

Decline in Dental Fluorosis Severity during Adolescence: A Cohort Study

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Abstract

Dental fluorosis occurs from overingestion of fluoride during tooth formation. However, there is little evidence in the literature on whether or how fluorosis prevalence and severity change over time after tooth eruption. Permanent dentition dental examinations were conducted at ages 9, 13, 17, and 23 as part of the Iowa Fluoride Study, which has followed a cohort from birth. Fluorosis was assessed using the Fluorosis Risk Index (FRI) and Russell's criteria for differential diagnosis. Measures of fluorosis severity at the person and tooth level were calculated: second highest FRI score at the person level (the maximum FRI score for each tooth was determined and the tooth with the second highest maximum FRI score was used) and highest FRI score at the tooth level. At both the person and tooth levels, a decline in mild to moderate fluorosis severity was observed across adolescence and young adulthood. Across each pair of adjacent examinations at the person level, for participants with a baseline second highest FRI of 0, most participants stayed at 0 (82% to 91%). Many participants with a baseline second highest FRI of 1 had a follow-up score of 0 (47% to 54%), while about a third had a follow-up score of 1 (34% to 38%), and a lower percentage had an increase to a score of 2 (9% to 15%). For participants with baseline second highest FRI score of 2, between 25% and 44% of participants had follow-up FRI scores each of 0, 1, and 2. Similar patterns were observed at the tooth level. These results were consistent with most of the existing, limited literature. Overall, fluorosis severity, which was initially mild to moderate, tended to decline during adolescence and young adulthood. Additional study of how this trend affects esthetic perceptions of fluorosis is warranted.

Keywords: fluoride(s), enamel, epidemiology, pediatric dentistry, preventive dentistry, tooth wear

Introduction

Fluorides form the cornerstone of dental caries prevention throughout the world; however, excessive ingestion of fluoride during tooth development can result in dental fluorosis (McDonagh et al. 2000). While most dental fluorosis in the United States is mild or very mild, nearly all studies of fluorosis have been conducted with children or adolescents, with very little information on fluorosis in young adults (Clark 1994; Whelton et al. 2004; Anthonappa and King 2015). Thus, it is largely unknown whether fluorosis becomes more or less prominent over time, especially into late adolescence and young adulthood.

Do et al. (2016) and Wong et al. (2016) recently showed statistically significant declines in the prevalence and severity of mild to moderate fluorosis in the permanent dentition during adolescence using cohort studies. Although Do et al. (2016) and Wong et al. (2016) provide evidence for a decline in fluorosis prevalence and severity in the permanent dentition, they only examined participants twice and did not examine the timing of this trend. In addition, no studies assessed whether similar trends exist in a modern US cohort.

This analysis used permanent dentition fluorosis exam data from the Iowa Fluoride Study (IFS) to determine whether there were changes in fluorosis severity in the permanent dentition at the person and tooth levels, examining trends through adolescence and young adulthood.

Methods

The Iowa Fluoride Study

The IFS followed a birth cohort recruited in Iowa maternity wards from 1992 to 1995, with the primary goal of estimating fluoride intakes of individual participants and studying associations between these intakes, dental caries, and fluorosis outcomes. At 6 mo postrecruitment, 1,387 participants had responded to follow-up. After obtaining parental consent, individual fluoride intakes were estimated using beverage intake and brushing frequency questionnaires sent every 3 to 6 mo starting at birth (Levy et al. 2001; Marshall et al. 2008). The IFS was approved by the Institutional Review Board of the University of Iowa and conforms to STROBE guidelines for human observational studies.

Caries and fluorosis exams were conducted on the permanent dentition at ages 9, 13, 17, and 23 y. After obtaining parental consent and participant assent (participant consent

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after age 18), these examinations were carried out by trained and calibrated examiners using a portable dental chair, exam light, and mouth mirror, with examiners blinded to previous study results. Before examination, participants' teeth were brushed and dried by quickly wiping the entire maxillary arch with gauze prior to fluorosis scoring and repeating the process for the mandibular arch. Russell's criteria, as well as location, color, and texture of each potential lesion, were used to differentiate fluorosis from other enamel defects (Russell 1961; Slayton et al. 2001).

