ORIGINAL REPORT: EPIDEMIOLOGICAL RESEARCH

Dental fluorosis trends in United States oral health surveys: 1986–2012

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A supplemental appendix to this article is available online.

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Dental Fluorosis Trends in United States Oral Health Surveys: 1986–2012

C. Neurath[1], H. Limeback[2], B. Osmunson[3], M. Connett[4], V. Kanter[5], C. R. Wells[6]

Abstract: *Introduction: Dental fluorosis has been assessed only three times in nationally representative oral health surveys in the USA. The first survey was conducted by the National Institute of Dental Research (NIDR) in 1986-1987. Subsequently, the National Health and Nutrition Examination Surveys (NHANES) conducted fluorosis assessments from 1999-2004 and more recently in 2011-2012. A large increase in prevalence and severity of fluorosis occurred between the 1986-1987 and 1999-2004 surveys.*

Objectives: *To determine whether the trend of increasing fluorosis continued in the 2011-2012 survey.*

Methods: *We analyzed publicly available data from the latest NHANES 2011-2012 survey, calculating fluorosis prevalence and severity using three measures: person-level Dean's Index score, total prevalence of those with Dean's Index of very mild and greater, and Dean's Community Fluorosis Index (CFI). We examined these fluorosis measures by several socio-demographic factors, and compared results to the two previous surveys. Analyses accounted for the complex design of the surveys to provide nationally representative estimates.*

Results: *Large increases in severity and prevalence were found in the NHANES 2011-2012 survey compared to the previous surveys, for all socio-demographic categories. For ages 12-15 years, an age range displaying fluorosis most clearly, total prevalence increased from 22% to 41% to 65% in the 1986-1987, 1999-2004, and 2011-2012 surveys, respectively. The rate of combined moderate and severe increased the most, from 1.2% to 3.7% to 30.4%. The CFI increased from 0.44 to 0.67 to 1.47. No clear differences were found in fluorosis rates between categories for most of the socio-demographic variables in the 2011-2012 survey.*

Conclusion: *Large increases in fluorosis prevalence and severity occurred. We considered several possible spurious explanations for these increases but largely ruled them out based on counter-evidence. We suggest several possible real explanations for the increases.*

Knowledge Transfer Statement:
The results of this study greatly increase the evidence base that objectionable dental fluorosis has increased in the USA. Dental fluorosis is an undesirable side effect of too much fluoride ingestion during early years of life. The presented evidence can be used by policy makers and professionals to weigh the risks and benefits of water fluoridation and early exposure to fluoridated toothpaste.

Keywords: fluoride(s), dental health survey(s), epidemiology, dental public health, risk factor(s), enamel

Introduction

Dental fluorosis is a developmental defect characterized by hypomineralized enamel. Its prevalence and severity are easily measured and are well-validated biomarkers of fluoride exposure in children from birth to about age 8 years (Mascarenhas 2000; Fejerskov et al. 1990; National Research Council [NRC] 2006).

Three nationally representative surveys have measured dental fluorosis in the USA since community water fluoridation began in 1945: the National Institute of Dental Research (NIDR) survey in 1986-1987; the National Health and Nutrition Examination Survey (NHANES) in 1999-2004; and most recently the NHANES 2011-2012 (National Institute of Dental and Craniofacial Research [NIDCR] 1992a; NIDCR 1992b; Centers for Disease Control [CDC] 2018).

From Trendley Dean's first studies of fluorosis in the 1930s through the NHANES 1999-2004 survey, the prevalence and severity of fluorosis in the USA increased (Dean 1942; Beltrán-Aguilar et al. 2010). This increase was an impetus for the US Public Health Service (PHS) decision to reduce its recommended fluoride level in drinking water to 0.7 mg/L in 2015 (PHS 2015). The PHS decision did not reference the most recent NHANES results from 2011-2012.

We analyzed the cross-sectional NHANES 2011-2012 data and calculated descriptive statistics on fluorosis

prevalence and severity by several socio-demographic variables. We compare the results to the two previous surveys and discuss possible explanations for the increases in prevalence and severity.

Methods

The NHANES surveys are comprehensive health and nutrition surveys designed to be representative of the USA non-institutional population and comparable between survey years (CDC 2018). The NHANES 1999-2004 and 2011-2012 cycles included fluorosis assessments and socio-demographic questionnaires, as did the NIDR 1986-1987 oral health survey. The data are publicly available (NIDCR 1992a; NIDCR

1992b; CDC 2018). NHANES 2013-2014 data on water fluoride concentration, fluoride supplement usage, and fluoride toothpaste usage was also used in evaluating possible explanations for fluorosis rates. However, no fluorosis data is yet available from the NHANES 2013-2014 survey (CDC 2018).

All three fluorosis surveys measured fluorosis at the tooth level, scoring every permanent tooth in each child by Dean's Index. We assigned a person-level Dean's Index score as the lesser score of the two most affected teeth (Dean 1942).

