.3%	•	7.9%	•	5.9%		5.0%	• • • • • • • • • • • • • • • • • • • •
Private	3.4%		3.5%		4.9%		2.2%	
Sample size	57,960	•	22,420	•	14,390	•	21,150	

treatment supplementary analyses add evidence that it is exposure to fluorine itself—as opposed to the social, economic, political, or other factors that lead some communities to implement fluoridation practices—that shapes cognition.

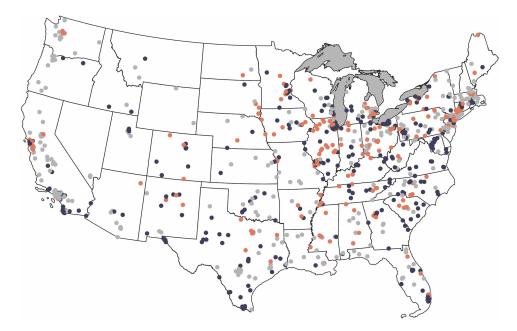
Given the data at our disposal, we are unable to fully explain the positive conditional association between fluoride exposure and adolescent academic achievement. On one hand, being exposed to sufficient (but not excessive) amounts of fluoride may causally affect academic achievement via improved oral health or other mechanisms. On the other hand, in our observational study the conditional associations may be due to unobserved student- or community-level confounding. At a minimum, however, our results cast doubt on the

assertion that exposure to recommended levels of fluoride reduce academic achievement or cognitive functioning.

Debates about water fluoridation policy and practice in the United States should be informed by research (i) on the consequences of exposure to fluoride at levels recommended by the US Department of Health and Human Service and as routinely observed in the country; (ii) on representative samples of people living in the United States; and (iii) that can adjust for key (mainly spatial) confounders.

#### Limitations

Although our analyses are innovative in several ways—for example, it is the first longitudinal, population-based study of a representative



**Fig. 1. Fluoride exposure category for HS&B:80 schools.** Dots depict the location of HS&B:80 high schools; we have introduced a small amount of spatial perturbation to protect the identities of the schools. Blue dots indicate that students in those schools were exposed to sufficient levels of fluoride from conception through grade 12; gray dots indicate that students were never exposed to sufficient fluoride through grade 12; and orange dots indicate that students were exposed to sufficient levels of fluoride at some point during childhood.

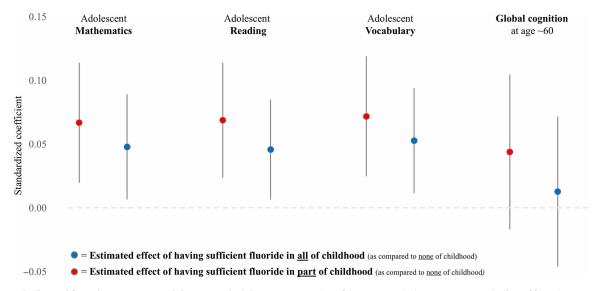


Fig. 2. Estimated effects of fluoride exposure on adolescent and adult cognition. 95% confidence intervals depicting estimated effect of fluoride exposure relative to insufficient exposure throughout childhood; models adjust for family socioeconomic background, demographic attributes, and spatial location. These analyses exclude a very small number of cases ( $n = \sim 110$ ) for whom we lack information about the year in which municipalities began to fluoridate their water. The analyses also exclude students ( $n = \sim 200$ ) in the small number of schools in Alaska and Hawaii. Analyses of adolescent cognitive outcomes include 57,960 students in the base year survey; analyses of cognition at age  $\sim 60$  restricted to the 13,260 panelists who responded in 2021. See table 52 for full details and model results. Source: High School and Beyond, 1980. Sample sizes have been rounded to the nearest 10.

sample to investigate the cognitive outcomes of people exposed to levels of fluoride in the range routinely observed in the United States—some limitations are worth noting. First, and most seriously, we would have preferred more complete information about where panelists lived from conception through late adolescence; we are forced to place them in the communities in which they went to

secondary school. Second, we would have preferred to know how much fluoride panelists consumed; instead, we proxy that with information about water chemistry. Especially given that the half-life of fluoride is just a few hours, this may be the only practical exposure measurement strategy in a community-based sample. Third, in estimating effects on adult cognition, we would have preferred to

have information about fluoride exposures across the adult life course. Despite these limitations, our results provide strong evidence that exposure to fluoride—at levels ordinarily seen in the United States and of relevance to policy debates about municipal water fluoridation—has benefits for adolescent cognition and is, at worst, not harmful for later-life cognitive functioning.