For each permanent tooth, the incisal/occlusal edge and 3 buccal zones (cervical, middle, and incisal/occlusal thirds of the buccal surface) were scored using the Fluorosis Risk Index (FRI) (Pendrys 1990). The FRI originally was chosen to provide zone-specific fluorosis outcomes that could be matched with very specific timing of fluoride intakes. Based on this scoring system, each zone was scored as having no fluorosis (scored as 0); questionable fluorosis (less than 1/2 of the zone affected by white striations), scored as 1; mild to moderate fluorosis (greater than 1/2 of the zone affected by white striations), scored as 2; severe fluorosis (pitting, staining, or deformity), scored as 3; or nonfluoride opacity with no fluorosis, which was counted as no fluorosis (scored as 0).

To assess interrater reliability, duplicate exams were performed at each age and κ scores accounting for multiple raters were calculated (Gwet 2008). There were 3 examiners at each age, but not the same 3—the first examiner carried out exams at all ages; the second examiner at ages 9 and 13; the third at age 9 only; the fourth at ages 13, 17, and 23; and the fifth at ages 17 and 23.

At age 9, the permanent incisors and first molars were erupted and scored for most participants. At ages 13, 17, and 23, the buccal surfaces of all permanent teeth present (excluding third molars) were scored for fluorosis. Therefore, we separately analyzed early-erupting teeth (incisors and first molars), late-erupting teeth (canines, premolars, and second molars), and maxillary incisors (most visible teeth).

Statistical Analysis

Changes in fluorosis severity between adjacent exams were assessed at the person and tooth levels. At the person level, we calculated the person level second highest FRI score (PL2FRI) for early- and late-erupting teeth, as well as the maxillary incisors, by finding the maximum fluorosis score for each tooth within the tooth group, ranking the teeth from highest FRI score to lowest, and using the FRI score of the second highest tooth. At the tooth level, we examined changes in the maximum FRI score for each tooth, examining separately the early- and late-erupting teeth, as well as maxillary incisors. When examining changes in fluorosis severity across all time points, we limited the calculation of person and tooth level fluorosis severity measures to zones examined at all ages. When examining changes in fluorosis severity at a pair of adjacent time points, we limited the calculation of person and tooth level fluorosis severity measures to zones examined at both ages.

To study the change in fluorosis severity across time, we summarized the number of participants or teeth with each level of PL2FRI or maximum tooth level FRI at each age. Goodman and Kruskal's γ statistic was used to quantify the trend in fluorosis severity for each tooth group and severity measure, and the standard asymptotic standard error was used to test for a statistically significant decline in PL2FRI with age. Gamma statistics range from -1 to $+1$ and can be conceptualized as correlation coefficients for ordinal variables (Agresti 2012). At the tooth level, permutation methods were used to adjust the standard error for within-participant correlation of teeth at each age. However, neither approach for computing standard errors accommodates within-participant temporal correlation across ages, which could lead to artificially low values. Therefore, we cautiously interpreted the significance of these tests.

Next, we cross-tabulated the changes in PL2FRI or maximum FRI score between adjacent exams. For each tooth level cross-tabulation table, we calculated the net fluorosis decrement—the number of teeth with lower maximum FRI scores minus the number of teeth with higher maximum FRI scores. In addition, within each participant and tooth group, we calculated the net fluorosis decrement within participants.

Then, we provided information from the cross-tabulation tables in grouped bar plots to facilitate visualization of the trend over time. At the person level, error bars representing 95% confidence intervals (CIs) based on the inversion of the binomial score test were overlaid on the figure for cross-tabulation cells with ≥ 10 participants. At the tooth level, 95% CIs were based on formulating generalized linear models for binary outcomes using a logit link function and fitting the models using generalized estimating equations to accommodate intra-person clustering (PROC GENMOD, SAS version 9.4; SAS Institute).

