EPA

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Fluoride:
Dose-Response Analysis
For Non-cancer Effects

Dental Fluorosis:
Evaluations of Key Studies

Health and Ecological Criteria Division
Office of Water

January, 2008

U.S. Environmental Protection Agency
Washington, D.C.

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ACKNOWLEDGMENTS

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The summaries included in this report were prepared by C. Wood, S. Milanez, D. Glass, S. Garcia, S. Goldhaber, and V. Dobozy. Summary reviewers included J.M. Donohue and T. Duke of the Health and Ecological Criteria Division, Office of Science and Technology, Office of Water, U.S. EPA; and D. Glass, D. Opresko and A. Watson of ORNL.

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INTRODUCTION

Prior to initiating the dose-response analysis for severe dental fluorosis, the Office of Water (OW) critically evaluated the studies that had been cited and utilized by the National Research Council (NRC, 2006) in their report *Fluoride in Drinking Water: A Scientific Review of EPA's Standards*. Additional studies identified in the OW initial literature search (2006) were also evaluated. Critical information fields examined and summarized include endpoint studied, type of study and population studied, exposure period and assessment, characterization of study groups, analytical methods and study design, parameters monitored, statistical methods employed, results (including critical tables and figures) authors' conclusions, critical references and definitions, profiler's appraisal, and critical review of the profiler's assessment.

This document is a compilation of the study evaluations arranged alphabetically by the name of the lead author. Dental fluorosis studies identified and added to the dose-response analysis for the non-cancer effects document after its external peer review were not evaluated in this fashion.

STUDY SUMMARIES

Dental Fluorosis

Acharya, S. 2005. Dental caries, its surface susceptibility and dental fluorosis in South India. International Dental Journal, 55(6): 359-64.

<table>
<tr><td></td><td></td></tr>
<tr><td>ENDPOINT STUDIED:</td><td>Dental fluorosis and dental caries</td></tr>
<tr><td></td><td></td></tr>
<tr><td>TYPE OF STUDY:</td><td>Cross-sectional survey</td></tr>
<tr><td></td><td></td></tr>
<tr><td>POPULATION STUDIED:</td><td>India/Karnataka State (Deccan Peninsula). 544 schoolchildren (301 males and 243 females) aged 12-15 years old from five different villages (Nallur, Naganur, Doddabathi, Kundawada and Holesirigere) within Karnataka State (Davangere District) were studied. All children were native to the region.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>CONTROL POPULATION:</td><td>none</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE PERIOD:</td><td>Schoolchildren that were continuous residents of the studied villages since birth and ranged in age from 12-15 years.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE GROUPS:</td><td>The number of children examined in each village and the fluoride concentration identified in the water supply for the village are provided in the table below. All children were in approximately the same socioeconomic status and sorghum was the main staple food item. Water was obtained in the villages from bore wells and was either pumped to a centralized storage tank where residents obtained water through a tap on the tank or through the Accelerated Rural Water Supply which distributed the bore well water to the consumers. The wells were approximately 15-18 years old.
<table>
<tr><th>Name of Village</th><th>No. of children examined</th><th>Fluoride conc. of water</th></tr>
<tr><td>Nallur</td><td>163</td><td>0.43 ppm</td></tr>
<tr><td>Naganur</td><td>49</td><td>0.72 ppm</td></tr>
<tr><td>Kundawada</td><td>96</td><td>1.10 ppm</td></tr>
<tr><td>Doddabathi</td><td>81</td><td>1.22 ppm</td></tr>
<tr><td>Holesirigere</td><td>155</td><td>3.41 ppm</td></tr>
</table></td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE ASSESSMENT:</td><td>Only drinking water was analyzed for fluoride content in this study. The fluoride content in food and beverages (i.e. tea) was not measured. Information regarding food habits was asked of the participants but data characterizing consumption or fluoride concentrations were not included for the assessment.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>ANALYTICAL METHODS:</td><td>Information about the age of the wells (15-18 years old) and the fact that the water supply had been from a constant source was obtained from the local and village councils and the Public Health Engineering Dept. of Davangere District. The analytical method used to measure fluoride in the wells was the ion selective electrode method developed by the Orion Research Incorporated Laboratories Products Group, USA. The model used was (94.09, 96.09) electrode 720A from Orion Instruments. Information about other parameters measured in the water was not included in the paper.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>STUDY DESIGN</td><td>544 schoolchildren (301 males and 243 females) aged 12-15 years old from five different villages (Nallur, Naganur, Doddabathi, Kundawada and Holesirigere) within Karnataka State (Davangere District) were studied. The age distribution was 170 (31.2%) in the 12-13 year old group, 201 (36.9%) in the 13-14 year old group and 173 (31.8%) in the 14-15 year old group.

Dental examinations were performed one time on the children in their schools. Children were examined under natural light while sitting on a chair or stool. Children were assessed for the presence and degree of fluorosis and the evidence of caries.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>PARAMETERS MONITORED:</td><td>The author of this paper (S. Acharya) was the dental examiner for the study and was trained in the WHO criteria for assessing fluorosis and caries prior to the start of the study. Dean's</td></tr>
</table>

criteria (1942) were used to assess fluorosis, and the Community Fluorosis Index (CFI) (Dean 1942) was calculated to assess the public health significance of fluorosis from each village.

Dental caries were assessed using the DMFS index (Klein et al. 1938). The type of carious lesion present was also recorded: pit and fissure lesions or smooth surface lesions. Occlusal, lingual and buccal pit and fissure lesions were classified under pit and fissure lesions. Proximal lesions and lesions on buccal, lingual and occlusal and incisal surfaces other than pit and fissures were classified under smooth surface lesions.

STATISTICAL METHODS:

All data analysis was done on Minitab Statistical Software (Version 13). The Karl Pearson coefficient for correlation and simple regression analysis was used to measure the correlation between fluoride concentration in the drinking water and dental caries. The F test was used for estimation of statistical significance and statistical significance was considered when $p < 0.05$.

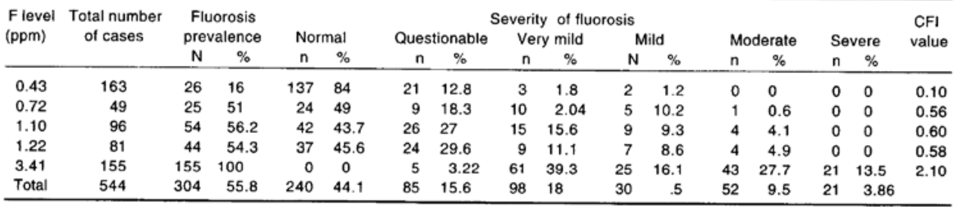
A sub-sample of 10% of the schoolchildren was re-examined for fluorosis and dental caries with one-day intervals between examinations to assess intraexaminer variability; Cohen's Kappa coefficient was found to be 0.88, indicating a high level of agreement.

RESULTS:

Dental fluorosis

Table 2 is copied directly from Acharya (2005) showing the prevalence and severity of fluorosis associated with exposure to water with varying fluoride concentrations. The prevalence of fluorosis increased from 16% at 0.43 ppm F to 100% at 3.41 ppm F and the degree of fluorosis severity increased as fluoride levels increased. The Community Fluorosis Index (CFI) increased from 0.10 at 0.43 ppm F to 2.10 at 3.41 ppm F, making the 3.41 ppm community one of marked health significance.

Table 2 Prevalence and severity of fluorosis in relation to differing water fluoride levels



F level (ppm)	Total number of cases	Fluorosis prevalence		Severity of fluorosis												CFI value
				Normal		Questionable		Very mild		Mild		Moderate		Severe		
		N	%	n	%	n	%	n	%	N	%	n	%	n	%	
0.43	163	26	16	137	84	21	12.8	3	1.8	2	1.2	0	0	0	0	0.10
0.72	49	25	51	24	49	9	18.3	10	2.04	5	10.2	1	0.6	0	0	0.56
1.10	96	54	56.2	42	43.7	26	27	15	15.6	9	9.3	4	4.1	0	0	0.60
1.22	81	44	54.3	37	45.6	24	29.6	9	11.1	7	8.6	4	4.9	0	0	0.58
3.41	155	155	100	0	0	5	3.22	61	39.3	25	16.1	43	27.7	21	13.5	2.10
Total	544	304	55.8	240	44.1	85	15.6	98	18	30	.5	52	9.5	21	3.86	

PROFILER'S NOTE: The prevalence and severity of fluorosis is given for each village was assessed; however, the greatest variance in data were when fluoride levels went from 1.22 ppm to 3.14 ppm. Acharya (2005) discusses the high level of fluoride present within this region of India due to the use of phosphate fertilizers causing fluoride levels to be increased in foods such as sorghum and rice (Anasuya et al. 1997) and the heavy consumption of tea in India; however, actual consumption of water or these other fluoride sources were not addressed in the study.

Dental caries

Acharya (2005) states that caries incidence and severity were highest in the children living in the area with the lowest fluoride (0.43 ppm) concentration, and that there was a statistically significant negative ($r = -0.16$) correlation between water fluoride levels and the mean DMFS, showing a declining trend with increasing level of fluoride (see Table 1 and Figure 1 copied directly from Acharya, 2005). The pit and fissure lesions also showed a decrease with increasing water fluoride levels, however, this trend was not observed with smooth surface lesions. Dental caries also was stated to be more prevalent in the older children and in the females.

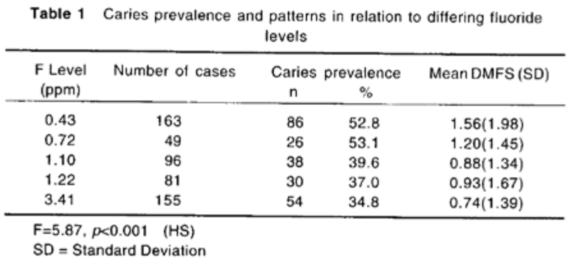


Table 1 Caries prevalence and patterns in relation to differing fluoride levels

F Level (ppm)	Number of cases	Caries prevalence n	%	Mean DMFS (SD)
0.43	163	86	52.8	1.56(1.98)
0.72	49	26	53.1	1.20(1.45)
1.10	96	38	39.6	0.88(1.34)
1.22	81	30	37.0	0.93(1.67)
3.41	155	54	34.8	0.74(1.39)

F=5.87, $p<0.001$ (HS)
SD = Standard Deviation

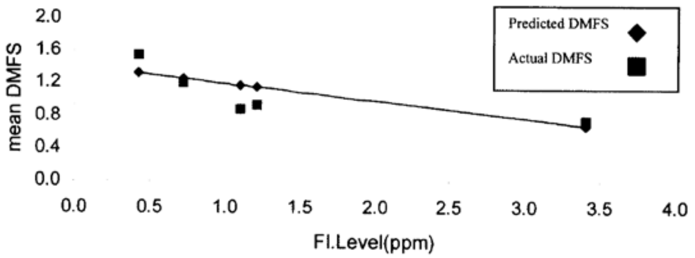


Figure 1. Correlation and regression between water fluoride levels and mean DMFS values. Correlation Coefficient: – 0.16; Regression Equation: 1.42 – 0.22 (F level). An inverse correlation was seen between water fluoride levels and mean DMFS which was statistically significant.

PROFILER'S NOTE: While the prevalence of caries did decrease as the fluoride level increased, the trend was not as strong for the DMFS score. The mean DMFS score for the 1.10 ppm fluoride level group was actually less than that at 1.22 ppm (see Table 1 above). The biggest difference in caries prevalence and mean DMFS scores was when the lowest and highest fluoride levels were compared. From the data provided, the profiler could not agree that the trend of increasing dental caries with age and in females occurred.

Caries surface patterns

The number of pit and fissure lesions as compared to smooth surface lesions are shown in Table 3 copied directly from Acharya (2005). The number of pit and fissure lesions decreased as the fluoride levels increased.

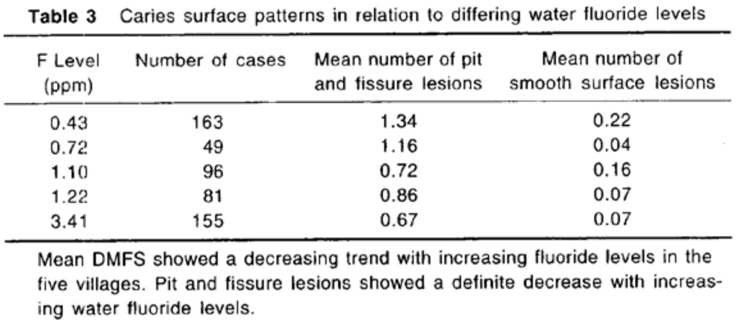


Table 3 Caries surface patterns in relation to differing water fluoride levels

F Level (ppm)	Number of cases	Mean number of pit and fissure lesions	Mean number of smooth surface lesions
0.43	163	1.34	0.22
0.72	49	1.16	0.04
1.10	96	0.72	0.16
1.22	81	0.86	0.07
3.41	155	0.67	0.07

Mean DMFS showed a decreasing trend with increasing fluoride levels in the five villages. Pit and fissure lesions showed a definite decrease with increasing water fluoride levels.

Of the 544 children examined, 234 had caries; however, only 10 filled tooth surfaces were found, indicating insufficient oral health care in the region.