We used Dean's Community Fluorosis Index (CFI) as a group-level measure of severity, taking a mean of the assigned person-level scores (unaffected = 0, questionable = 0.5, very mild = 1, mild = 2, moderate = 3, severe = 4) (Dean 1942). Our third measure of fluorosis was total

prevalence, the percentage of children with a fluorosis score of "very mild" or higher.

The NHANES and NIDR surveys each used several calibrated examiners and almost identical criteria for assigning Dean's Index scores and for differentiating between fluorosis and non-fluoride enamel defects (NIDCR 1992a; CDC 2018; Dye et al. 2008).

For comparisons between surveys, we focused our analyses on ages 12-15 years. We calculated descriptive statistics for three measures of fluorosis – Dean's Index, total prevalence, and CFI – by the socio-demographic variables of age, gender, race/ethnicity, poverty level, county of birth (in USA/outside USA), and parent's education level.

Figure 1. Dean's Index score frequency distribution for children ages 12-15 years, comparing changes across the three national surveys in the USA.
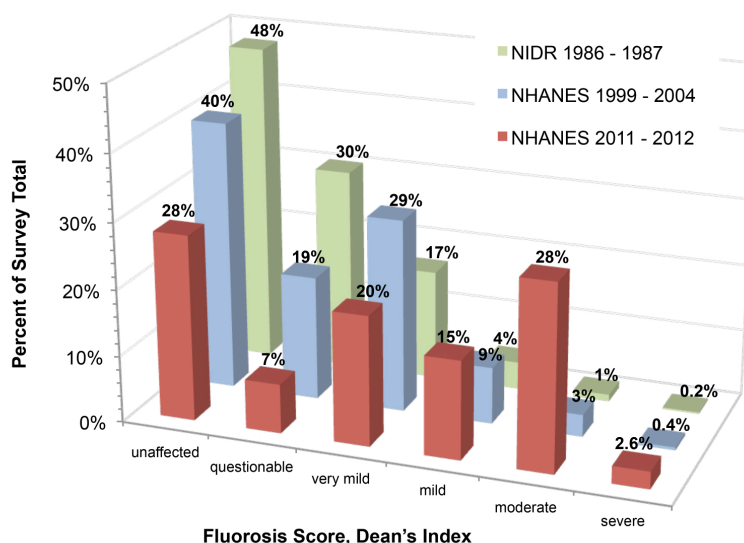
	unaffected	quest.	very mild	mild	moderate	severe
NIDR 1986–1987	**47.8** (40.6, 55.1)	**30.4** (25.4, 36.0)	**16.5** (12.1, 22.2)	**4.1** (2.9, 5.7)	**1.0** (0.6, 1.5)	**0.2** (0.1, 0.4)
NHANES 1999–2004	**40.3** (35.1, 45.7)	**18.6** (15.7, 22.0)	**28.9** (25.8, 32.3)	**8.5** (7.0, 10.3)	**3.3** (2.5, 4.5)	**0.4** (0.2, 0.8)
NHANES 2011–2012	**27.9** (19.5, 38.3)	**7.4** (4.9, 11.0)	**19.5** (14.9, 25.0)	**14.8** (11.5, 18.9)	**27.9** (18.3, 40.1)	**2.6** (1.1, 6.1)

(95% confidence interval)

All three surveys used complex multistage probability sampling to select the individuals by several socio-demographic and geographic factors. We accounted for this by using individual NHANES-provided weights and survey design information to obtain nationally representative estimates and 95% confidence intervals for percentages and numbers affected. Approximate estimates of the number of people in the USA with fluorosis were calculated by summing the NHANES individual sampling weights of the affected sample of NHANES participants. The sample weight of each NHANES participant equals the number of people in the USA population that participant represents. Analyses were

Table.

Comparison of dental fluorosis in three national surveys of the USA, ages 12-15 years, by socio-demographic variables.[a]