Then, for the middle 2 baseline FRI categories (i.e., PL2FRI of 1 or 2), we calculated the difference between baseline and follow-up FRI scores and conducted Wilcoxon signed-rank tests stratified by baseline fluorosis severity to determine whether the probability of having a lower follow-up FRI score was significantly greater than the probability of having a higher follow-up score, indicating a significant decline in fluorosis severity. A clustered version of this test was conducted for tooth level statistics using the *clusrank* package in R (R Development Core Team 2008; Jiang 2018).

A significance level of 0.05 was used for all tests, and non-directional P values were used for all tests except the Wilcoxon signed-rank tests because we were testing for a decrease in fluorosis severity.

Results

Most IFS participants were within the target "year" for examinations, and the sample was approximately half female and almost all non-Hispanic White (Table 1). In 2007 (when participants were approximately ages 12 to 15), most participants lived in households with an income \geq \$60,000 and had mothers with at least a 4-y college degree.

Table 1. Demographic Information for Iowa Fluoride Study Participants at Each Fluorosis Exam.

Characteristic	Target Age of Fluorosis Exam (y)			
	9	13	17	23
Sample size	629	549	464	342
Mean (SD) of actual age	9.3 (0.7)	13.5 (0.6)	17.8 (0.7)	23.5 (0.6)
% Female	50.7	50.6	53.0	56.7
% Non-Hispanic White	94.9	94.9	94.8	95.9
% Households with income \geq \$60,000 in 2007	67.9	67.6	68.1	67.7
% Mothers with \geq 4-y college degree in 2007	50.4	49.6	50.8	53.7

A version of this table limited to the participants included in Figures 1 and 2 is provided in Appendix Table 3A, and a version of this table limited to the participants included in Table 2 is provided in Appendix Table 3B.

Table 2. Second Highest FRI Score (Count [%]) at the Person Level Using Only Surfaces Available at All Time Points.

Tooth Type (γ , 2-Sided P Value)	Second Highest FRI Score	Age 9 (n = 282) (Permanent Teeth Only)	Age 13 (n = 282)	Age 17 (n = 282)	Age 23 (n = 282)
Early-erupting teeth (-0.31, <0.0001)	0	109 (38.7)	149 (52.8)	187 (66.3)	186 (66.0)
	1	74 (26.2)	79 (28.0)	58 (20.6)	67 (23.8)
	2	96 (34.0)	54 (19.2)	36 (12.8)	28 (9.9)
	3	3 (1.1)	0 (0.0)	1 (0.4)	1 (0.4)
			(n = 291)	(n = 291)	(n = 291)
Late-erupting teeth (-0.36, <0.0001)	0		127 (43.6)	183 (62.9)	209 (71.8)
	1		101 (34.7)	76 (26.1)	61 (21.0)
	2		63 (21.7)	31 (10.7)	19 (6.5)
	3		0 (0.0)	1 (0.3)	2 (0.7)
			(n = 278)	(n = 278)	(n = 278)
Maxillary incisors (-0.33, <0.0001)	0	127 (45.7)	165 (59.4)	198 (71.2)	204 (73.4)
	1	67 (24.1)	74 (26.6)	53 (19.1)	51 (18.4)
	2	83 (29.9)	39 (14.0)	27 (9.7)	22 (7.9)
	3	1 (0.4)	0 (0.0)	0 (0.0)	1 (0.4)

FRI, Fluorosis Risk Index.

Kappa statistics were calculated for person and tooth level outcomes after combining participants or teeth with an FRI of 2 and 3 due to low rates of severe fluorosis. The weighted averages of the person and tooth level κ scores over all exams were 0.31 and 0.37, respectively.