STUDY AUTHORS' CONCLUSIONS:

There was a highly significant negative correlation between water fluoride levels and dental caries. Dental fluorosis also increased with increasing fluoride levels. Caries surface patterns were defined as either pit and fissure or smooth surface lesions, with pit and fissure lesions more common than smooth surface lesions. Pit and fissure lesions showed a decreasing trend with increasing fluoride levels but this trend was not observed with smooth surface lesions. Overall, water fluoride was an important factor associated with low caries prevalence.

Acharya (2005) also observed that low caries and small numbers of smooth surface lesions occurred in the teeth of children from areas with low fluoride concentrations in drinking water. Acharya hypothesizes that this may be due to the "very active local economy" of food produce and food items, in which interexchange of food produced (either grown or cooked) in

		communities with high- and medium-fluoride wells is frequently bought, exchanged, sold and consumed in communities supplied by low-fluoride water wells. Acharya (2005) considers this exchange to result in a "'halo' effect." Consumption of tea (considered a considerable source of F), salt and other condiments may also be factors.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Anasuya, A., S. Bapurao and P.K. Paranjape. 1997. Fluoride and silicon intake in normal and endemic fluorotic areas. J. Trace Elements Med. Biol., 10:149-155. Klein, H. C.E. Palmer and J.V. Knutson. 1938. Studies on dental caries I. Dental status and dental needs of elementary school children. Public Health Rep., 53: 751.
PROFILER'S REMARKS	***DFG/12-06 and 12/14/2006***	Data showed a dose-response to fluoride concentrations in the water as the severity of fluorosis; the CFI increased when fluoride concentrations went from 1.22 ppm to 3.14 ppm. For fluoride concentrations between 0.72 and 1.22 ppm, there was not much of a dose-response and the health significance based on the CFI was borderline. The study did not present the data based on age levels or gender so the profiler could not confirm all of Acharya's (2005) conclusions. While Acharya (2005) discussed the other possible sources of fluoride that have been documented in the area, there were no data provided to characterize them. The study did use accepted standards of assessment such as Dean's index for fluorosis. Statistical analysis appears to be adequate. The study also indicated a decreased amount of caries as the fluoride levels increased in the water.
PROFILER'S ESTIM. NOEL/NOAEL		This study was not designed to be suitable for development of a NOAEL for fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL		This study was not designed to be suitable for development of a LOAEL for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor (X), Medium (_), Strong (_) Data showed increased severity of fluorosis and an increased CFI when the fluoride levels went from 1.22 to 3.14 ppm but there was not much difference in those exposed to 0.72 to 1.22 ppm making a clear dose-response not evident. In addition, the authors note likely confounding due to dietary fluoride intake by villagers who are also supplied with low-F drinking water. Therefore, the study does not have a potential to be used for dose-response modelling.
CRITICAL EFFECT(S):		Dental fluorosis and dental caries

Akpata, E.S., Z. Fakiha and N. Khan. 1997. Dental fluorosis in 12-15-year-old rural children exposed to fluorides from well drinking water in the Hail region of Saudi Arabia. Community Dent Oral Epidemiol 25:324-7.

ENDPOINT STUDIED:	Dental caries and fluorosis (permanent teeth).
TYPE OF STUDY:	Prevalence study.
POPULATION STUDIED:	Saudi Arabia/Hail region: Children aged 12-15 years; selected for study participation by a two-stage stratified cluster sampling technique. Hail villages were stratified according to the fluoride concentrations of the wells used (see Table 1). Each stratum of fluoride concentration was allocated a sample size proportional to its population. Forty-two primary and intermediate schools, chosen by simple random sampling technique from a total of about 155 were visited and a sample of classrooms with children aged 12-15 years was selected by the same technique. The 2355 children (approximately equal numbers of boys and girls) examined were life-long residents of the villages and had no obvious nutritional deficiencies. Those who obtained their drinking water from more than one well were excluded from the study. Informed consent for study participation was obtained from the community heads and school authorities.
CONTROL POPULATION:	None.
EXPOSURE PERIOD:	12-15 yr; from time of birth to1993.
EXPOSURE GROUPS:	0.50-0.79; 0.80-1.09; 1.10-1.39; 1.40-1.69; 1.70-1.99; 2.00-2.29 or >2.30 ppm fluoride in well water. Of the 1083 wells in the Hail region of Saudi Arabia, 87 popularly used for drinking water were selected for analyses. The wells were at least 20 years old and about 300 m deep. The wells contained ground water, possibly located at the confined aquiferous earth stratum and consequently, significant seasonal variation in the fluoride concentration of well water was unlikely. The study authors note that the amount of time the children spent in air-conditioned rooms might have influenced water drinking habits, and thereby affected fluoride intake; however, this factor was not quantified.
EXPOSURE ASSESSMENT	The study author note that the data suggest other sources of fluoride exposure such as foods, beverages and infant formula, although fluoride intake from these sources was not quantified.
ANALYTICAL METHODS:	Fluoride levels in the 87 wells selected for analysis were measured by the ion-specific electrode method. (Taves, 1968)
STUDY DESIGN	The objective of the study was to investigate the relationship between fluoride levels in well drinking water, severity of dental fluorosis and dental caries in the Hail region of Saudi Arabia. A random sample of 2355 children aged 12-15 years was examined for dental caries following the WHO criteria (WHO, 1977). Their teeth were then examined for dental fluorosis using the Thylstrup and Fejerskov Index (TFI; see NRC, 2006, pages 88-89). A reproducibility test was conducted on 20 subjects to test for intra-examiner agreement.
PARAMETERS MONITORED:	Dental caries was evaluated following the WHO criteria. Dental fluorosis was evaluated using the modified TFI. The teeth were dried with gauze, illuminated with a pocket torch, and the facial tooth surfaces examined for fluorosis. To calibrate the three examiners against the principal investigator, 20 subjects were examined for dental caries and dental fluorosis of tooth #11. The calibration was repeated until intra-examiner level of agreement gave a Cohen's Kappa statistic of at least 0.75. At each session during the field work, about 10% of subjects were examined a second time and the reproducibility measured; this resulted in intra-examiner level of agreement varying between 0.76-0.80 and 0.78-0.84 in the diagnoses of dental fluorosis and dental caries, respectively.

STATISTICAL METHODS: Chi-square tests, simple linear regression analysis and analysis of covariance were used to assess the statistical significance of the association between fluoride levels in well drinking water, severity of dental fluorosis and caries occurrence.

RESULTS: The study population is presented in Table 1 taken directly from Akpata, 1997.

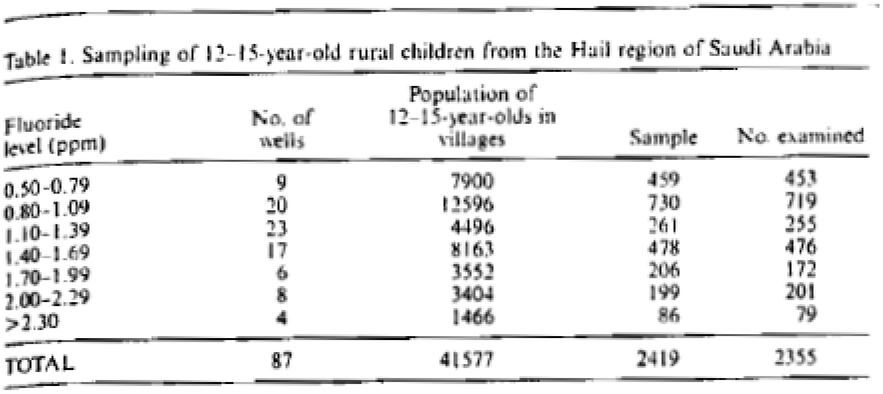


Table 1. Sampling of 12–15-year-old rural children from the Hail region of Saudi Arabia

Fluoride level (ppm)	No. of wells	Population of 12–15-year-olds in villages	Sample	No. examined
0.50-0.79	9	7900	459	453
0.80-1.09	20	12596	730	719
1.10-1.39	23	4496	261	255
1.40-1.69	17	8163	478	476
1.70-1.99	6	3552	206	172
2.00-2.29	8	3404	199	201
>2.30	4	1466	86	79
TOTAL	87	41577	2419	2355

Study results in Tables 2-3 and Figures 1-3 are shown directly from Akpata, 1997.

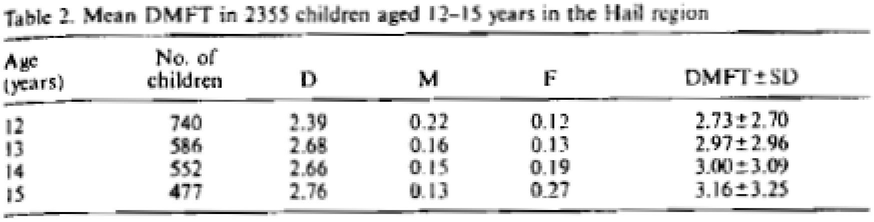


Table 2. Mean DMFT in 2355 children aged 12–15 years in the Hail region

Age (years)	No. of children	D	M	F	DMFT ± SD
12	740	2.39	0.22	0.12	2.73 ± 2.70
13	586	2.68	0.16	0.13	2.97 ± 2.96
14	552	2.66	0.15	0.19	3.00 ± 3.09
15	477	2.76	0.13	0.27	3.16 ± 3.25

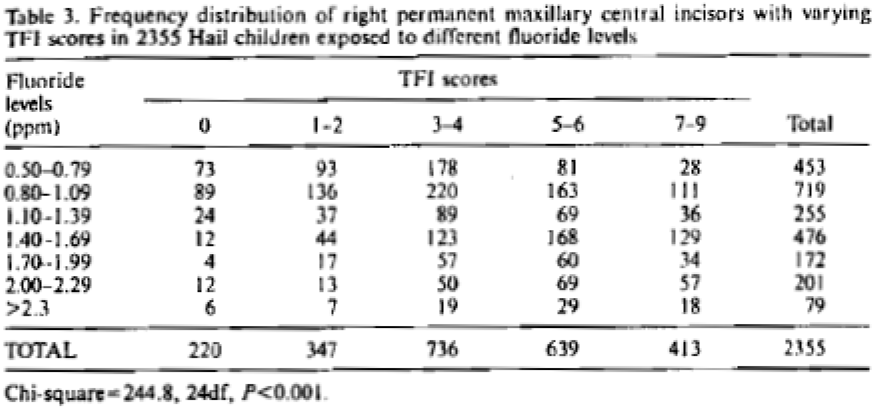


Table 3. Frequency distribution of right permanent maxillary central incisors with varying TFI scores in 2355 Hail children exposed to different fluoride levels

Fluoride levels (ppm)	TFI scores					
	0	1-2	3–4	5–6	7-9	Total
0.50–0.79	73	93	178	81	28	453
0.80–1.09	89	136	220	163	111	719
1.10-1.39	24	37	89	69	36	255
1.40-1.69	12	44	123	168	129	476
1.70-1.99	4	17	57	60	34	172
2.00–2.29	12	13	50	69	57	201
>2.3	6	7	19	29	18	79
TOTAL	220	347	736	639	413	2355

Chi-square = 244.8, 24df, $P<0.001$.

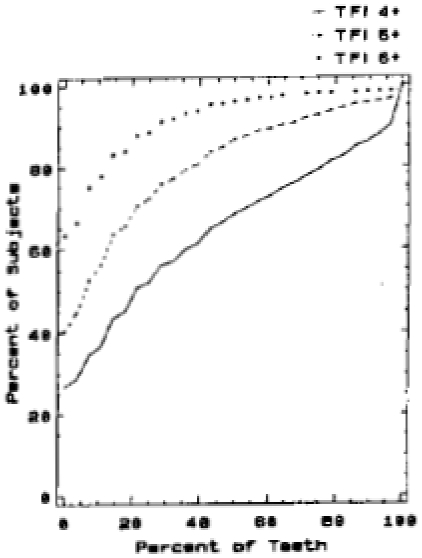


Fig. 1. Percentage cumulative frequency curves, illustrating the proportion of teeth in 12–15-year-old Hail children with TFI scores of 4+, 5+ and 6+.