Socio-demographic variable Measure Category	NIDR[b] 1986-1987	NHANES[b] 1999-2004	NHANES 2011-2012
All			
Sample size, n[c]	11,800	3,364	599
Weighted n, millions	13.24	15.75	16.59
Dean's Index score			
Moderate & Severe[d]	1.2 (0.9, 1.7)	3.7 (2.8, 4.9)	30.4 (21.3, 41.5)
Prevalence[e]	21.8 (16.2, 28.6)	41.2 (36.7, 45.9)	64.7 (54.6, 73.6)
CFI[f]	0.44 (0.36, 0.51)	0.67 (0.59, 0.74)	1.47 (1.16, 1.77)
Gender			
Prevalence[e]			
Male	22.9 (16.8, 30.4)	41.9 (37.2, 46.7)	62.9 (50.0, 74.2)
Female	20.6 (15.4, 27.1)	40.5 (35.1, 46.2)	66.6 (57.8, 74.4)
CFI[f]			
Male	0.46 (0.38, 0.54)	0.70 (0.62, 0.77)	1.35 (1.04, 1.66)
Female	0.42 (0.34, 0.49)	0.65 (0.57, 0.73)	1.59 (1.23, 1.95)
Race			
Prevalence[e]			
White	21.6 (15.4, 29.4)	36.1 (30.7, 41.9)	69.3 (56.3, 79.8)
Black	25.4 (16.5, 36.9)	57.9 (50.9, 64.7)	65.3 (57.1, 72.7)
Mex.-Amer.[g]	–	43.9 (35.3, 52.8)	54.7 (37.1, 71.3)
Other Hisp.[g]	–	35.1 (27.8, 43.0)	50.2 (34.6, 65.8)
Asian[g]	–	–	70.5 (50.8, 84.6)
Other race[g]	–	–	54.9 (42.0, 67.1)
CFI[f]			
White	0.43 (0.34, 0.51)	0.60 (0.51, 0.69)	1.59 (1.21, 1.96)
Black	0.50 (0.38, 0.63)	0.96 (0.85, 1.08)	1.42 (1.21, 1.63)
Mex.-Amer.[g]	–	0.73 (0.55, 0.91)	1.28 (0.69, 1.87)
Other Hisp.[g]	–	0.50 (0.42, 0.58)	1.03 (0.78, 1.28)
Asian[g]	–	–	1.68 (1.26, 2.11)
Other race[g]	–	–	1.21 (0.70, 1.72)
Poverty[h]			
Prevalence[e]			
poorest	26.0 (19.6, 33.6)	41.5 (34.5, 48.8)	59.5 (46.3, 71.4)
middle	19.4 (9.3, 36.2)	43.6 (38.0, 49.3)	62.4 (49.8, 73.5)
not poor	18.9 (12.0, 28.6)	38.3 (33.7, 43.1)	69.5 (59.2, 78.2)
CFI[f]			
poorest	0.51 (0.40, 0.62)	0.66 (0.56, 0.77)	1.28 (0.97, 1.60)
middle	0.40 (0.26, 0.54)	0.71 (0.62, 0.80)	1.40 (0.97, 1.83)
not poor	0.40 (0.28, 0.52)	0.64 (0.57, 0.71)	1.60 (1.31, 1.89)

Table (continued).

Comparison of dental fluorosis in three national surveys of the USA, ages 12-15 years, by socio-demographic variables.[a]

Socio-demographic variable Measure Category	NIDR[b] 1986-1987	NHANES[b] 1999-2004	NHANES 2011-2012
Parent Education[g]			
Prevalence[e]			
no high school	–	42.8 (33.8, 52.3)	59.2 (40.1, 75.8)
some high school	–	39.6 (31.9, 47.9)	67.0 (50.0, 80.4)
high school grad.	–	39.3 (33.3, 45.6)	67.3 (52.9, 79.1)
some college	–	43.6 (37.3, 50.0)	59.8 (46.3, 71.9)
college grad.+	–	38.9 (32.2, 46.0)	70.3 (57.2, 80.8)
CFI[f]			
no high school	–	0.69 (0.57, 0.82)	1.32 (0.76, 1.88)
some high school	–	0.65 (0.52, 0.79)	1.59 (1.06, 2.11)
high school grad.	–	0.66 (0.56, 0.76)	1.52 (1.14, 1.90)
some college	–	0.70 (0.61, 0.80)	1.28 (0.83, 1.73)
college grad.+	–	0.65 (0.54, 0.75)	1.66 (1.33, 2.00)

[a] All results except sample size n values are weighted to account for survey design as described in the text; numbers in parentheses indicate 95% confidence intervals.

[b] Fluorosis score results differ slightly from those reported in Beltrán-Aguilar et al. (2010) for NIDR 1986-1987 and NHANES 1999-2004. For NHANES 1999-2004 the difference is explained by Beltrán-Aguilar et al using the age at time of interview to categorize by age while we used age at exam which produced a slightly different age group sample.

[c] Number of children ages 12-15 years in the survey, unweighted.

[d] Percent with Dean's Index scores of moderate or severe

[e] Total prevalence, percent with fluorosis scores of very mild or greater.

[f] CFI, Community Fluorosis Index, a mean numerical fluorosis score which integrates prevalence and severity.

[g] Some race and parent education categories not available for NIDR 1986-1987 or NHANES 1999-2004.

[h] The categories of the poverty variable were based on the ratio of the family income to the federal poverty level. For the NIDR 1986-1987 survey, values were based on mean county-level family income and poverty level obtained from USA Census data for 1980. The NIDR 1986-1987 data file includes coded county of residence. The categories were based on tertiles of poverty ratio. For both NHANES surveys the poverty ratio was provided at individual-level. For the NHANES surveys, the category "poorest" had a poverty ratio less than 1; the category "middle" had a ratio from 1–3; and the category "not poor" had a ratio of 3 or higher.

conducted with Stata 15.1 from StataCorp LLC, College Station, TX and JMP 13 from SAS Institute, Inc., Cary, NC.