At age 9, cervical zones were not scored for many participants due to incomplete eruption, and at age 13, 28.8% of participants had some form of orthodontic treatment. Most participants had relatively few missing values at the 17- and 23-y exams. A sensitivity analysis with additional inclusion criteria based on the number of nonmissing teeth or zones was also conducted, and the results (not shown) were very similar to those presented here.

Table 2 summarizes PL2FRI across age. For all 3 tooth groups, the percentages of participants with PL2FRI of 1 and 2 tended to decline, the percentage with PL2FRI of 0 increased, and the percentage with a PL2FRI of 3 was very low. These results, in addition to γ statistics significantly <0 (γ -0.31 to -0.36, P < 0.0001), indicate a general decline in questionable and mild fluorosis throughout adolescence and young adulthood.

In Table 3, the percentages of teeth with maximum FRI scores of 0 to 3 at each age follow trends similar to PL2FRI.

The decline in fluorosis appears to slow between 17 and 23, also reflecting patterns seen in Table 2. The γ statistics for each tooth group range from -0.29 to -0.32 (P < 0.0001).

Based on the net within-participant fluorosis decrement for maxillary incisors of 0.73 teeth, participants had 0.73 more maxillary incisors with a decrease in fluorosis severity than an increase in fluorosis severity from ages 9 to 13, on average (SD = 1.79). The net within-participant fluorosis decrements for the maxillary incisors were 0.40 (SD = 1.68) and 0.17 (SD = 1.65) for ages 13 to 17 and 17 to 23, respectively. In addition, when considering all maxillary incisors examined at each pair of exams, we saw net decrements of 380 (18.8% of all teeth examined), 170 (10.1%), and 52 (4.3%) at ages 9 to 13, 13 to 17, and 17 to 23, respectively.

Appendix Tables 1 and 2 provide cross-tabulation tables upon which Figures 1 and 2 are based. Figure 1 uses clustered bar charts to summarize changes in PL2FRI on maxillary incisors between adjacent exams at the person level, stratified by baseline fluorosis severity. Small sample sizes precluded detailed analysis of participants with baseline PL2FRIs of 3. For baseline PL2FRI scores of 1 and 2, the signed-rank test showed that the probability of having a lower follow-up

Table 3. Maximum Tooth Level FRI Score (Count [%] of Teeth) Using Only Surfaces Available at All Time Points.

Tooth Type (γ , 2-Sided P Value)	Maximum Tooth-Level FRI Score	Age 9 (n = 3,269) (Permanent Teeth Only)	Age 13 (n = 3,269)	Age 17 (n = 3,269)	Age 23 (n = 3,269)
Early-erupting teeth (-0.31, <0.0001)	0	2,249 (68.8)	2,577 (78.8)	2,791 (85.4)	2,847 (87.1)
	1	572 (17.5)	460 (14.1)	333 (10.2)	314 (9.6)
	2	439 (13.4)	229 (7.0)	137 (4.2)	102 (3.1)
	3	9 (0.3)	3 (0.1)	8 (0.2)	6 (0.2)
			(n = 4,251)	(n = 4,251)	(n = 4,251)
Late-erupting teeth (-0.29, <0.0001)	0		2,871 (67.5)	3,368 (79.2)	3,543 (83.4)
	1		955 (22.5)	677 (15.9)	588 (13.8)
	2		422 (9.9)	197 (4.6)	116 (2.7)
	3		3 (0.1)	9 (0.2)	4 (0.1)
		(n = 1,068)	(n = 1,068)	(n = 1,068)	(n = 1,068)
Maxillary incisors (-0.32, <0.0001)	0	547 (51.2)	683 (64.0)	792 (74.2)	831 (77.8)
	1	271 (25.4)	258 (24.2)	192 (18.0)	170 (15.9)
	2	247 (23.1)	126 (11.8)	80 (7.5)	61 (5.7)
	3	3 (0.3)	1 (0.1)	4 (0.4)	6 (0.6)

FRI, Fluorosis Risk Index.