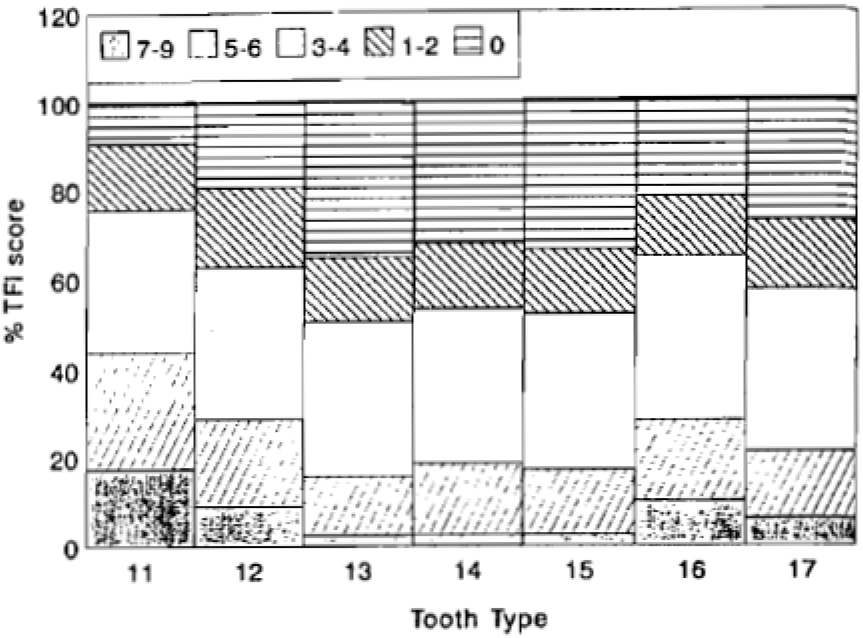
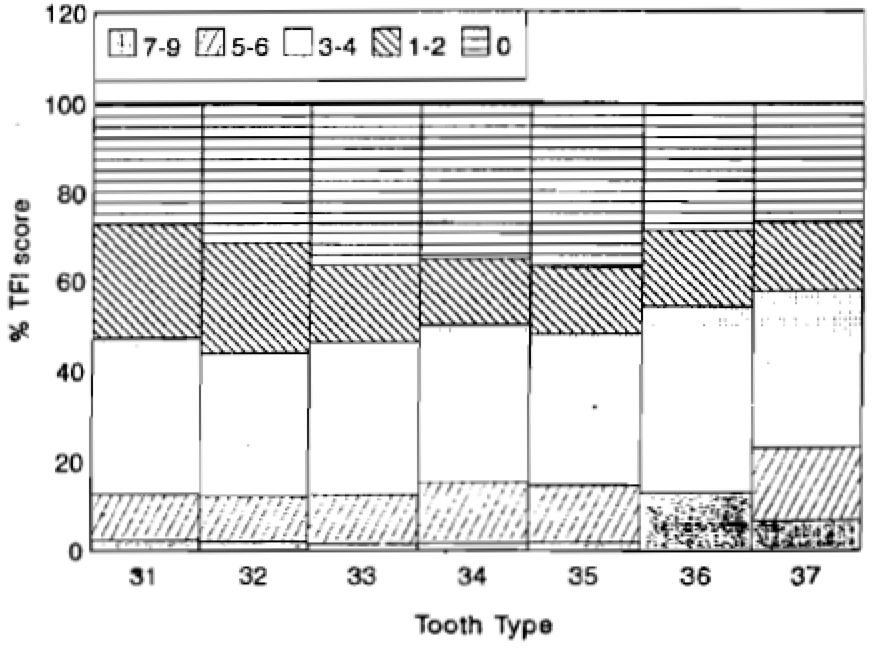


Fig. 2. Percentage frequency distribution of TFI scores in maxillary tooth types of 12–15-year-old Hail children exposed to 0.5–2.8 ppm fluoride from well water.

		 *Fig. 3.* Percentage frequency distribution of TFI scores in mandibular tooth types of 12–15-year-old Hail children exposed to 0.5-2.8 ppm fluoride from well water.
STUDY AUTHORS' CONCLUSIONS:		The study authors concluded that the strong association between fluoride levels in well drinking water and the severity of dental fluorosis indicates that fluoride from well water is a significant factor in the etiology of dental fluorosis in the Hail region. Although there was a statistically significant relationship between DMFT (decayed, missing or filled teeth) and fluoride levels, the R^2 value was very low, indicating that fluoride in well water made little contribution to the variability of caries experience in Hail children.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		World Health Organization. Oral health surveys: basic methods. Geneva: WHO, 1977. Taves, D.R. 1968. Determination of submicromolar concentrations of fluoride in biological samples. Talentia 15:1015-23.
PROFILER'S REMARKS	***Initials/Date*** VAD/03-09-07	The study results are not representative of the U.S. population since the study was conducted in Saudi Arabia. The study didn't account for other sources of fluoride exposure in addition to the drinking water. The study report indicated that attempts have been made within the past decade by some of the Hail rural population to defluoridate their well drinking water by sedimentation and distillation. These practices may have reduced the actual fluoride concentrations in the drinking water of some children in the study. Although there may have been confounding factors, such as additional fluoride intake through food or beverage consumption, the data do show a trend towards increasing severe fluorosis with increasing fluoride concentration in well water (about 6% at 0.5-0.79 ppm to greater than 20% at 1.40 ppm and higher. Although the incidences of severe fluorosis are higher in this study, comparisons can be made to the Galagan and Lamason (1953) study from the southwest US where similar climatic conditions occur.
PROFILER's ESTIM. NOAEL		The study design did not identify a no-flurosis intake dose.
PROFILER'S ESTIM. LOAEL		Fluorosis, including severe fluorosis, was reported at all levels of fluoride concentration in the drinking water. Therefore, the LOAEL was 0.50-0.79 ppm.

SUITABILITY FOR DOSE RESPONSE MODELING	Not suitable,(_); Poor (_); Medium (X); Strong (_)
CRITICAL EFFECTS:	Dental fluorosis and caries (permanent teeth)

Awadia, A.K., Birkeland, J.M., Haugejorden, O., and Bjorvatn, K. 2000. An Attempt to Explain Why Tanzanian Children Drinking Water Containing 0.2 or 3.6 mg Fluoride Per Liter Exhibit a Similar Level of Dental Fluorosis. Clin Oral Invest 4: 238-244.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Cohort
POPULATION STUDIED:	Africa, Tanzania: 80 school children of African ethnicity, ages 8-16 years old, from the urban community of Arusha, Tanzania where the fluoride level in the drinking water is 3.6 mg/l.
CONTROL POPULATION:	96 school children of African ethnicity, ages 8-16 years old, from the rural community of Kibosho, Tanzania where the fluoride level in the drinking water is 0.2 mg/l.
EXPOSURE PERIOD:	A structured interview was conducted to collect information relating to the child's first 6 years of life. The enamel formation of upper central incisors is normally finished at approximately 3.5 years after birth. Thus, the use of tooth 21 (upper left central incisor) in the analyses restricted relevant fluoride exposure to a limited period of life.
EXPOSURE GROUPS:	Subjects were from two northern Tanzanian communities. Kibosho (altitude 1300 m) is a rural community of approximately 20,000 inhabitants (mostly of the Wachagga tribe with African ethnicity) and has a historical water fluoride concentration of 0.05-0.56 mg/l. Arusha (altitude 1400 m) is an urban community of 135,000 inhabitants (multi-ethnic and multi-tribal) and has a historical water fluoride concentration of 3.5-3.6 mg/l. Data is based on findings over 20 years. Children were selected from four schools in Arusha (every third child was randomly selected from the schools' attendance records, n=80) and from one school in Kibosho (all children in grades 3-5, n= 96). The average age was significantly lower in Arusha (10.4±1.8 years) than in Kibosho (12.4±1.7 years). There was no gender difference between or within areas. Magadi, a fluoride-containing salt added to weaning food and to 'adult' food, may be an important source of fluoride in Kibosho. On a dry weight basis, a magadi sample has been shown to contain 1.5 mg F/g. An estimated intake of 0.44 g magadi per adult per day would give a fluoride exposure of 0.7 mg/day. However, there is marked variability in fluoride content of magadi (160 to 1750 mg/l). The amount and the fluoride content of consumed magadi could not be assessed in the current study.
EXPOSURE ASSESSMENT:	Dental fluorosis prevalence and severity were measured; comparisons were made on TFI scores from tooth 21. Information regarding variables assumed to be related to dental fluorosis during the first 6 years of life was collected from questionnaires consisting of two parts; the subjects answered one part and the accompanying parent(s) (mainly mothers), the other part.
ANALYTICAL METHODS:	Data on how fluoride concentrations in the water supply were measured were not included in the study report. Fluoride content in magadi was not determined in the study.
STUDY DESIGN	The study included two cohorts of school children from two communities in northern Tanzania. One study population was from Arusha (n=80, age 10.4±1.8 years), a multi-ethnic and multi-tribal urban community with a water fluoride concentration of 3.6 mg/l. The other study population was from Kibosho (n= 96, age 12.4±1.7 years), a rural community consisting primarily of Wachagga tribe members with African ethnicity and with a water fluoride concentration of 0.2 mg/l. Children were selected from four schools in Arusha (every third child was randomly selected from the schools' attendance records, n=80) and from one school in Kibosho (all children in grades 3-5).

	Information regarding variables assumed to be related to dental fluorosis during the first 6 years of life was collected from questionnaires consisting of two parts; the subjects answered one part and the accompanying parent(s) (mainly mothers), the other part. Variables included: fluid intake; diet, including weaning food (i.e., lishe—porridge containing ground maize, beans, peanuts, and fishmeal; and kiborou—beans and bananas cooked with magadi, a fluoride-containing salt); toothpaste use; parent occupation; and general health. The prevalence and severity of dental fluorosis was measured as follows: Examinations: Subjects were examined for dental fluorosis under indirect light while seated on a chair. Prior to the clinical examination, the teeth were wiped clean with cotton gauze and isolated with cotton rolls. One examiner graded dental fluorosis on the facial surfaces of all permanent teeth using the Thylstrup and Fejerskov Index (TFI). Substantial intra-examiner agreement of the recordings has been reported earlier (Cohen's kappa 0.74). To standardize conditions and allow comparison with previous findings, the TFI score for tooth 21 (upper left central incisor) was used to characterize the severity of fluorosis in a subject. No radiographs were taken during the surveys.
PARAMETERS MONITORED:	Dental fluorosis was measured using the Thylstrup and Fejerskov Index (TFI). No radiographs were taken during the surveys. The TFI score for tooth 21 (upper left central incisor) was used to characterize the severity of fluorosis in a subject.
STATISTICAL METHODS:	Data were analyzed using the statistical package for social sciences (SPAA for PC version 9.0). Distribution of subjects according to background variables was assessed by chi-square tests (with Yates's continuity correction). The average total fluid intake in the two areas was compared using the Student's *t*-test. The Mann-Whitney *U* test was used to compare the distribution of fluorosis between areas and background variables. Spearman's rank correlation coefficient (r_s) was employed to assess the strength of the bivariate association between the dependent variable (TFI score on tooth 21) and the independent variables. Stepwise multiple linear regression analyses (SMLRA) was applied to control for confounding and to estimate explained variance in the dependent variables. The SMLRA was run for the whole group (inter-area) and within areas. The intra-area analyses were carried out in an attempt to further explain the difference in the level of fluorosis between the areas. Variables logically important for the development of dental fluorosis were selected for the regression model rather than variables found to be significant in bivariate analyses. The level of significance was 5% ($p<0.05$).
RESULTS:	
Dental fluorosis	Figure 1 was copied directly from Awadia et al. (2000) and summarizes the frequency distribution of children according to the severity of dental fluorosis, recorded on tooth 21. The prevalence (TFI $\geq$1) was not significantly different between the communities. The median TFI score on tooth 21 was four in both areas. The severity of dental fluorosis was significantly lower in Kibosho (0.2 mg F/l) than in Arusha (3.6 g mg F/l) (p=0.008). There were no significant differences between genders.

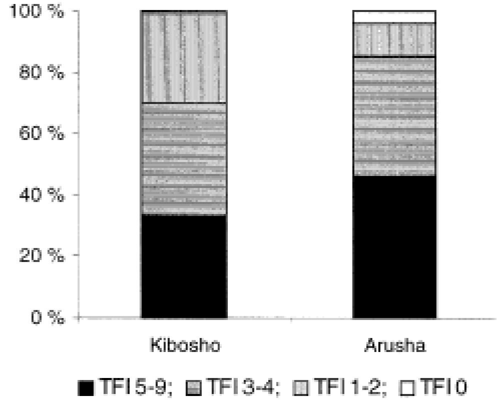
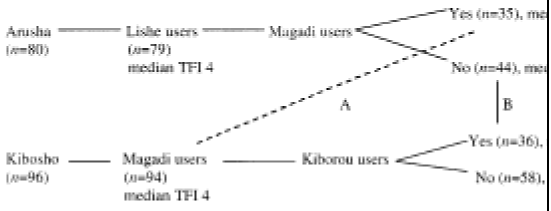


Fig. 1 Frequency distribution (%) of children according to the severity of dental fluorosis recorded by the TF Index on tooth 21 in Kibosho (0.2 mg fluoride/l; *n*=96) and Arusha (3.6 mg fluoride/l; *n*=80)

Figure 2 also was copied directly from Awadia et al. (2000) and summarizes the distribution of children and median TFI scores on tooth 21 according to area and dietary practices. When comparing dental fluorosis among magadi users (comparison *A* in Figure 2), the scores in Kibosho (TFI=4, n=94) were significantly lower than in Arusha (TFI=5, n=35, p=0.002). The TFI scores among users of both magadi and kiborou in Kibosho (TFI=4, n=36, comparison *B* in Figure 2) did not differ significantly from the severity in magadi non-users in Arusha (n=44, p=0.93).

Fig. 2 Distribution of children and median TFI scores on tooth 21 according to area and dietary practices in Kibosho (0.2 mg fluoride/l; *n*=96) and Arusha (3.6 mg F/l; *n*=80). *Dotted lines A* and *B* indicate compared groups



PROFILER’S NOTE: The profiler agrees that the prevalence of dental fluorosis was similar between the two regions (median TFI scores of 4), but that the severity of fluorosis was lower in Kibosho (average TFI score would probably reflect this if it were calculated). Further, when considering magadi use, the TFI score was lower in Kibosho compared to Arusha (4 vs. 5), and in Arusha, magadi users (TFI=5) had a higher TFI score compared to non-users (TFI=4) in the same area.