Results

The NIDR 1986-1987, NHANES 1999-2004, and NHANES 2011-2012 surveys assessed fluorosis in 38,781 (ages 6-19); 16,051 (ages 6-49); and 2,283 (ages 6-19) participants, respectively. The frequency distributions of Dean's Index fluorosis scores for the three surveys are shown in Figure 1 for the age group 12-15 years. The Table shows fluorosis total prevalence and CFI for each year by socio-demographic factors.

Fluorosis prevalence and severity increased dramatically across the surveys. Moderate and severe scores increased the most, reaching rates of 28% moderate and 2.6% severe in children age 12-15 in

Figure 2. Relationship between age and Community Fluorosis Index (CFI) for the three national fluorosis surveys in the USA. From polynomial regression models, cubic for NHANES 2011-2012 and NIDR 1986-1987, quartic for NHANES 1999-2004; 95% confidence intervals shown with shading; regression lines and confidence intervals are weighted to account for survey design. All models statistically significant with F test p<0.01. The three surveys had different age ranges.
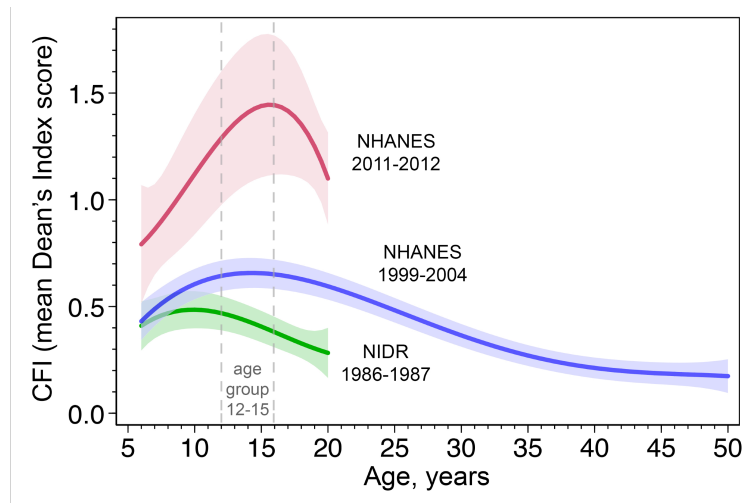
NHANES 2011-2012. Combined moderate plus severe rates were over 8 times greater than in 1999-2004 and 25 times greater than in 1986-1987. Large increases occurred in each succeeding survey for all age groups, races/ethnicities, income levels, country of birth, and for both genders (Table and Appendixes 1, 2).

When stratified by age, those 12-15 years had the greatest prevalence and severity. Details of the relationship between age and severity of fluorosis are shown in Figure 2 with polynomial models regressing CFI against age. The relationship between age and CFI differed somewhat across the three surveys, but all had increases from age 6 to a peak between age 10 and 16, and then declined.

Absolute declines with age were greatest in the NHANES 2011-2012 survey, but proportional declines were greatest in NIDR 1986-1987. The CFI for NHANES 2011-2012 declined from a peak of 1.4 at age 15 to 1.1 by age 20 for a proportional decline of 27%. In NIDR 1986-1987 the CFI declined from 0.47 to 0.30, a decline of 36%. The NHANES 1999-2004 absolute decline was from 0.65 to 0.60 at age 20, an 8% decline. Considering the width of the 95% confidence intervals, the differences in proportional declines in the three surveys may not be statistically significant.

In the NHANES 2011-2012 survey, females had a higher rate of moderate fluorosis than males (35% vs. 22%) and higher CFI (1.59 vs. 1.35) but neither difference was assessed as statistically significant based on overlap of their 95% confidence limits. For race/ethnicity, the Asian category had the highest CFI (1.68) and highest rate of moderate fluorosis (32%), followed by Whites (31%) and then Blacks (29%). Both earlier surveys found substantially higher prevalence and severity in Blacks than Whites, but by NHANES 2011-2012, they had reached similarly high rates. In NHANES 2011-2012, the CFI and rates of moderate fluorosis increased as poverty level decreased, but differences were not statistically significant. Nor were significant differences seen between those born outside the USA versus inside the USA. No significant differences were found between levels of parent's education. Details by socio-demographic variables are provided in Appendixes 1 and 2.