PL2FRI was significantly greater than the probability of having a higher follow-up PL2FRI ($P \leq 0.0006$) for all tooth groups and pairs of adjacent exams (Fig. 1 and Appendix Fig. 1). This figure illustrates a declining trend in questionable and mild to moderate fluorosis between adjacent exams.

Figure 2 presents results for tooth level maximums for maxillary incisors, which are very similar, likely because there are only 4 maxillary incisors. Figures for the early- and late-erupting teeth corresponding to the person and tooth level outcomes can be found in Appendix Figures 1 and 2. Appendix Tables 3 to 5 summarize the demographic information, person and tooth level outcomes, respectively, for the participants included in Appendix Figures 1 and 2. Appendix Figure 3 provides photographs taken at the fluorosis exams demonstrating decline in fluorosis severity on the anterior teeth.

The 95% CIs for the transition from a PL2FRI of 1 to 0 are entirely above the 95% CIs for participants who stayed at a PL2FRI of 1 for late-erupting teeth from 13 to 17 and 17 to 23 (Fig. 1 and Appendix Fig. 1). This indicates that a significantly higher proportion of participants had a decline from 1 to 0, compared to the proportion who stayed at 1. At the tooth level, 95% CIs for the transition from a maximum FRI of 1 to 0 are entirely above the 95% CIs for teeth that stayed at a maximum FRI of 1 for all tooth groups and pairs of adjacent ages analyzed, with the exception of the maxillary incisors from 17 to 23.

To assess transitions for participants with a baseline PL2FRI of 2, we dichotomized participants with a decrease from a baseline PL2FRI of 2 and participants who stayed at PL2FRI of 2 or saw an increase, and we calculated binomial confidence intervals. The 95% CI for the percentage of participants with a decrease in fluorosis score was uniformly higher than the participants with a steady or increasing FRI score for all tooth groups from 9 to 13 and 17 to 23, as well as maxillary incisors from 13 to 17.

For baseline tooth level maximum FRI scores of 1 or 2, dichotomized 95% CIs for the percentage of teeth with a

decrease in fluorosis score were uniformly higher than the percentage of teeth with steady or higher FRI scores for all tooth groups and age ranges, except for maxillary incisors with a baseline maximum FRI of 1.

Discussion

Overall, our results confirm that very mild, mild, and moderate fluorosis tends to decrease in severity during adolescence. This trend continues into young adulthood and appears to slow in the early 20s. This was observed at both the person and tooth levels, although we also saw consistency within each participant and tooth between adjacent exams.

The strengths of our analysis include the series of 4 dental examinations and long-term follow-up, detailed differential diagnosis between fluorosis and other enamel defects, and consistency of results across person and tooth level measures of fluorosis severity. The limitations include homogeneity of the cohort, small numbers of severe fluorosis cases, declining sample size over time, and some inconsistency between examiners, which has been an ongoing challenge in fluorosis scoring (Whelton et al. 2004; National Center for Health Statistics 2019). We observed a decline in interrater agreement over time, especially at the last 2 exams. This is likely due to inter-examiner variability from changes in examiners, as well as intra-examiner variability. We had no intention initially of studying patterns over time based on earlier assumptions that fluorosis severity would not change. Therefore, examiner recalibrations after age 13 did not emphasize dental fluorosis as much but instead emphasized consistency in scoring caries over fluorosis. In a sensitivity analysis, we observed that the 2 examiners who examined participants at ages 13, 17, and 23, as well as 17 and 23, respectively, were more likely than the examiner who conducted exams at all ages to score a tooth or person with fluorosis (or more severe fluorosis), indicating that

examiner differences were likely not responsible for the declining trend. Please see additional discussion in the Appendix.