Background variables

Table 3 was copied directly from Awadia et al. (2000) and summarizes the frequency distribution of subjects according to categories on background variables (n=176). The fluid intake included water (Kibosho, 0.4±0.14 l; Arusha, 0.6±0.28 l) and tea (Kibosho, 0.3±0.11 l; Arusha, 0.4±0.22 l). The average total fluid intake was significantly lower in Kibosho than in Arusha (0.7±0.23 l vs. 1.0±0.38 l, p<0.01). The difference in total fluid intake could be related to either the different interviewer in the two areas or the different tribes and living conditions. Boiling of drinking water was less common in Kibosho (44%) than in Arusha (72%, p<0.001).

Regarding weaning food, 99% of subjects in Arusha and 61% in Kibosho had used lishe; 39% in Kibosho used kiborou, made with fluoride-containing magadi. Significantly more subjects in Kibosho used magadi than in Arusha (98% vs. 45%, respectively). The type of magadi or the amounts consumed during critical periods for developing dental fluorosis could not be determined.

During the pre-school period, toothpaste was reported to be used by 41% of the subjects in Kibosho and 94% in Arusha. It was not possible to distinguish between fluoridated and non-fluoridated toothpaste but most toothpaste on the market in Tanzania contains fluoride.

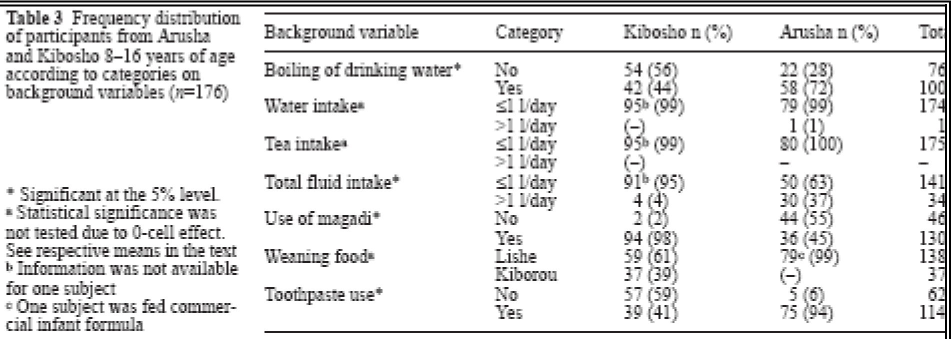


Table 3 Frequency distribution of participants from Arusha and Kibosho 8–16 years of age according to categories on background variables (*n*=176)

Background variable	Category	Kibosho n (%)	Arusha n (%)	Tot
Boiling of drinking water*	No	54 (56)	22 (28)	76
	Yes	42 (44)	58 (72)	100
Water intake[a]	≤1 l/day	95[b] (99)	79 (99)	174
	>1 l/day	(–)	1 (1)	1
Tea intake[a]	≤1 l/day	95[b] (99)	80 (100)	175
	>1 l/day	(–)	–	–
Total fluid intake*	≤1 l/day	91[b] (95)	50 (63)	141
	>1 l/day	4 (4)	30 (37)	34
Use of magadi*	No	2 (2)	44 (55)	46
	Yes	94 (98)	36 (45)	130
Weaning food[a]	Lishe	59 (61)	79[c] (99)	138
	Kiborou	37 (39)	(–)	37
Toothpaste use*	No	57 (59)	5 (6)	62
	Yes	39 (41)	75 (94)	114

* Significant at the 5% level.
[a] Statistical significance was not tested due to 0-cell effect. See respective means in the text
[b] Information was not available for one subject
[c] One subject was fed commercial infant formula

Table 4 was copied directly from Awadia et al. (2000) and summarizes Spearman's rank correlation coefficient between TFI score on tooth 21, age, dietary practices, habits and liquid intake (n=171-176). Area and fluid intake were significantly associated with the TFI score in bivariate correlation analyses. Area correlated significantly with several independent variables. Use of magadi was significantly associated with mother's occupation (peasantry) and hence with area of residence in the bivariate analyses.

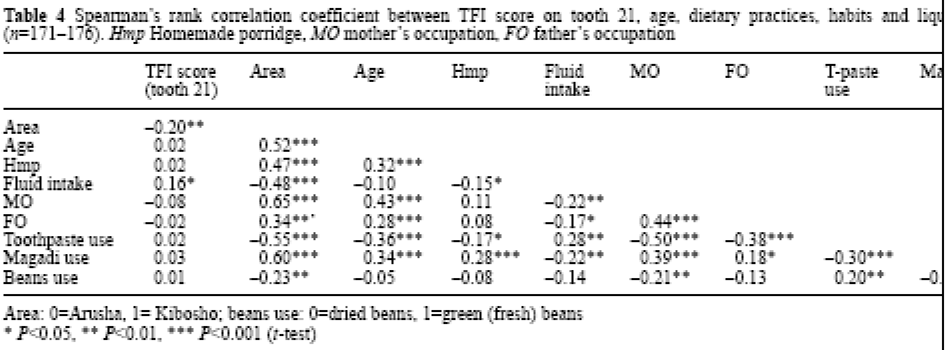


Table 4 Spearman's rank correlation coefficient between TFI score on tooth 21, age, dietary practices, habits and liqu (*n*=171–176). *Hmp* Homemade porridge, *MO* mother's occupation, *FO* father's occupation

	TFI score (tooth 21)	Area	Age	Hmp	Fluid intake	MO	FO	T-paste use	Ma
Area	–0.20**								
Age	0.02	0.52***							
Hmp	0.02	0.47***	0.32***						
Fluid intake	0.16*	–0.48***	–0.10	–0.15*					
MO	–0.08	0.65***	0.43***	0.11	–0.22**				
FO	–0.02	0.34**'	0.28***	0.08	–0.17*	0.44***			
Toothpaste use	0.02	–0.55***	–0.36***	–0.17*	0.28**	–0.50***	–0.38***		
Magadi use	0.03	0.60***	0.34***	0.28***	–0.22**	0.39***	0.18*	–0.30***	
Beans use	0.01	–0.23**	–0.05	–0.08	–0.14	–0.21**	–0.13	0.20**	–0.

Area: 0=Arusha, 1= Kibosho; beans use: 0=dried beans, 1=green (fresh) beans
* $P<0.05$, ** $P<0.01$, *** $P<0.001$ (*t*-test)

Table 5 was copied directly from Awadia et al. (2000) and summarizes the stepwise multiple linear regression analyses with TFI score on tooth 21 as the dependent variable (n=176). When the variables age, area, total fluid intake, magadi use, weaning food use, and mother's occupation were used in the SMLRA, the area accounted for 3.2% of the variance in the TFI score. The use of magadi increased the variance that could be accounted for by 2.9% when the total explained variance was 5.0%. In Kibosho, age explained 5.7% of the variance in TFI score in SMLRA (p=0.02). In Arusha, magadi use significantly explained 3.7% of the variance in TFI score.

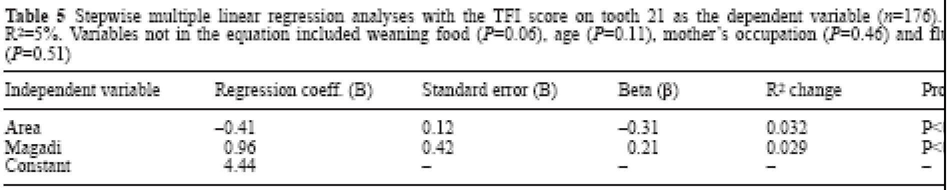


Table 5 Stepwise multiple linear regression analyses with the TFI score on tooth 21 as the dependent variable (*n*=176). R^2=5%. Variables not in the equation included weaning food (*P*=0.06), age (*P*=0.11), mother's occupation (*P*=0.46) and fl (*P*=0.51)

Independent variable	Regression coeff. (B)	Standard error (B)	Beta (β)	R^2 change	Pro
Area	–0.41	0.12	–0.31	0.032	P<
Magadi	0.96	0.42	0.21	0.029	P<
Constant	4.44	–	–	–	–

PROFILER'S NOTE: The profiler agrees that the participants differed significantly regarding practices related to food habits such as boiling of drinking water, use of magadi, and type of weaning food.

STUDY AUTHORS' CONCLUSIONS:

A modest but significant difference in the severity of dental fluorosis was found when comparing children of two Tanzanian communities using drinking water with different concentrations of fluoride. Use of magadi (shown to contain high amounts of fluoride and to be related to severity of dental fluorosis in other studies) and a traditional weaning food cooked with magadi (kiborou) may partly explain the high prevalence and severity of fluorosis in the rural population (Kibosho) with a lower socio-economic level and with drinking water containing only 0.2 mg F/l.

		The fluoride concentration of the drinking water (18-fold), degree of urbanization and tribe were the obvious differences between areas. The participants differed significantly regarding practices related to food habits such as boiling of drinking water, use of magadi, and type of weaning food. Except for area, use of magadi and weaning food, none of the above mentioned factors explained a significant proportion of the variance of the TFI scores in the multivariate analyses and total explained variance was only 5%. Given the different fluid intake levels (0.7 in Kibosho vs. 1.0 l in Arusha) and the fluoride concentrations (0.2 vs. 3.6 mg F/l) in the drinking water, the fluoride intake in Arusha corresponds to approximately 3.5 mg F/day. Thus, alternative sources of fluoride are required to explain the level of fluorosis observed in Kibosho. Magadi users had significantly higher TFI scores in Arusha. Statistically, the effect of magadi could not be established in Kibosho since only two subjects were non-users. Magadi may be an important source of fluoride in Kibosho. Whether the use of magadi and/or the traditional weaning food (kiborou) is primarily related to tribe, area, urbanization, or socio-economic level could not be determined. The less frequent use of toothpaste in the rural community supports the notion that factors related to living conditions may affect the severity of dental fluorosis.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		No references or definitions are cited.
PROFILER'S REMARKS	***Initials/date SJG/ 2/14/07***	The study was well-conducted and had adequate study design. However, the study was not designed for development of a dose response to fluoride as the emphasis was on monitoring dental fluorosis in children and on attempting to explain other factors besides fluoride in the drinking water that may contribute to fluorosis. Higher prevalence and severity of fluorosis was expected in Arusha where the fluoride in the drinking water was 18-fold higher than in Kibosho. However, based on the study design, the prevalence of dental fluorosis did not differ significantly between areas, but the severity was significantly higher in Arusha (3.6 mg F/l) according to TFI scores on tooth 21. Apart from fluoride in the drinking water, other sources of fluoride (magadi) may partly explain the relatively high prevalence and severity of fluorosis in Kibosho (0.2 mg F/l). Limitations of the study included: o The amount and the fluoride content of consumed magadi could not be assessed. o Water intake was estimated at the subject's present age. o The duration of breast-feeding was not considered and the possible protective influence of breast-feeding could not be assessed from these data.
PROFILER'S ESTIM. NOEL/NOAEL		Study design was not suitable for development of a NOAEL for fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL		Study design was not suitable for development of a LOAEL for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor (_), Medium (_), Strong (_) While the study was well-conducted, the study design was not conducive to provide data for a dose-response. The study indicated similar prevalence of dental fluorosis in children of both communities, but slightly higher severity of fluorosis in children living in the community with greater fluoride concentration in the drinking water (Arusha). The study did not address any issues of caries, plaque or gingivitis.
CRITICAL EFFECT(S):		Prevalence and severity of dental fluorosis

Bharati, P., A. Kubakaddi, M. Rao and R.K. Naik. 2005. Clinical symptoms of dental and skeletal fluorosis in Gadag and Bagalkot districts of Karnataka. J. Hum. Ecol., 18(2): 105-107.

ENDPOINT STUDIED:	Dental and skeletal fluorosis
TYPE OF STUDY:	Case control
POPULATION STUDIED:	India/ 6 villages in Gadag and 2 villages of Bagalkot District: 532 male and female subjects surveyed from 6 villages in the Mundargi taluk (Gadag district) and 300 male and female subjects surveyed from 2 villages in the Hungund taluk (Bagalkot district). Ten percent of the households from each village were chosen for the study with at least one member of the household exhibiting fluorosis. All members of the households chosen were part of the study sample. PROFILER'S NOTE: The ages or range of ages of the participants were not included in the study report.
CONTROL POPULATION:	None described
EXPOSURE PERIOD:	Not described. PROFILER'S NOTE: The profiler assumes since all members of the household were included in the study that some of the participants (i.e. parents) had received long-term exposures to the fluoride levels.
EXPOSURE GROUPS:	Only fluoride levels in drinking water were provided. Water in the Mundargi taluk ranged from 4.0 to 10.5 ppm (Bharati and Meera Rao, 2001; Bharati, 1996) and water in the Hungund taluk ranged from 2.04 to 3.2 ppm (Kubakaddi, 2001). PROFILER'S NOTE: The applicability of this study for use in developing United States' guidelines is limited as the values of fluoride exposure are much higher than those found typically in the U.S. drinking water supply.
EXPOSURE ASSESSMENT:	Participants were only assessed for the exposure to fluoride through the drinking water.
ANALYTICAL METHODS:	Analytical methods were not described. Only ranges for the fluoride level in the water were provided; no other water parameters were measured.
STUDY DESIGN	The study was conducted in 6 villages of Mundargi taluk (Gadag district) and 2 villages of Hungund taluk (Bagalkot district) in India that historically had fluoride levels ranging from 2.04 to 10.5 ppm fluoride. In each village, 10% of the households were selected with the criteria for selection being that one person in the family was affected with fluorosis. A checklist was developed using available literature and consultation with a nutritionist to record the clinical symptoms of fluorosis. The symptoms were recorded by personally interviewing each individual in the families chosen and by observations with the help of local doctors. The symptoms were then tabulated and percentages calculated.
PARAMETERS MONITORED:	No parameters used for scoring either the dental or skeletal fluorosis were described. The dental fluorosis was observed by examination (see Table 1) and the skeletal fluorosis by clinical symptoms described by the participants (see Table 2).
STATISTICAL METHODS:	No statistical methods were described.
RESULTS:	
Dental fluorosis	Table 1 below is copied directly from Bharati et al. (2005). In Mundargi taluk, out of 532 participants, 328 (61.65%) had either dental fluorosis (25%), skeletal fluorosis (5.45%) or both (31.20%). Among the 300 participants of Hungund taluk, 194 (64.67%) had either dental fluorosis (35%), skeletal fluorosis (17%) or both (12.67%). In the Mundargi taluk,

browning of the teeth was the most common symptom of dental fluorosis followed by pain and pus in teeth. Ninety five subjects had pitting and swelling and 86 participants had lost their teeth. In Hungund taluk, lack of luster was the most common symptom followed by browning of teeth with about 6 participants having lost their teeth. Overall, dental fluorosis was more severe in Mundargi.