Figure 4. Histograms. **(A)** NHANES 2011-2012 distribution of county-level Community Fluorosis Index, County CFI, for ages 12-15 years. Each county's CFI is calculated accounting for NHANES individual sample weights. Then, each County CFI is weighted by that county's total population. The resulting frequency distribution reflects that of the USA population represented by the sampled counties. Counties were defined by the NHANES variables –"stratum" and "PSU" – but identities of actual counties sampled are not available in the publicly released NHANES data. County frequencies weighted by county populations. **(B)** NHANES 2013-2014 frequency distribution of tap water fluoride concentration for individuals age 0-19 years; weighted with NHANES individual sample weights so as to be representative of the USA population (CDC 2018). Heavy red lines are smoothed density curves.
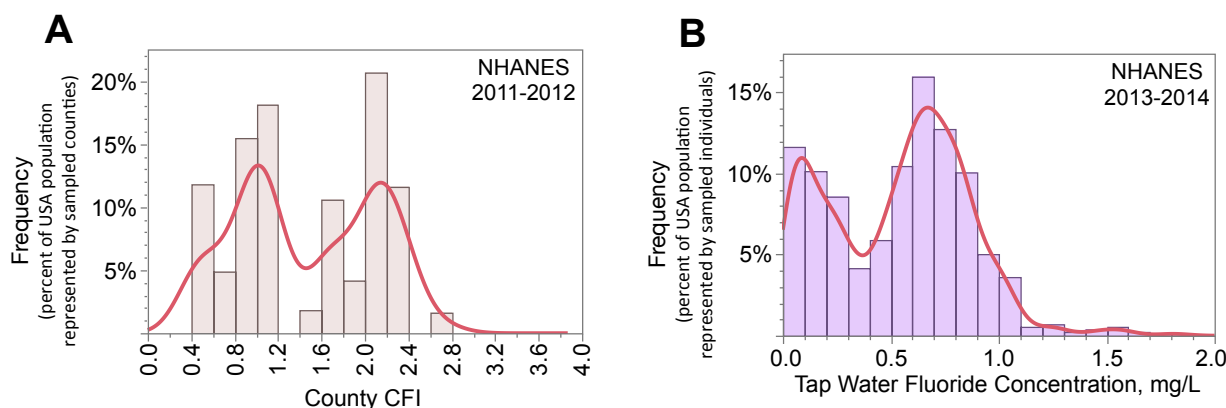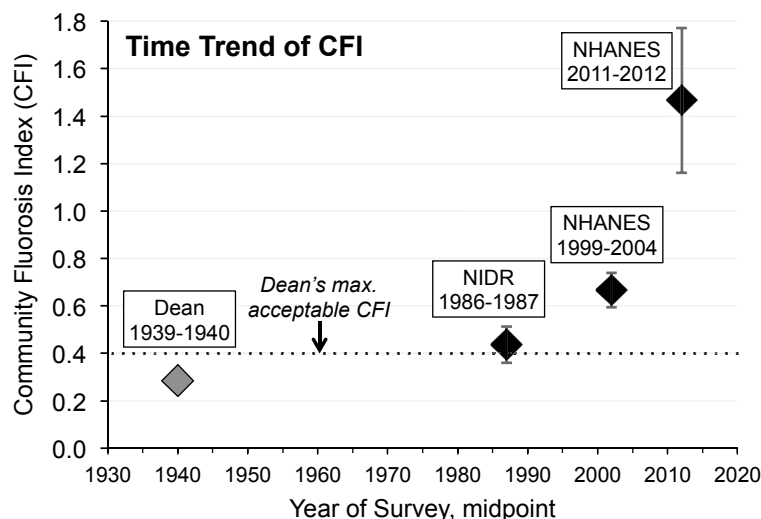
Figure 3. Community Fluorosis Index (CFI) for national surveys of the USA, ages 12-15 years, by survey years midpoint. Error bars show 95% confidence intervals. Dashed line at CFI of 0.4 is Dean's maximum acceptable CFI for artificially fluoridated water (Dean 1951). See Appendix 3 for details of CFI estimate for Dean's 1939-1940 survey.

The increase in fluorosis prevalence and severity over time, measured by CFI, is shown in Figure 3. An estimate of the CFI in 1939-1940 for the entire USA (Appendix 3), based on early surveys by Dean, is included in this graph. At that time, there was no artificial fluoridation, fluoride toothpaste, fluoride dental treatments, or fluoride supplementation in the USA.

We estimated the approximate number of children in the USA with dental fluorosis in 2011-2012 by summing the NHANES sample weights of all individuals within a subgroup. Out of 32 million children age 12-19 in the USA, about 20 million had fluorosis of degree very mild or higher, with 8 million having moderate, and 0.7 million severe.

To assess whether the surveys were likely to have obtained a sample of children representative of the USA population distribution of water fluoride levels we created two histograms, one for the frequency of county-level CFI in NHANES 2011-2012 (counties are actually pseudo-PSUs) and the other of tap water fluoride concentration for each participant in NHANES 2013-2014 (Figure 4A and 4B). The CFI score for each county was calculated using individual survey sample weights and then the CFI distribution was weighted by county population. All 31 counties sampled by NHANES had participants in the 12-15 year age range of interest. The tap water fluoride concentration distribution was weighted by individual sample weights, and was derived from 4,100 children age 0-19 years in the NHANES 2013-2014 sample. Survey participants' tap water fluoride concentration was not obtained in the 2011-2012 survey (CDC 2018).