The prevalence and severity of dental fluorosis among US children according to 1999–2004 National Health and Nutrition Examination Survey (NHANES) data were similar to our sample based on secondary Dean's index score data collected at ages 13, 17, and 23 of the IFS (Beltrán-Aguilar et al. 2010). A comparison of the distributions of Dean's index scores from IFS and NHANES data is provided in Appendix Table 6. Overall, the trend of declining FRI scores is reflected in our Dean's index results. In addition, the distribution of Dean's index scores for IFS participants at age 13 is very similar to the distribution of Dean's index scores from the NHANES data for adolescents aged 13 to 15. Recently, NHANES reported a higher fluorosis prevalence for US children during 2011–2016 compared to 1999–2004 (National Center for Health Statistics 2019). Authors of the data quality report claim that a true prevalence increase from 1999–2004 to 2011–2016 is biologically implausible, assuming constant fluorosis severity after eruption. However, based on our analysis, it would be more realistic to assume a decline in fluorosis prevalence during adolescence and young adulthood, casting further doubt on increasing fluorosis prevalence in the United States.

Our results agree with 3 of the 4 studies that examined changes in fluorosis in cohorts over time. Aasenden and Peebles (1978) outlined follow-up fluorosis exams of 51 children in Massachusetts, aged 12 to 17, with baseline exams at ages 7 to 12. Dean's index was used, and there was an overall decline in mean fluorosis score during adolescence for participants with mild to moderate fluorosis during childhood. Wong et al. (2016) carried out fluorosis examinations of a cohort of Hong Kong children at ages 12 ($n = 668$) and 15 ($n = 432$). The incisors and first molars were scored using the Developmental Defects of Enamel (DDE) index, and authors found a statistically significant decline in person and tooth level prevalence and severity of diffuse opacities (fluorosis) for each tooth type considered (central incisors, lateral incisors, and first molars). Do et al. (2016) reported on follow-up examinations at ages 16 to 22 ($n = 314$) for 677 South Australian participants examined initially at ages 8 to 14. The Thylstrup and Fejerskov Index was used to assess