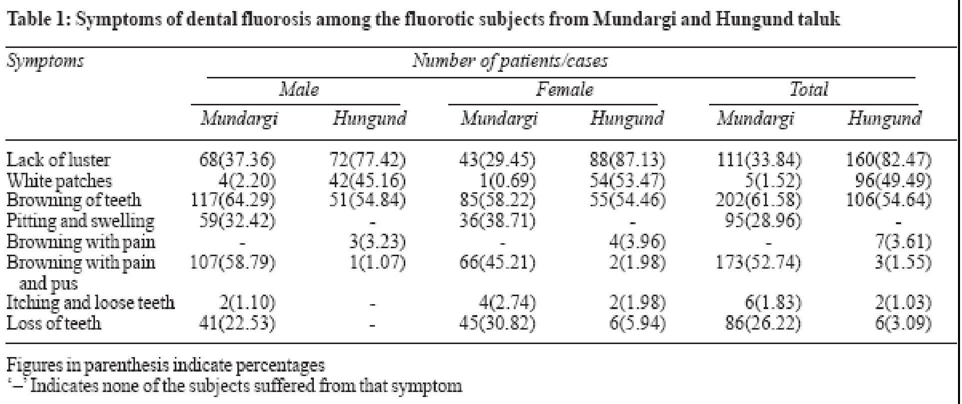


Table 1: Symptoms of dental fluorosis among the fluorotic subjects from Mundargi and Hungund taluk

Symptoms	*Number of patients/cases*					
	Male		*Female*		*Total*	
	Mundargi	*Hungund*	*Mundargi*	*Hungund*	*Mundargi*	*Hungund*
Lack of luster	68(37.36)	72(77.42)	43(29.45)	88(87.13)	111(33.84)	160(82.47)
White patches	4(2.20)	42(45.16)	1(0.69)	54(53.47)	5(1.52)	96(49.49)
Browning of teeth	117(64.29)	51(54.84)	85(58.22)	55(54.46)	202(61.58)	106(54.64)
Pitting and swelling	59(32.42)	-	36(38.71)	-	95(28.96)	-
Browning with pain	-	3(3.23)	-	4(3.96)	-	7(3.61)
Browning with pain and pus	107(58.79)	1(1.07)	66(45.21)	2(1.98)	173(52.74)	3(1.55)
Itching and loose teeth	2(1.10)	-	4(2.74)	2(1.98)	6(1.83)	2(1.03)
Loss of teeth	41(22.53)	-	45(30.82)	6(5.94)	86(26.22)	6(3.09)

Figures in parenthesis indicate percentages
'–' Indicates none of the subjects suffered from that symptom

PROFILER'S NOTE: The profiler agrees that the number of more severe findings were observed in the higher fluoride area, Mundargi taluk; however, if the authors had provided the data based on age groups and length of exposure, more useful information for establishing a dose response would have been available for evaluation. Also, more details in how the authors determined signs and symptoms are needed.

Skeletal fluorosis

Table 2 below is copied directly from Bharati et al. (2005). For skeletal fluorosis, tingling and numbness of extremities, back pain and bending were observed in a high number of females in both areas. Males in both areas had more joint and knee pain. A higher percentage of females were unable to walk properly or do normal work compared to males in Hungund but the opposite was true in Mundargi taluk. Overall, skeletal fluorosis was more severe in Mundargi taluk (the high-F communities).

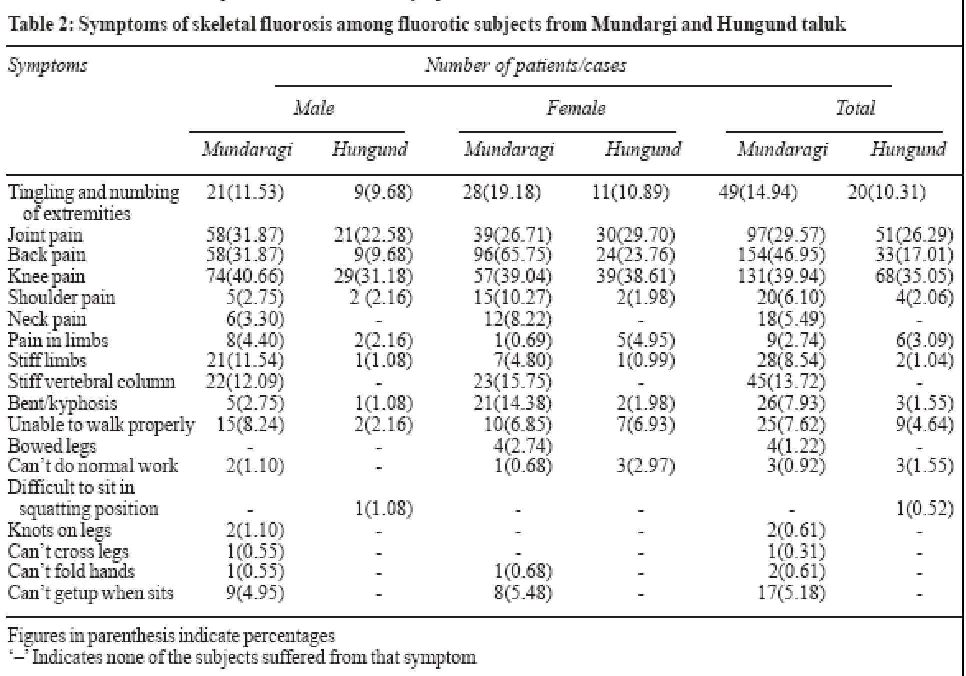


Table 2: Symptoms of skeletal fluorosis among fluorotic subjects from Mundargi and Hungund taluk

Symptoms	*Number of patients/cases*					
	Male		*Female*		*Total*	
	Mundaragi	*Hungund*	*Mundaragi*	*Hungund*	*Mundaragi*	*Hungund*
Tingling and numbing of extremities	21(11.53)	9(9.68)	28(19.18)	11(10.89)	49(14.94)	20(10.31)
Joint pain	58(31.87)	21(22.58)	39(26.71)	30(29.70)	97(29.57)	51(26.29)
Back pain	58(31.87)	9(9.68)	96(65.75)	24(23.76)	154(46.95)	33(17.01)
Knee pain	74(40.66)	29(31.18)	57(39.04)	39(38.61)	131(39.94)	68(35.05)
Shoulder pain	5(2.75)	2 (2.16)	15(10.27)	2(1.98)	20(6.10)	4(2.06)
Neck pain	6(3.30)	-	12(8.22)	-	18(5.49)	-
Pain in limbs	8(4.40)	2(2.16)	1(0.69)	5(4.95)	9(2.74)	6(3.09)
Stiff limbs	21(11.54)	1(1.08)	7(4.80)	1(0.99)	28(8.54)	2(1.04)
Stiff vertebral column	22(12.09)	-	23(15.75)	-	45(13.72)	-
Bent/kyphosis	5(2.75)	1(1.08)	21(14.38)	2(1.98)	26(7.93)	3(1.55)
Unable to walk properly	15(8.24)	2(2.16)	10(6.85)	7(6.93)	25(7.62)	9(4.64)
Bowed legs	-	-	4(2.74)		4(1.22)	-
Can't do normal work	2(1.10)	-	1(0.68)	3(2.97)	3(0.92)	3(1.55)
Difficult to sit in squatting position	-	1(1.08)	-	-	-	1(0.52)
Knots on legs	2(1.10)	-	-	-	2(0.61)	-
Can't cross legs	1(0.55)	-	-	-	1(0.31)	-
Can't fold hands	1(0.55)	-	1(0.68)	-	2(0.61)	-
Can't getup when sits	9(4.95)	-	8(5.48)	-	17(5.18)	-

Figures in parenthesis indicate percentages
'–' Indicates none of the subjects suffered from that symptom

PROFILER'S NOTE: The profiler agrees that the number of more severe findings were observed in the higher fluoride area, Mundargi taluk; however, giving the data based on age groups and length of exposure would have provided more useful information in establishing a dose response.

Also, more details in how the symptoms were determined are needed.

STUDY AUTHORS' CONCLUSIONS:		The people of Mundargi and Hungund taluk consuming water containing more than 2 ppm of fluoride were suffering from both dental and skeletal fluorosis. Major symptoms of dental fluorosis included lack of luster, browning, pain, pus and untimely loss of teeth. Skeletal fluorotic symptoms observed included tingling and numbing of extremities, pain in joints and knee, bending, stiff limbs, stiff vertebral column and unable to carry out the routine duties. Preventative measures in these villages in the form of a supply of safe drinking water and/or defluoridation of water is needed.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Bharati, P. 1996. Nutritional status and occurrence of fluorosis in selected villages of Mundargi Taluk in Dharwad District. PhD. Thesis, University of Agricultural Sciences, Dharwad. Bharati, P. and Meera Rao. 2001. Epidemiology of fluorosis in Dharwad district. Journal of Human Ecology. 14 (1): 37-42. Kubakaddi, A.B. 2001. Epidemiology of fluorosis and educational intervention in Hungund Taluk. M.H. Sc. Thesis, University of Agricultural Sciences, Dharwad. PROFILER'S NOTE: The two references that are thesis publication are not likely to be retrieved.
PROFILER'S REMARKS	***Initials/date DFG/1-07***	The study severely lacked details that could have been used for developing a dose response. The ages of the participants including their length of exposure to the fluoride, actual fluoride levels measured in the water (including analysis techniques), details on other sources of fluoride, using a widely-accepted method for measuring the degree of fluorosis and applying statistical techniques to the data were either not performed or not provided. Application of the findings of this report to exposure conditions in the United States is limited, as the levels of F concentration in US domestic drinking water are usually much lower. Despite the incomplete documentation and limited application of these findings to the US domestic drinking water debate, this paper adds background information to the limited dataset on skeletal fluorosis. No other sources of F, such as food or tea, etc., were reported in Bharati et al (2005). Focus of the study was on documenting the clinical signs of fluorosis. Water fluoride levels for the individual households were not reported, and no evaluation was made of confounding factors. Although the data did show that the community with lower fluoride levels had fewer cases of severe fluorosis, the data are insufficient for a dose-response analysis. Further, the populations studied are not comparable (regarding dental hygiene and diet) to North American domestic water consumers.
PROFILER'S ESTIM. NOEL/NOAEL		The study is not suitable for developing a NOAEL for fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL		The study is not suitable for developing a LOAEL for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable ( ), Poor (X), Medium ( ), Strong ( ) PROFILER'S NOTE: This study supports the hypothesis that the incidence of decayed and missing teeth is increased when dental fluorosis is severe, especially in areas where access to dental care is poor. There is a dramatic difference between the two populations for decay and other severe dental problems. Although this study lacks details and is incomplete, the results could possibly be combined with more robust studies for weight-of-evidence that participants exposed to ≥ 2 ppm showed signs of dental and skeletal fluorosis, noting that a key piece of information missing

	was length of exposure.
CRITICAL EFFECT(S):	Dental and skeletal fluorosis

Bottenburg, P., D. Declerck, W. Ghidey, K. Bogaerts, J. Vanobbergen and L. Martens. 2004. Prevalence and determinants of enamel fluorosis in Flemish schoolchildren. Caries Research, 38:20-28

ENDPOINT STUDIED: Dental fluorosis

TYPE OF STUDY: Cross-sectional survey of dental fluorosis prevalence and severity

POPULATION STUDIED: Belgium/Flanders: A representative cohort of Flemish schoolchildren (all born in 1989) and selected from Dept. of Education records such that each child in Flanders had an equal selection probability (stratified cluster sampling without replacement). Table 1 is copied directly from Bottenburg et al. (2004) and provides the gender, age, number and geographic location of the selected schoolchildren. For the final study, only data on 4,128 children were used. The study protocol was approved by the Ethics Committee (Catholic Univ. of Leuven) in cooperation with the Dept. of Education and Flemish Regional Administration.