Discussion

The dramatic increases in prevalence and severity of dental fluorosis found in the latest NHANES 2011-2012 survey are unprecedented. The rates are not only high compared to the previous national surveys, they are also higher than in most other countries with widespread community water fluoridation. The lower rates reported in other countries, however, may in part be a result of their surveys only assessing some teeth, rather than all teeth. Many surveys only assess anterior teeth, omitting the molars which may have the highest degree of fluorosis. NHANES and NIDR assessed all teeth which is the method established by Dean and recommended by the World Health Organization (WHO) (Dean 1942; WHO 2013).

To check whether abridged methods that assess fewer teeth underestimate person-level scores we applied Canada's abridged method (restricted to the four maxillary incisors) to the NHANES 2011-2012 data (Canadian Health Measures Survey [CHMS] 2010). Moderate dental fluorosis at ages 12-15 years decreased from 28% with all teeth to 9% with four teeth, and severe decreased from 2.6% to 0.7% (Appendix 4). Other researchers also found rates of moderate plus severe decrease greatly when molars are excluded (Colquhoun 1984; Medina-Solis et al. 2008). Australia and New Zealand surveys use such abridged methods.

The relationships between CFI and age (Figure 2) may reflect the increase in numbers of erupted permanent teeth from age 6 to about 12 producing a rising CFI that reaches a peak when all the teeth are erupted. The CFI then slowly declines as attrition of the outer fluorosed enamel and other factors progressively obscure its clinical features (Dean 1942; Fejerskov et al. 1990). The CFI versus age curves may also reflect short-term secular trends in fluoride exposures across birth cohorts.

Possible Explanations for Large Increases in Fluorosis

The scale of the increase in fluorosis over time in the USA, culminating in the very high rates in NHANES 2011-2012, prompted us to consider possible explanations. To explain the timing of the increases it is important to recognize the lag between when excessive fluoride exposure affects the developing enamel and when the surveys assessed the erupted permanent teeth. Fluorosis is caused by excessive exposures from birth to about age 8 years (and older for 3rd molars). Children who are assessed for fluorosis at ages 12-15 will have had their relevant exposures 4 to 15 years previous. Therefore, fluorosis in 12-15 year olds for the three surveys reflects exposures in the years 1971-1983, 1984-2000, and 1996-2008. Our search for explanations first considers whether NHANES may have overestimated fluorosis rates, and then examines possible reasons for a genuine increase in fluorosis.

Could NHANES Have Overestimated Fluorosis?

Was Sampling Representative of Water Fluoride in USA? Each two-year NHANES cycle samples people from about 30 counties in the USA. We considered whether, by chance, a disproportionate number of the selected counties in NHANES 2011-2012 might have had artificial fluoridation, or high natural water fluoride. Either situation could have led to an overestimate of national fluorosis rates. However, examination of the individual county fluorosis rates showed a bimodal distribution of CFI consistent with the expected bimodal distribution of water fluoride concentration in the USA (Figure 4A), caused by the 60:40 mix of population with artificially fluoridated versus unfluoridated water. The NHANES 2013-2014 survey, which measured each child's tap water fluoride concentration, also showed a bimodal distribution (Figure 4B) (CDC 2018).

In Figure 4A, two counties had CFIs above 2.6, conceivably due to high natural water fluoride. However, even if these are excluded as unrepresentative of the USA, the overall CFI is only lowered from 1.47 to 1.45. Given these findings, and the specific stratified sampling design of NHANES 2011-2012 (CDC 2018), the sample appears to be reasonably representative of the distribution of water fluoride levels in the USA.

Nevertheless, in the absence of individual-level home water fluoride information for the NHANES 2011-2012 survey and without any authoritative home water fluoride distribution available for the USA (as discussed in Appendix 3), we can not quantify how representative the water fluoride distribution is of the sampled children to the USA population. The absence of information in NHANES 2011-2012 on home water fluoride levels also prevents analyses to estimate the effect of water fluoride concentration on fluorosis rates and severity.

Diagnostic Criteria. We considered whether shifts in diagnostic criteria among surveys could produce spuriously high rates of fluorosis. This seems unlikely as the examination procedure manuals for all three surveys specified almost exactly the same criteria for scoring fluorosis, and the surveys were designed to be comparable to

each other (NIDCR 1992a; CDC 2018). Careful calibration procedures were used for the dental examiners within each two-year survey cycle and between cycles (Dye 2008). A single dentist was the "gold standard" reference dentist for all of the 2000-2004 and 2011-2012 surveys [*]. The NHANES 1999-2004 survey had two primary examiner dentists who conducted more than 90% of the exams. Six back-up examiners and the reference examiner conducted the remainder of the exams. The number of examiners in NHANES 2011-2012 has not been reported although it was probably similar to those for NHANES 1999-2004. The reference dentist trained all examiners for 40 hours before each survey cycle and maintained calibration through periodic checks during each cycle and annual retraining sessions. Relatively good intra- and inter-examiner reliability of fluorosis scoring was reported (mean weighted kappa=0.66; with weight of 1 for same Dean's Index score, 2/3 for scores one degree apart, and 1/3 for scores two degrees apart). The NIDR 1986-1987 survey used similar methods for training and calibrating dentist examiners but there are no reports of intra- or inter-examiner reliability. Thirteen primary examiners conducted more than 95% of the NIDR 1986-1987 exams and two back-up examiners conducted the remainder (NIDCR 1992a).