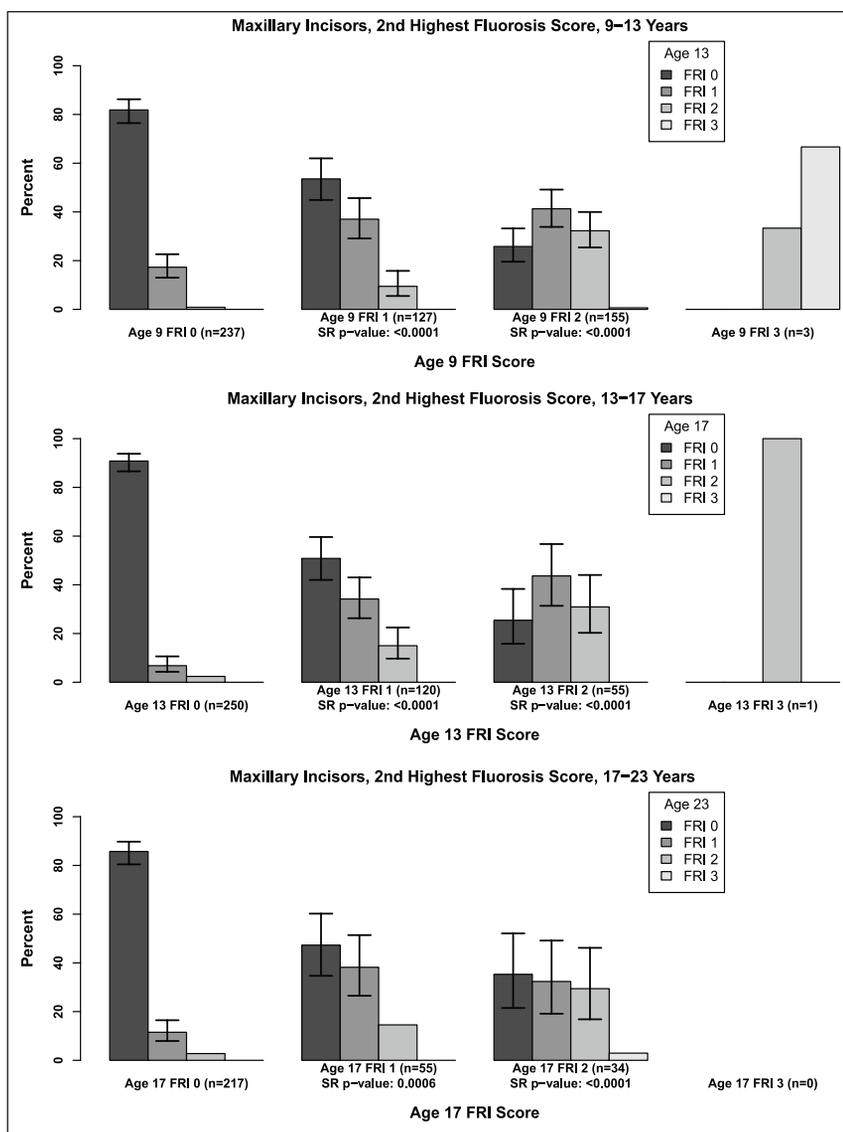


Figure 1. Cross-tabulations of person level, second highest Fluorosis Risk Index (FRI) scores on maxillary incisors. *P* values for the Wilcoxon signed-rank test (SR *P* value) are provided.

fluorosis severity at the person and tooth levels for maxillary teeth (central incisors at the person level and incisors, canines, and first premolars at the tooth level). The authors observed a significant decline in very mild and mild dental fluorosis at the tooth level. In contrast, 1 study that used the DDE index to assess changes in enamel defects from ages 9 to 12 for 176 of 666 originally examined New Zealand children did not show a significant decline in diffuse opacities (fluorosis) and saw a slight, nonsignificant increase in the number of participants with diffuse opacities from ages 9 to 12 (de Liefde 1988). The differences between our results and the New Zealand study could be due to their smaller sample size, differences in study design (following up on all children with enamel defects at baseline and also following up on a sample from participants unaffected at baseline), or the relatively low prevalence of