Table 1. Sample characteristics of 11-year-old Flemish schoolchildren (n = 5,071)

Category	Characteristic	Children	%
Gender	male	2,668	52.6
	female	2,403	47.4
Geographic localization (province)	Antwerp	1,440	28.4
	Flemish Brabant	728	14.3
	Limburg	871	17.2
	Eastern Flanders	1,161	22.9
	Western Flanders	871	17.2
Urbanization level	city	549	10.8
	town	1,230	24.3
	suburb	954	18.8
	countryside	2,338	46.1
Educational type	private	3,414	67.3
	state	685	13.5
	province/municipal	972	19.2

PROFILER'S NOTE: The fluoride concentration associated with each individual province was not included in the study.

CONTROL POPULATION: none

EXPOSURE PERIOD: Children were first examined at age 7 (1996) and then yearly with the final examination taking place at age 12 (2001). Data in the study report was obtained when the children were 11 years old in 2000.

EXPOSURE GROUPS: Children born in 1989 in five different provinces in Flanders (Northern part of Belgium) from 3 different levels of educational systems were chosen for this study. Although originally there were 5,071 boys and girls, the data presented were based on 4,128 due to children moving, illness or other unavoidable circumstances. All children were exposed to drinking water with a fluoride concentration range of 0.47 to 1.47 mg/L.

EXPOSURE ASSESSMENT: Children were exposed to tap water which had fluoride concentrations ranging from 0.04 to 1.47 mg F/L with a median value of 0.16 mg F/L and a 75th percentile of 0.26 mg F/L. No other water quality parameters were included. Children and/or their parents were questioned on the use of fluoride supplements/toothpaste, tooth-brushing habits and diet.

ANALYTICAL METHODS:	Fluoride concentrations had been measured electrochemically in the water of different municipalities since 1982. The long-term fluoride concentration in the municipal drinking water was obtained from regional authorities (AMINAL, Brussels), water distribution organizations (Vlaamse Watermaatschappij, Heverlee) or municipal authorities; analytical techniques were not further characterized by the authors. The authors obliquely indicate that local water supplies were not artificially fluoridated: "The presence of fluorosis in a region with generally low natural fluoride concentrations in the drinking water and no artificial water fluoridation could be confirmed in the present study."
STUDY DESIGN:	Male and female schoolchildren from five different provinces within Flanders, Belgium were used in the study. Data were collected on a total of 4, 128 children. See Table 1 under Study Population for more details. The sample population was chosen using a technique of stratified cluster sampling without replacement. Children were first examined at age 7 and then yearly until age 12. Examinations were performed in a mobile dental clinic. Teeth were examined for evidence of fluorosis and caries after teeth were dried using compressed air. Questionnaires were given to the parents of the children and included the following information: teeth brushing habits, use of fluoride toothpaste, use of fluoride supplements, and dietary habits. Data for general health and urbanization level was supplied by the school health records.
PARAMETERS MONITORED:	Fluorosis was recorded one time at subject age 11 (in 2000) and on the buccal surface of fully erupted permanent teeth using the Thylstrup/Fejerskov index (TFI) (1978). (see Section 2 for description) Caries were scored at cavitation level in all deciduous and permanent teeth using a WHO/CPITN type E probe. Caries data were expressed as DMFT or DMFS in the permanent dentition or dmft and dmfs in the primary teeth. On the day of the examination, the dentist explained tooth brushing, provided dietary counselling, and distributed educational material.
STATISTICAL METHODS:	Descriptive statistics were calculated to obtain frequency distributions of different variables. Statistical analysis was also done on possible risk factors concerning prevalence and severity of fluorosis. Univariable logistic regression analysis was performed to establish the effects of the variables on the prevalence of fluorosis. Using "severity" as a continuous variable, an analysis of variance (ANOVA) was performed using the same variables as independent variables: 1) medical history, 2) sex of child, 3) level of urbanization, 4) tooth brushing frequency, 5) age tooth brushing began, 6) quantity of toothpaste used, 7) use of fluoride-containing dentrifice, 8) use of children's toothpaste, 9) use of systemic fluoride supplements, 10) age started supplements, 11) how supplements were given (in milk/not in milk), 12) administration of fluoride supplements up to age 3, 13) regularity of taking supplements, and 14) long-term mean fluoride concentration in the water system. Non-parametric tests using Wilcoxon two-sample test statistics were performed to find differences between groups of children. A simple logistic regression was used to establish a relationship between fluorosis prevalence as explanatory variable and caries experience in the deciduous and permanent dentition as outcome variable. Chi-square tests were performed to establish relationships between time points of eruption for teeth of the same quadrant (early = central incisors, and late = canines and premolars) and TFI score to evaluate possible differences in fluorosis severity between these 2 groups of teeth. Clinical examiners were pre-calibrated according to kappa values achieved after evaluation of examiner scoring of projected slides illustration various degrees of fluorosis and caries. On this basis, some candidate examiners were rejected from further participation.
RESULTS:	
Dental fluorosis	In the study, most teeth were free of fluorosis and few had a TFI exceeding 3; three individuals had a TFI of 5. Statistics indicated that brushing frequency, tap water fluoride concentration, receiving fluoride supplements and taking fluoride supplements without milk

all had a significant effect of the odds ratio for developing fluorosis. ANOVA identified no variables significantly influencing severity. Figure 1 is copied directly from Bottenberg et al. (2003). Chi-square test results were significant for severity differences between tooth 11 and 13 (p = 0.049), tooth 21 and 24 (p = 0.021) and tooth 11 and 14 (p = 0.005). Differences between teeth 21 and 23 were not significant.

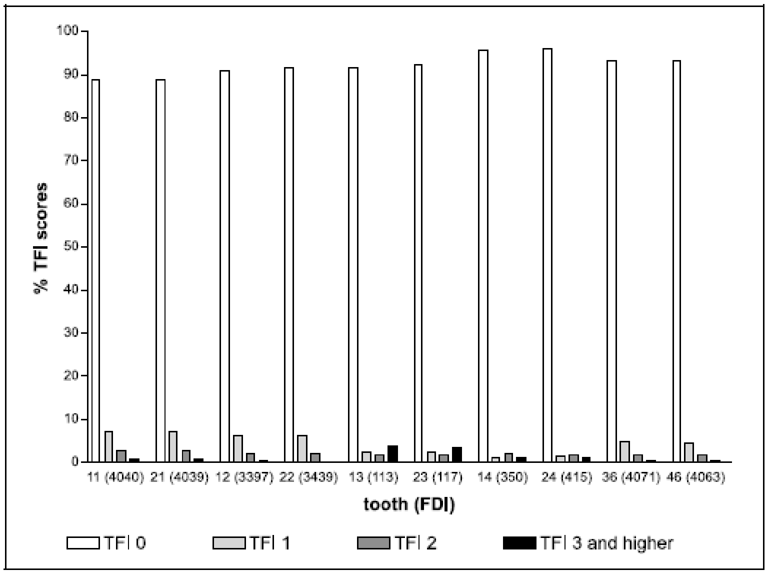


Fig. 1. Percentage distribution of fluorosis scores by tooth type (FDI two-digit system) and TFI. Numbers in parentheses refer to the number of fully erupted teeth available for examination.

PROFILER’S NOTE: While fluorosis was observed, most subjects did not exhibit a TFI score that was considered adverse. The article states that the teeth were grouped and presented in Figure 1 above by the FDI two-digit system. In the FDI system, the first digit refers to the quadrant (1 upper right, 2 upper left, 3 lower left and 4 lower right). The second digit refers to the tooth type, i.e., 1 = central incisor, 2 = laterals, 3 = canines, 4 = first molars, up through 8 which are the third molars.

Dental caries

Table 6 was copied directly from Bottenberg et al. (2004). The author stated that both in the primary and permanent dentition, decayed, missing, and filled teeth or surfaces were significantly (p<0.001) lower in children showing signs of fluorosis.

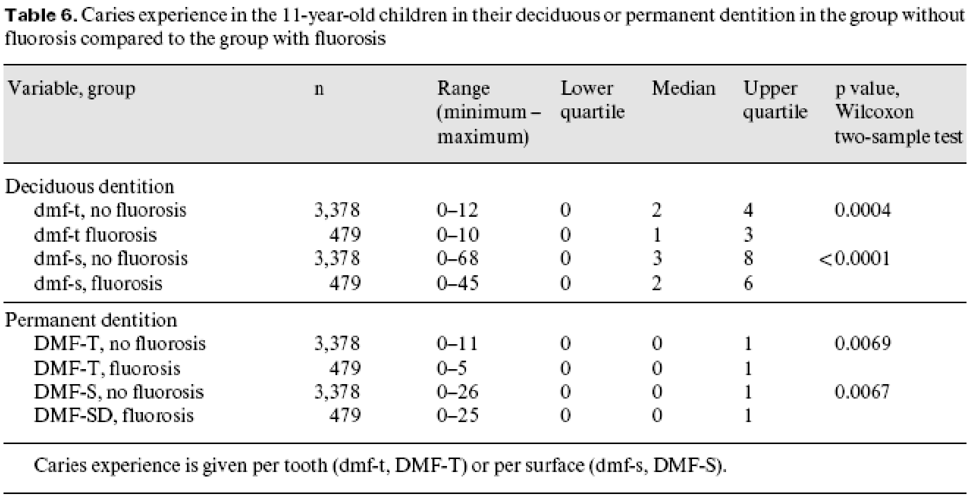


Table 6. Caries experience in the 11-year-old children in their deciduous or permanent dentition in the group without fluorosis compared to the group with fluorosis

Variable, group	n	Range (minimum – maximum)	Lower quartile	Median	Upper quartile	p value, Wilcoxon two-sample test
Deciduous dentition						
dmf-t, no fluorosis	3,378	0–12	0	2	4	0.0004
dmf-t fluorosis	479	0–10	0	1	3	
dmf-s, no fluorosis	3,378	0–68	0	3	8	<0.0001
dmf-s, fluorosis	479	0–45	0	2	6	
Permanent dentition						
DMF-T, no fluorosis	3,378	0–11	0	0	1	0.0069
DMF-T, fluorosis	479	0–5	0	0	1	
DMF-S, no fluorosis	3,378	0–26	0	0	1	0.0067
DMF-SD, fluorosis	479	0–25	0	0	1	

Caries experience is given per tooth (dmf-t, DMF-T) or per surface (dmf-s, DMF-S).

PROFILER’S NOTE: Although the data show there were less decayed, missing and filled teeth or surfaces, the TFI scores indicated fluorosis at a level that was not considered adverse, as most values were below 3.

Other variables considered.

Table 5 was copied directly from Bottenburg et al. (2004) and shows the statistical significance of all parameters measured. Tooth brushing frequency, fluoride supplement usage, taking fluoride supplements without milk and tap water fluoride concentration (>0.7 mg/L) were significant risk factors when the presence of fluorosis on at least one tooth was used as outcome variables.

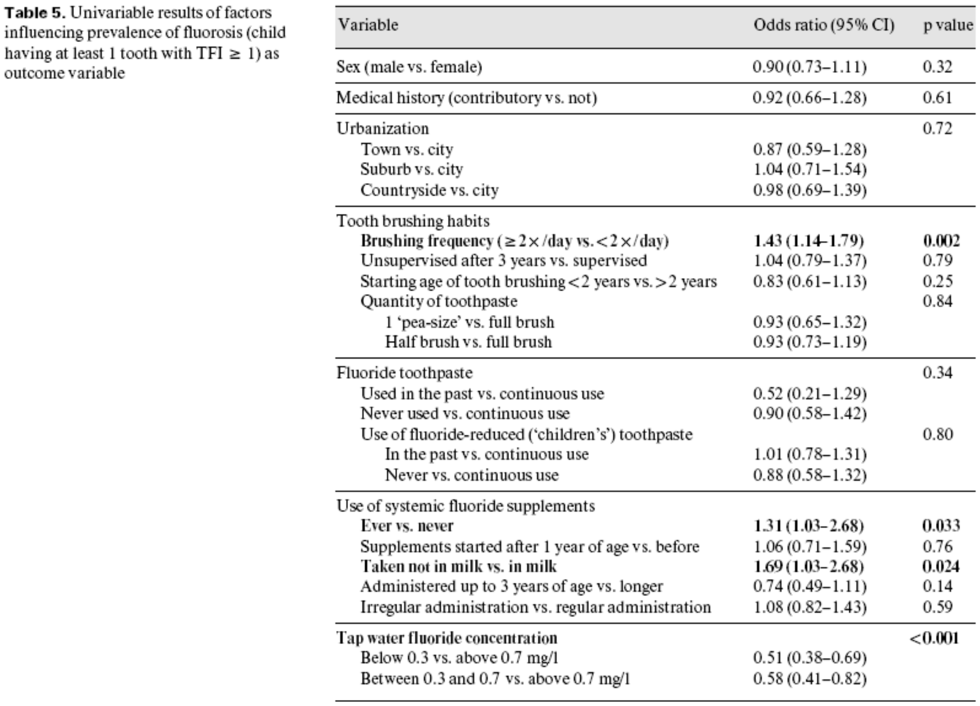


Table 5. Univariable results of factors influencing prevalence of fluorosis (child having at least 1 tooth with TFI ≥ 1) as outcome variable