Misdiagnosis of Molar-Incisor Hypoplasia (MIH) for Fluorosis. We also considered whether misdiagnosis of MIH as fluorosis could explain the large increase in fluorosis. MIH often displays as enamel opacities which might be confused for fluorosis.

This explanation would require MIH prevalence to have increased greatly between 1971 and 2006, but we could find no evidence in the literature for such an increase. Studies from the 1940s to 1960s in low water fluoride areas found rates of non-fluoride opacities ranging from 12% to 84% (Small and Murray 1978). Only two recent, limited area, MIH prevalence studies are reported for the USA, finding prevalences of 23% and 29% (Schwendicke et al. 2018).

Misdiagnosis of MIH for fluorosis also seems unlikely because the NHANES

assessment criteria explicitly distinguishes between white opacities with diffuse borders characteristic of fluorosis and those typical of MIH with demarcated borders, often yellow to orange, on first permanent molars (CDC 2018).

One study found that moderate and severe fluorosis masked non-fluoride opacities occurring on the same tooth (Wenzel and Thylstrup 1982). It is therefore possible the rate of MIH was high in the NHANES 2011-2012 children but high rates of genuine moderate and severe fluorosis masked some of the MIH. Moreover, the NHANES scoring system only allows a single diagnosis per tooth, so a fluorosis diagnosis could override a tooth having both MIH and fluorosis, even if the fluorosis were relatively mild. On the other hand, co-occurring MIH and fluorosis on the same tooth might accentuate the severity of fluorosis, resulting in a falsely higher fluorosis score.

To investigate further whether MIH misdiagnosed as fluorosis could explain the high rates of fluorosis, we examined the NHANES data at specific tooth level (Appendix 4). A distinguishing characteristic of MIH is that permanent molars are usually the most affected teeth, with incisors sometimes being affected, but to a lesser degree. Other teeth are rarely affected beyond small opacities that would not be misdiagnosed as moderate or severe fluorosis (Ghanim et al. 2017). Given these diagnostic characteristics, we flagged as possible MIH those children with no other teeth besides molars or incisors scored moderate or severe.

We found 47% of all children age 12-15 in the NHANES 2011-2012 survey could meet this criterion of possibly being MIH misdiagnosed as fluorosis. This is likely an upper limit. Nevertheless, if we assume they all have only MIH, removing them from the 30% classified as moderate and severe fluorosis by NHANES yields a "corrected" rate of about 14%. This is still almost four times greater than the 1999-2004 rate and suggests much of the large increase in 2011-2012 is in fact true fluorosis.

Explanations for a Genuine Increase in Fluorosis

Fluoride Supplements and School Fluoride Rinse Programs. Two factors

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[*] Personal communication from Dr. Bruce Dye, NIDCR, March 28, 2018.

have the potential to increase fluorosis risk, but seem unlikely to explain the very large increases found in NHANES 2011-2012. Previous studies found fluoride supplements increase fluorosis risk; however, the recommended dose was reduced twice between 1971 and 2003 (Fomon et al. 2000; Mascarenhas 2000). Furthermore, use of supplements has decreased over time. In the NIDR 1986-1987 survey, 25% of children ages 5-14 years had taken supplements, but this declined to 14% by NHANES 2013-2014 (Appendix 5). School fluoride rinse programs have also declined between the 1980s and 2008 so are also unlikely to explain the large increases in fluorosis rates (Kentucky DPH 2018).

Water Fluoridation. The percentage of Americans with artificial water fluoridation increased over the period 1971-2008, from about 45% to 64%, for a 43% increase over the 1971 rate (CDC 2016). There may also have been a "multiplier effect" with increasing consumption of processed foods, beverages, and infant formula made with fluoridated water.

Infant Formula. From 1971 to 1998, there was an increase in infant formula feeding by about 50% and a corresponding reduction in cow's milk feeding for infants age 4-12 months, resulting in an estimated net increase in high fluoride intake days of about 50% (Fomon et al. 2000). Cow's milk is very low in fluoride while formula made up with fluoridated tap water is relatively high. Studies have found formula feeding increases risk of fluorosis (Fomon et al. 2000; Mascarenhas 2000).