#### **MATERIALS AND METHODS**

We use data from the HS&B:80, which began as a nationally representative probability sample of 58,270 sophomores and seniors in 1020 American high schools in 1980. A randomly selected subset of 26,820 sample members were selected for follow-up and have been reinterviewed on several occasions through 2021 (15). Complete descriptions of our data, measures, and analytic approach appear in the Supplementary Materials.

Using geolocations of HS&B:80 schools and under the assumption that sample members were conceived and raised in the community where they attended high school, we characterize sample members' fluoride exposure from conception through secondary school using archival data on (i) municipal water system fluoridation practices and (ii) naturally occurring fluoride levels as measured in untreated well water. First, we extracted records from the 1967 through 1993 editions of the US Department of Health and Human Service's Fluoridation Census (16, 17). These records indicate which US localities supplemented municipal drinking water with fluoride and the month and year in which they began doing so. Second, we used US Geological Survey data (18) that characterize fluoride levels in untreated groundwater as measured in 38,105 US wells between 1988 and 2017.

From 1962 to 2015, the US Department of Health and Human Services (19) recommended community water fluoridation levels of between 0.7 and 1.2 mg/liter; in 2015, the recommendation was lowered to 0.7 mg/liter (20). We use a measure of fluoride exposure that can take on three possible values. First, students were classified as consistently exposed to insufficient levels of fluoride if—at both the time of their conception and at the time of their secondary school academic achievement tests—they lived in places that (i) did not use municipal water fluoridation and (ii) had naturally occurring fluoride levels below 0.7 mg/liter. Second, students were classified as consistently exposed to sufficient levels of fluoride if—at both the time of their conception and at the time of their secondary school academic achievement tests—they lived in places that (i) used municipal water fluoridation or (ii) had naturally occurring fluoride levels at or above 0.7 mg/liter. Third, students were classified as exposed to sufficient levels of fluoride for part of childhood if they lived in places that implemented municipal water fluoridation at some point after their conception but before the time of their secondary school achievement tests. Notably, too few HS&B:80 students attended schools in communities with fluoride levels greater than 1.2 mg/liter to include this category.

We characterize adolescent cognitive performance among all HS&B:80 students in 1980 using test scores in reading comprehension, vocabulary, and mathematics (21) in the 12th grade. We characterize global cognitive functioning at age ~60 using a measure derived from a hierarchical item response theory model (22, 23) that combines information from—and accounts for shared variance across—measures of memory, fluency, and attention administered to HS&B:80 sample members who participated in 2021.

We estimate a series of ordinary least squares regression models; SEs are adjusted to account for the school-based clustered sampling design. Missing data are handled through multiple imputation with chained equations. All models adjust for students' self-reported gender, race and ethnicity, family socioeconomic background, urbanicity, and region.

#### **Supplementary Materials**

This PDF file includes:

Supplementary Materials and Methods Tables S1 to S3 Fig. S1

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disease and related dementias to CogniScreen Inc. and Tau Biosciences Inc. He has equity in both companies. He has also provided paid consultation services related to cognitive assessment to Cognition Therapeutics Inc. He is on the Medical Advisory Board and provides paid consultation services related to Alzheimer's disease to Cognito Therapeutics Inc. He is a paid scientific consultant for work involving cognitive assessment to IQVIA. He is a member of the Scientific Advisory Board for CogState and serves as a member of a DSMB for the University of Illinois, A.M.B. is a compensated section editor for the journal Alzheimer's & Dementia. The other authors declare that they have no competing interests. Data and materials availability: Data from the HS&B:80 cohort are available to all United States-based researchers via a restricted use data license from the US Department of Education's Institute for Education Sciences (IES). To obtain a license to use the HS&B:80 data, go to: https://ies.ed. gov/about/restricted-use-data. The IES Data Security Office can also be contacted by email (IESData.Security@ed.gov) or via US Mail (Department of Education, 400 Maryland Ave, SW, Room 1 W126, Washington, DC 20202). The measures of fluoride exposure described in the Supplementary Materials are available via the HS&B:80 project website at https:// edshareproject.org/ and on Zenodo (https://doi.org/10.5281/zenodo.16953271). All code used is available openly on Zenodo. All other data needed to evaluate the conclusions in this paper are present in the paper and/or the Supplementary Materials.

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