Variable	Odds ratio (95% CI)	p value
Sex (male vs. female)	0.90 (0.73–1.11)	0.32
Medical history (contributory vs. not)	0.92 (0.66–1.28)	0.61
Urbanization		0.72
Town vs. city	0.87 (0.59–1.28)	
Suburb vs. city	1.04 (0.71–1.54)	
Countryside vs. city	0.98 (0.69–1.39)	
Tooth brushing habits		
Brushing frequency (≥ 2× /day vs. < 2× /day)	**1.43 (1.14–1.79)**	**0.002**
Unsupervised after 3 years vs. supervised	1.04 (0.79–1.37)	0.79
Starting age of tooth brushing < 2 years vs. > 2 years	0.83 (0.61–1.13)	0.25
Quantity of toothpaste		0.84
1 ‘pea-size’ vs. full brush	0.93 (0.65–1.32)	
Half brush vs. full brush	0.93 (0.73–1.19)	
Fluoride toothpaste		0.34
Used in the past vs. continuous use	0.52 (0.21–1.29)	
Never used vs. continuous use	0.90 (0.58–1.42)	
Use of fluoride-reduced (‘children’s’) toothpaste		0.80
In the past vs. continuous use	1.01 (0.78–1.31)	
Never vs. continuous use	0.88 (0.58–1.32)	
Use of systemic fluoride supplements		
Ever vs. never	**1.31 (1.03–2.68)**	**0.033**
Supplements started after 1 year of age vs. before	1.06 (0.71–1.59)	0.76
Taken not in milk vs. in milk	**1.69 (1.03–2.68)**	**0.024**
Administered up to 3 years of age vs. longer	0.74 (0.49–1.11)	0.14
Irregular administration vs. regular administration	1.08 (0.82–1.43)	0.59
Tap water fluoride concentration		**<0.001**
Below 0.3 vs. above 0.7 mg/l	0.51 (0.38–0.69)	
Between 0.3 and 0.7 vs. above 0.7 mg/l	0.58 (0.41–0.82)	

STUDY AUTHORS' CONCLUSIONS:

Fluorosis was present in about 10% of the children examined with most having a TFI of 1. Tooth brushing frequency, fluoride supplement use and tap water fluoride concentration (>0.7 mg/L) were significant risk factors when the presence of fluorosis on at least one tooth was used as outcome variables. Children having fluorosis had a lower risk of caries. Signs of fluorosis are low in the prevalence and severity in Flemish children and correlated to a lower caries experience. A higher proportion of teeth with TFI scores ≥2 was observed in later and slower mineralizing teeth such as canines and premolars; nevertheless, the authors point out that consideration of these latter data require precaution given the low number of late-mineralizing teeth observed among subjects.

Bottenberg et al (2004) recommend that, if fluoride sources are to be eliminated in the future, preference should be given to elimination of fluoride supplements (rather than decrease in toothpaste use or brushing frequency).

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

PROFILER'S REMARKS

Initials/date DFG 12/15/2006

The study did not correlate the incidence of fluorosis with a specific concentration of fluoride and most of the schoolchildren exhibited fluorosis in the range that is not considered adverse. The study adequately addressed all of the other variables that contribute to the fluoride exposure of a child. This study did correlate reduced caries incidence with higher levels of fluorosis, and also compared the degree of fluorosis severity in early-erupting and late-erupting teeth.

PROFILER'S ESTIM. NOEL/NOAEL	Data are not suitable for estimating a NOAEL for dental fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL	Data are not suitable for estimating a LOAEL for dental fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (X), Poor (_), Medium (_), Strong (_) The study is unsuitable to be used for dose-response modelling between fluoride in water and degree of dental fluorosis; and, as presented, the data can not be used to ascertain the threshold for severe fluorosis.
CRITICAL EFFECT(S):	Dental fluorosis; the accumulative effect of low fluoride in the drinking water and other risk factors resulted in no adverse findings in Flemish children.

Brothwell, D. J. and H. Limeback. 1999. Fluorosis risk in grade 2 students residing in a rural area with widely varying natural fluoride. Community Dent. Oral Epdemiology. 27: 130-6.

Brothwell, D. and H. Limeback. 2003. Breastfeeding is protective against dental fluorosis in a nonfluoridated rural area of Ontario, Canada. J. Hum Lact, 19(4), p. 386-390

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Prevalence and Retrospective case-control study
POPULATION STUDIED:	Canada (Ontario): 1739 children in the 2nd grade (ages 7-8 years) from 55 out of 95 local schools in a rural, non-fluoridated area of Ontario, Canada were involved in dental screenings. From these, 1367 had erupted maxillary central incisors and were scored for fluorosis. The study population consisted of children with a TSIF score of ≥ 1. Of the 1367 children scored for fluorosis, only 752 (55%) of them returned with completed questionnaires and samples of their home drinking water to be evaluated for fluoride concentration. Of the 752, 175 had a TSIF score of ≥ 1.
CONTROL POPULATION:	As explained above under Population Studied, the same children were screened to be used in the control population. The criteria for the control population was a TSIF score of 0 and of the 752 children in the study, 577 had this score.
EXPOSURE PERIOD:	Based on the questionnaires, 39% of the children had lived in their current residence since birth and 64.8% resided at their home since age 3 or less.
EXPOSURE GROUPS:	Children included in this study were part of a mandatory health program requirement for the Wellington-Dufferin-Guelph Health Unit that provided dental disease surveillance. In the 55 schools chosen, 18 were high dental need schools, 30 moderate dental need schools and 7 low dental need schools based on the number of children with an urgent need for dental treatment from the previous year. Those children in the 2nd grade that were screened and had a TSIF score of ≥ 1 made up the study group population and those with a TSIF score of 0 were used as the controls.
EXPOSURE ASSESSMENT:	Water samples from the children's homes were tested for fluoride concentrations. Questionnaires included in the study inquired about breast feeding versus bottle feeding, use of fluoride supplements, age at which tooth brushing was started, type of toothpaste used, amount of toothpaste used, routine use of fluoridated mouthwash and any professional fluoride applications.
ANALYTICAL METHODS:	Fluoride levels in the water were measured at the Faculty of Dentistry, University of Toronto, using an Orion fluoride-specific electrode. The study states that the precision of the electrode in the range of fluoride was within 1%. No other parameters were measured in the water.
STUDY DESIGN	1739 children in the 2nd grade (ages 7-8 years) from 55 out of 95 local schools in a rural, non-fluoridated area of Ontario, Canada were involved in dental screenings. One examiner performed the dental examinations in each school clinic using a portable light, mirror, explorer and gauze. Central incisors were assessed for fluorosis by TSIF score. Those children given a TSIF score were sent home with a questionnaire that assessed the following areas for possible fluoride exposure: breast- vs. bottle-feeding, infant formula, skim milk, fluoride supplements, toothbrushing, professional fluoride treatment and fluoridated mouthwash. Also included were questions in regards to satisfaction of teeth appearance, years residing in area, household income and education level. A sample of tap water was requested and a sample vial provided.
PARAMETERS	Fluorosis was scored using the 8-point Tooth Surface Index of Fluorosis (TSIF) (Horowitz et al.

MONITORED:

1984). The examiner kept laminated cards detailing the criteria and example pictures of each grade during the examination.

Other possible fluoride exposures were identified using the questionnaire, as described under Study Design, and a sample of tap water was analyzed for fluoride levels.

PROFILER'S NOTE: Details regarding the TSIF index are included in Section 2 of the report.

STATISTICAL METHODS:

Data entry and analysis were done by the principal investigator using Epi-Info 5.0 and SPSS for Windows 7.5. Bivariate analysis was used to identify possible important predictors for prevalence and severity of fluorosis. Those indicating statistically significance *($P<0.05$)* on x^2, t-test, or ANOVA were entered into multiple logistic regression to assess independent effects. The relative effect of different variables was assessed by comparing resultant odds ratios and 95% confidence intervals.

Intra-examiner reliability for the single examiner in assessing TSIF grades for the participants was assessed by re-examining 55 students in one school 6 months after the initial examination. A weighted kappa score of 0.75 indicated very good agreement. The 6-month interval was used to lessen examiner recall.

Examiner training and calibration was done using sample photographs, concurrent in-school examinations, and by developing a diagnostic decision tree. Prior to the initial examinations, inter-examiner agreement when grading TSIF on 44 photographs was assessed. All photographs were independently assigned a TSIF score by the examiner and two investigators. A weighted kappa value of 0.89 showed excellent inter-examiner agreement in grading fluorosis.

RESULTS:

Dental fluorosis

Table 1 is copied directly from Brothwell and Limeback (1999) and shows the TSIF scores for the children in the study.

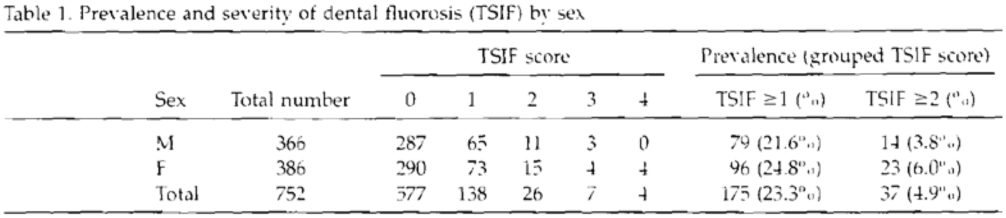


Table 1. Prevalence and severity of dental fluorosis (TSIF) by sex

		TSIF score					Prevalence (grouped TSIF score)	
Sex	Total number	0	1	2	3	4	TSIF ≥1 (%)	TSIF ≥2 (%)
M	366	287	65	11	3	0	79 (21.6%)	14 (3.8%)
F	386	290	73	15	4	4	96 (24.8%)	23 (6.0%)
Total	752	577	138	26	7	4	175 (23.3%)	37 (4.9%)

PROFILER'S NOTE: The study indicated that the majority of the children had a TSIF score of 0 and for those with evidence of fluorosis, most were given a TSIF score of ≤2. According to the NRC (2006), fluorosis is considered severe when the TSIF score is ≥5, indicating that none of the children examined exhibited severe fluorosis.

Variables associated with fluoride exposure

Table 4 was copied directly from Brothwell and Limeback (1999) and showed the results of the bivariate analysis. Bivariate analysis found that the fluoride exposures significantly (p<0.05) associated with fluorosis (TSIF ≥2) were home water fluoride concentration and fluoridated mouthwash use. Those associated with a TSIF ≥1 were home water F concentration, breast-feeding length, fluoridated mouthwash use and professional fluoride treatments. Logistic regression analysis for fluorosis (TSIF ≥1) showed the following had significant independent effects: home water F concentration, duration of breast-feeding, use of fluoride supplements and fluoridated mouthwash.

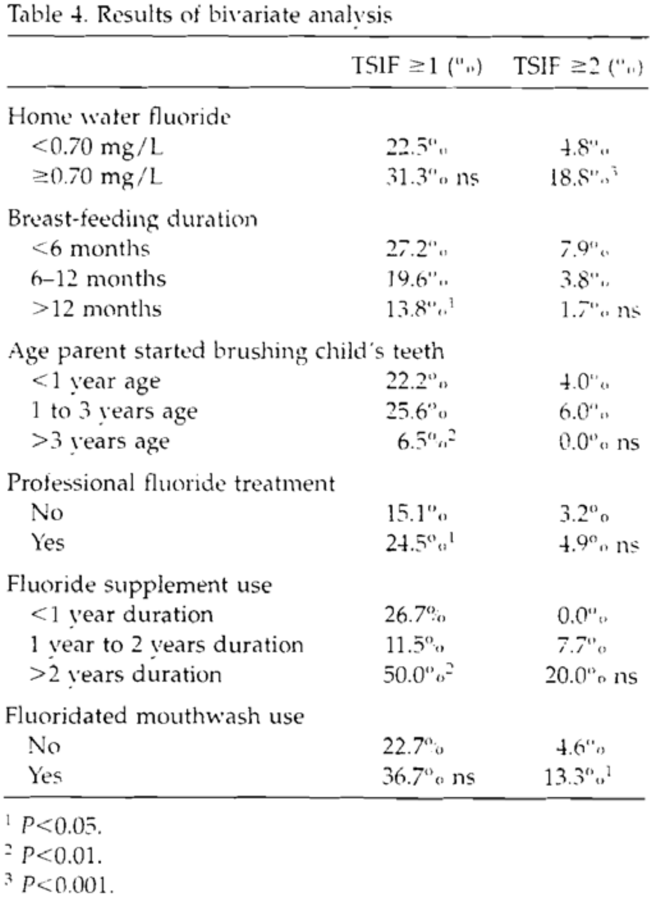


Table 4. Results of bivariate analysis

	TSIF ≥1 (%)	TSIF ≥2 (%)
Home water fluoride		
<0.70 mg/L	22.5%	4.8%
≥0.70 mg/L	31.3% ns	18.8%[3]
Breast-feeding duration		
<6 months	27.2%	7.9%
6–12 months	19.6%	3.8%
>12 months	13.8%[1]	1.7% ns
Age parent started brushing child's teeth		
<1 year age	22.2%	4.0%
1 to 3 years age	25.6%	6.0%
>3 years age	6.5%[2]	0.0% ns
Professional fluoride treatment		
No	15.1%	3.2%
Yes	24.5%[1]	4.9% ns
Fluoride supplement use		
<1 year duration	26.7%	0.0%
1 year to 2 years duration	11.5%	7.7%
>2 years duration	50.0%[2]	20.0% ns
Fluoridated mouthwash use		
No	22.7%	4.6%
Yes	36.7% ns	13.3%[1]

[1] $P<0.05$.
[2] $P<0.01$.
[3] $P<0.001$.