Fluoridated Toothpaste. Increased ingestion of fluoride toothpaste, especially amongst younger children, is another possible explanation. Marketing of toothpaste targeted toward children did not start until the mid-1980s (Stevenson 1988). This marketing included new candy and fruit flavors that would appeal to young children and were more likely to be ingested (Levy et al. 1992). Other marketing methods targeted young children with cartoon characters, bright colors, stripes and sparkles added to the toothpaste. Brushes with full loads were depicted, and pump dispensers were introduced, both of which may have caused children to use excessive toothpaste

(Basch et al. 2014; Stark 2018).   In 1997, the FDA required a warning on fluoride toothpaste labels but recent NHANES 2013-2014 questionnaire data suggests that the warning is still not being followed by many children. About 36% of children ages 2-5 used a full or half load of toothpaste rather than a pea-sized or smaller quantity (CDC 2018) (see Appendix 6).

Amoxicillin. Hong et al. (2011) found that amoxicillin use in early childhood could double the risk of fluorosis, especially in children with higher fluoride intakes. Amoxicillin use in children in the USA more than tripled between 1980 and 1998, reaching a rate of about 10% per year (McCaig et al. 1995). Increased use of amoxicillin together with increasing fluoride exposures may explain, in part, the increase in fluorosis across the three surveys.

Fluorinated Anesthetics That Produce High Peak Blood Fluoride. A previously unrecognized risk factor for fluorosis may be pediatric use of fluorinated anesthetics that can produce high peak serum fluoride levels of 10 µM (0.2 mg/L) or greater. Studies in rats show that short duration plasma fluoride peaks reaching this level can cause fluorosis (Angmar-Månsson and Whitford 1990). Pediatric surgeries under general anesthesia have increased greatly between 1975 and 2008. In children born around 1975, only 11% had experienced general anesthesia by age 5, but for those born around 2003 the rate had climbed to 42% (Wilder et al. 2009; Rabbits et al. 2010). During this same period, there was also a switch from pediatric anesthetics that caused relatively low serum fluoride levels (halothane) to those that cause high levels (sevoflurane and isoflurane) (NRC 2006).

Other Possible Explanations. Several explanations for the dramatic rise in fluorosis have not been carefully investigated but may be worth considering in future inquiries. They include increases in fluoride exposures from: ready-to-drink (bottled) tea (Tea Association of USA 2017), mechanically deboned meats (Fein and Cerklewski 2001), use of medications metabolizing to fluoride, and fluoride pesticide residues on foods (Stannard et al. 1991).

Dose-Response Considerations. Finally, the doses of fluoride required to cause the levels of fluorosis found in NHANES 2011-2012 can be estimated and are plausible. Fejerskov et al. (1990) estimated the dose-response relationship between total fluoride intake and CFI, using a large set of data. They found that a CFI of 1.5, as in NHANES 2011-2012, would be reached when the average intake in children was just 0.06 $mg/kg_{bodyweight}$/day (Fejerskov et al. Figure 4). A recent estimate of mean total fluoride intake for 0-5 year olds in the USA equals or exceeds 0.06 $mg/kg_{bodyweight}$/day, with fluoridated water, infant formula, and swallowed tooth paste the main contributors (Erdal and Buchanan 2005). Therefore, current exposures from these three sources appear sufficient to explain the rates of fluorosis found in NHANES 2011-2012.

Public Health Implications. Seventy years ago, Trendley Dean, the "father of fluoridation", stated that artificial fluoridation should cause almost no fluorosis of severity greater than very mild, and a CFI below 0.4 (Dean 1951). This admonition was based on the tradeoff between reducing caries and increasing fluorosis that he observed in his seminal studies. The NHANES 2011-2012 results, representative of the entire USA population with 60% fluoridation, show that the prevalence and severity of fluorosis now greatly exceed what Dean would have considered acceptable, with an estimated 20 million teenagers showing fluorosis, of which almost 9 million have degree moderate or severe. Both degrees are considered aesthetically objectionable, with possible psychological consequences, and may require expensive cosmetic dentistry to repair. Severe fluorosis may cause functional harm to the teeth from greater enamel attrition and higher risk of caries (NRC 2006). Recent studies in areas where fluorosis was due to fluoride in drinking water and where no fluoride toothpaste was used – thus avoiding the confounding benefit of the fluoride toothpaste – have found caries rates positively associated with fluorosis severity, especially of degree moderate and severe (Wondwossen et al. 2004). Thus, today's excessive ingestion of fluoride may actually be increasing decay in some children rather than decreasing it.

The implications of widespread overexposure go beyond the adverse effect of dental fluorosis. Accumulating evidence also suggests that current levels of fluoride exposure in the USA may be associated with developmental neurotoxicity and other adverse health effects (NRC 2006; Hirzy et al. 2016; Bashash et al. 2017).

Author Contributions

C. Neurath contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript. H. Limeback, B. Osmunson, and M. Connett contributed to conception, design, analysis, and interpretation, drafted and critically revised the manuscript. V. Kanter and C. R. Wells contributed to design, analysis, and interpretation, and critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

Acknowledgments

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