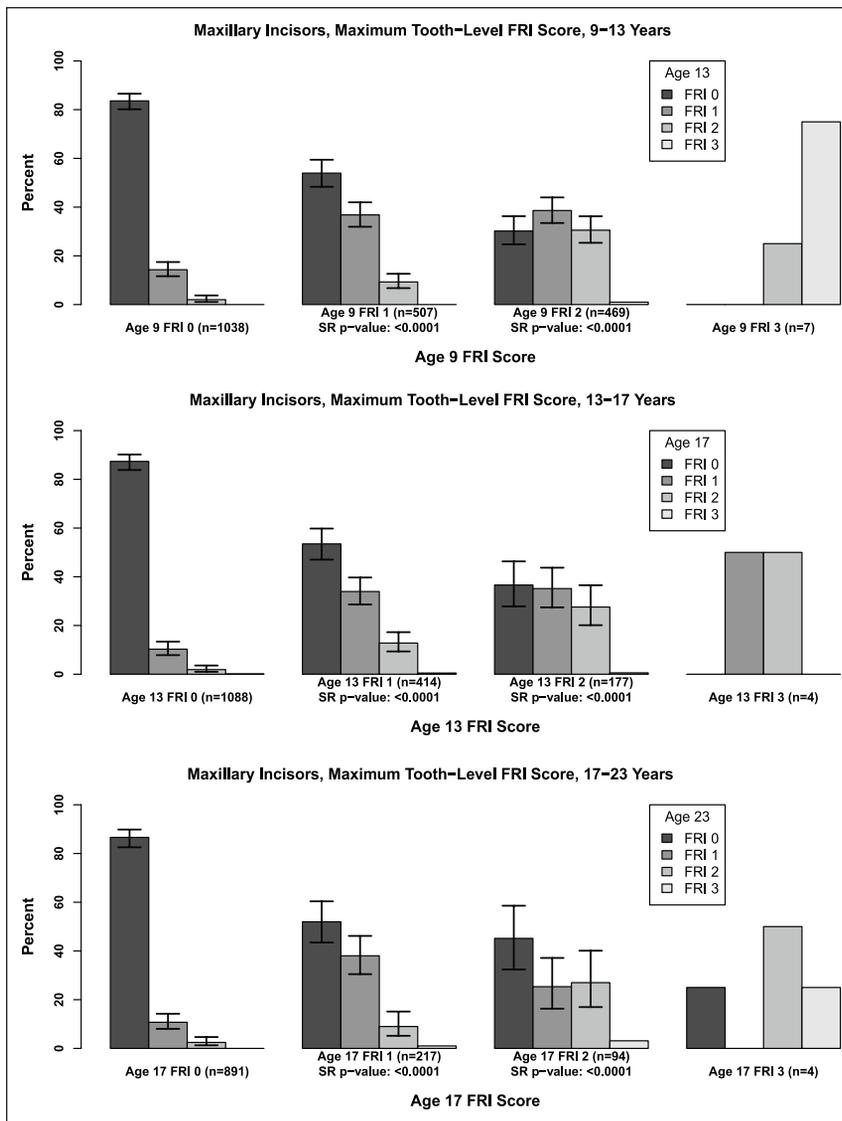


Figure 2. Cross-tabulations of tooth level maximum Fluorosis Risk Index (FRI) scores on maxillary incisors. *P* values for the Wilcoxon signed-rank test (SR *P* value), which adjusts for intraparticipant clustering of teeth, are provided.

diffuse opacities (18.9% had any baseline enamel defect vs. 35.4% of our participants having PL2FRI of 2 or 3 at age 9). Overall, our results agree with the majority of the limited published literature on changes in fluorosis prevalence and severity over time, provide evidence for this trend over multiple time points, and provide some evidence about when this trend starts to level off.

Previous authors have proposed that the biological mechanisms responsible for this trend are post-eruptive maturation and wear on tooth surfaces with mild fluorosis, possibly due to brushing, mastication, and/or demineralization (Do et al. 2016; Wong et al. 2016). In addition, remineralization of the enamel due to calcium and phosphate ions in the saliva could contribute to fluorosis fading (Wong et al. 2016). Although bleaching

may contribute to this decline, a separate analysis of participants who reported using any bleaching products at ages 11, 13, 17, 19, or 23 ($n = 189$) showed similar trends of decline in fluorosis severity relative to the overall results and participants who did not report using any bleaching products ($n = 475$) (results not shown). There were many fewer cases of higher fluorosis severity over time, and we suspect that some of these cases were due to measurement error.

Overall, there is growing clinical evidence for a decline in fluorosis severity during adolescence for all permanent teeth and into young adulthood to a lesser extent. These changes probably affect esthetic perceptions of fluorosis over time, decreasing fluorosis-related esthetic concerns for older adolescents and adults, but further study is needed. Researchers should consider this decline at the person and tooth levels when studying fluorosis in young adolescents, and policymakers should take this trend into consideration when setting fluoride intake recommendations. In conclusion, estimates of fluorosis prevalence or severity from childhood and early adolescence should not be used as lifelong measures of fluorosis, as this may lead to overestimates in adolescence and young adulthood.

Author Contributions

A.M. Curtis, contributed to conception, design, data analysis, and interpretation, drafted and critically revised the manuscript; S.M. Levy, J.J. Warren, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised the manuscript; J.E.

Cavanaugh, contributed to design, data analysis, and interpretation, drafted and critically revised manuscript; J.L. Kolker, K. Weber-Gasparoni, contributed to data acquisition and interpretation, critically revised the manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

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