Figure 3 was copied directly from Brothwell and Limeback (2003) and shows a statistically significant (p<0.05) difference in the amount of time children were breastfed and the rate of fluorosis. The longer breastfeeding occurred, the less fluorosis was observed.

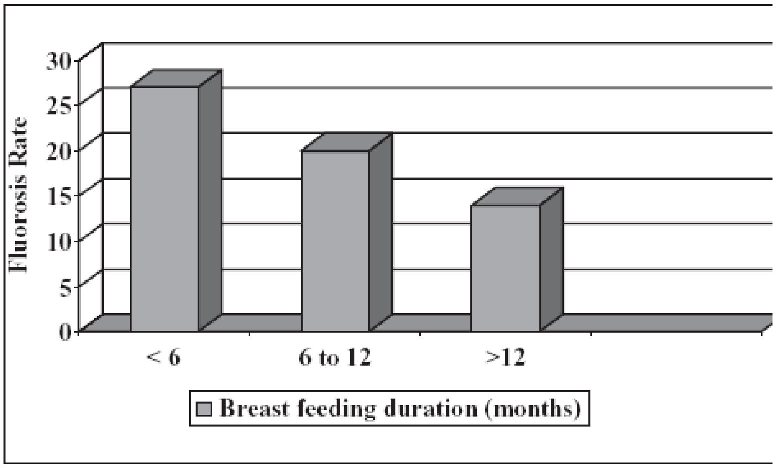


Figure 3. Unadjusted fluorosis rate by breastfeeding duration.

PROFILER'S NOTE: The profiler agrees with the findings.

STUDY AUTHORS' CONCLUSIONS:

The two journals reported on the same study but had two different objectives. The first article (1999) was a pilot study and identified risk factors that accounted for fluoride exposures in an area of non-fluoridated water. Brothwell and Limeback (1999) concluded 1) that fluorosis could be a concern even in non-fluoridated areas, 2) that fluoride supplements should not be given unless a home test for water fluoride level is performed and 3) that breast-feeding for more than

		6 months may be beneficial to preventing fluorosis in permanent incisors. In the second journal article regarding the same study, Brothwell and Limeback (2003) concentrated primarily on the conclusion that breastfeeding for ≥6 months may protect children from developing fluorosis in the permanent incisors.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		None
PROFILER'S REMARKS	***Initials/date: DFG/12-06***	The study adequately assessed most variables that contribute to a child's exposure to fluoride and reported on which would be more statistically significant providing direction for future studies. The degree of fluorosis observed in the report was not severe, however, and the profiler is unsure whether the same trends observed would be similar in areas of high fluoride or severe dental fluorosis. Adding the evidence of caries prevalence would have been helpful also to see if any correlations occurred between the degree of fluorosis and the fluoride exposures. The profiler agrees that breastfeeding longer than 6 months does appear to decrease the rate of fluorosis. This paper also includes information pertinent to relative source contribution analyses (Table 3 and others).
PROFILER'S ESTIM. NOEL/NOAEL		The data were not suitable for developing a NOAEL.
PROFILER'S ESTIM. LOEL/ LOAEL		The data were not suitable for developing a LOAEL.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( ) While the study was not suitable for indicating a dose-response, useful information as to what variables are important in assessing a child's total fluoride exposure was provided.
CRITICAL EFFECT(S):		Variables involved in assessing total fluoride exposure and the effect on dental fluorosis in young children.

Budipramana, E.S., A. Hapsoro, E.S. Irmawati and S. Kuntari. 2002. Dental fluorosis and caries prevalence in the fluorosis endemic area of Asembagus, Indonesia. International Journal of Pediatric Dentistry, 12:415-422.

ENDPOINT STUDIED: Dental fluorosis and caries

TYPE OF STUDY: Cross-sectional survey in an endemic fluorosis area.

POPULATION STUDIED: Indonesia/coastal East Java: Table 1 was copied directly from Budipramana et al. (2002) to characterize the study population of children. Gender was not specified; subject children (N= 474) were between 6-12 years old and lifetime residents of the village. All of the villages in the subdistrict of Asembagus, Indonesia had similar ethnic and socioeconomic status and drinking water supplied by local wells.

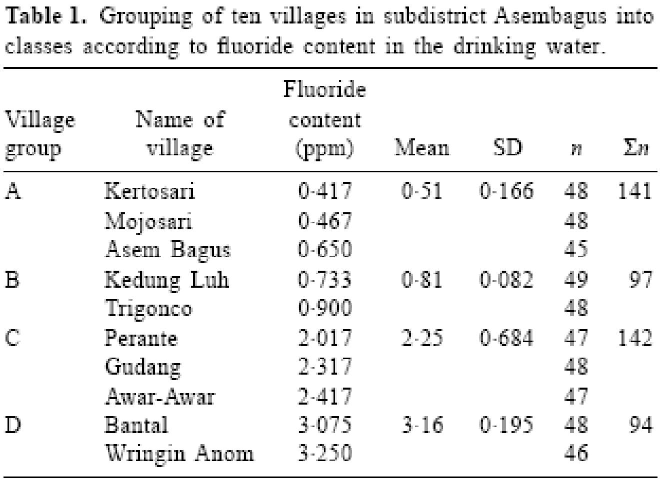


Table 1. Grouping of ten villages in subdistrict Asembagus into classes according to fluoride content in the drinking water.

Village group	Name of village	Fluoride content (ppm)	Mean	SD	*n*	Σ*n*
A	Kertosari	0·417	0·51	0·166	48	141
	Mojosari	0·467			48	
	Asem Bagus	0·650			45	
B	Kedung Luh	0·733	0·81	0·082	49	97
	Trigonco	0·900			48	
C	Perante	2·017	2·25	0·684	47	142
	Gudang	2·317			48	
	Awar-Awar	2·417			47	
D	Bantal	3·075	3·16	0·195	48	94
	Wringin Anom	3·250			46	

PROFILER'S NOTE: A confounder exists as Budipramana et al. (2002) state that in 1990, the local municipality attempted to supply water from another source to help reduce fluoride exposure. The water was considered low-fluoride (0.45 mg F/L); this attempt did not work as most of the inhabitants preferred to drink water from their own wells. The profiler is unsure if means that some of the older children (i.e. 9-12 year olds) in this study would have been exposed to this lower fluoride water (0.45 mg/L) for a period of time. The authors do not clearly state if this source of low fluoride water was actually in the villages presented in the study.

CONTROL POPULATION: None

EXPOSURE PERIOD: Subject children were 6-12 years old and were lifetime residents of the villages.

EXPOSURE GROUPS: Levels of fluoride concentrations in a sample of local drinking water are included in Table 1 above in the **Population Studied** section. Data were also collected on each child's dietary and residential history as well as drinking water consumption.

EXPOSURE ASSESSMENT: Children were assessed for exposure to fluoride in the drinking water as well as the main food items in their diet. As most of the protein diet was fish or mussels, water from the local river (the Banyu Putih River) and its fluoride concentration was (historically) measured.

ANALYTICAL METHODS: A total of three samples of water were collected in plastic containers from each village; one from each of the three different wells. Fluoride concentration in the water was determined using a Spectrophotometer UV-1201 (Shimatzu, Japan). No other water quality parameters were included in the study.

	PROFILER'S NOTE: The study states that the water samples were collected in October 1999 after a dry season and therefore, fluoride levels could have been higher than normal as the levels tended to rise after a drought and lower during the heavy rain periods. It is stated that 3 samples of water were obtained from 3 different wells within each village but the authors do not state if the samples were collected all at the same time.
STUDY DESIGN:	Gender of the study population was not specified; subjects were between 6-12 years old and lifetime residents of each study village. Subjects were chosen at random from 1 selected primary school in each of the 10 villages studied. All of the study villages were located in the subdistrict of Asembagus, Indonesia, and had similar ethnic and socioeconomic status. Children were examined for fluorosis and the incidence of caries under natural light using a sharp dental probe and mirror. Examinations for the study were performed one time during October 1999. Children were also questioned about the main food items in their diet.
PARAMETERS MONITORED:	The DMFT index was determined according to the standards of WHO (1997). The degree of fluorosis was determined using Dean's index (WHO 1997) as modified by Bischoff et al. (1976). The degree of fluorosis was graded 0-3 depending on the extent of pitting and mottling on the two teeth most affected; if the 2 teeth were unequally affected, the least affected tooth was considered. Four classes were derived: 1) normal teeth with no fluorosis. Scored as 0 2) teeth with white, opaque area with no brown staining. Classed as mild with a score of 1. 3) teeth with extensive white, opaque, mottling, irregularly scattered, brown staining and minute pitting. Classed as moderate with a score of 2 4) teeth with wide-spread brown staining and extensive pitting. Classed as severe with a score of 3. The community fluorosis index (CFI) (Dean 1942) was computed by using the following formula that calculates the average severity of scores. $\text{CFI} = \dfrac{\Sigma\ (\text{frequency x statistical weight})}{\text{No. of individuals}}$ PROFILER'S NOTE: The profiler located the paper by Bischoff et al. (1976) and the authors state they used their own method for determining the degree of fluorosis using Dean's index as a guide. Bischoff et al. (1976) only uses scores of 0-3 (see above) and Dean uses scores of 0-4 (see Section 2).
STATISTICAL METHODS:	Statistical analysis was conducted by using Kruskal-Wallis one-way ANOVA and multiple regression analysis.
RESULTS:	
Dental fluorosis	Table 3 is copied directly from Budipramana et al. (2002) and indicates the prevalence and degree of fluorosis for children in each village. Overall, 96% of the children examined had evidence of fluorosis, with most being graded as a 1 or 2, mild to moderate. There was a statistically significant (reported as p=0.000) difference in CFI between the village groups with the highest CFI being 2.03 in village group C (Perante, Gudang and Awar-Awar) which had a mean fluoride water concentration of 2.25 ppm.

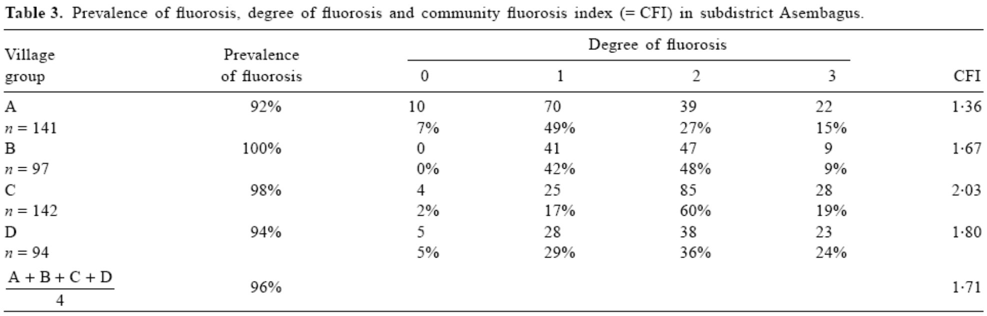


Table 3. Prevalence of fluorosis, degree of fluorosis and community fluorosis index (= CFI) in subdistrict Asembagus.

Village group	Prevalence of fluorosis	Degree of fluorosis 0	1	2	3	CFI
A	92%	10	70	39	22	1·36
n = 141		7%	49%	27%	15%	
B	100%	0	41	47	9	1·67
n = 97		0%	42%	48%	9%	
C	98%	4	25	85	28	2·03
n = 142		2%	17%	60%	19%	
D	94%	5	28	38	23	1·80
n = 94		5%	29%	36%	24%	
$\frac{A+B+C+D}{4}$	96%					1·71

PROFILER'S NOTE: From the data provided, the degree of fluorosis did not increase as the fluoride content in the water increased and the majority of cases were moderate (2).

Dental caries

Table 2 was copied directly from Budipramana et al. (2002) and shows the prevalence and distribution of caries in primary and permanent teeth. Reported means indicate that 62% of the children were caries-free for permanent teeth and 67% were caries-free for primary teeth. In this study, there were very few teeth diagnosed as missing or filled, so only data for diseased teeth (D_T- permanent or D_t- primary) were discussed. There were no statistically significant differences in the number of diseased teeth between groups of villages in either the permanent or primary teeth, but the number of diseased permanent teeth tended to increase as the fluoride levels increased. The number of diseased primary teeth decreased as the fluoride increased.

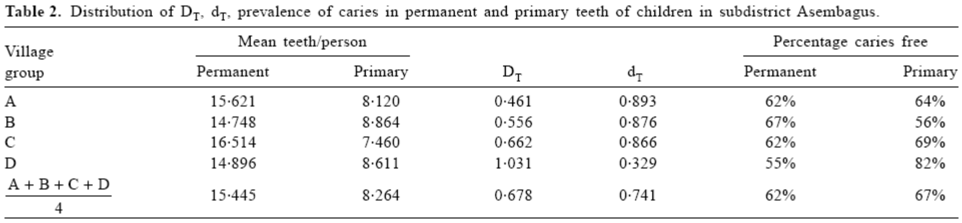


Table 2. Distribution of D_T, d_T, prevalence of caries in permanent and primary teeth of children in subdistrict Asembagus.

Village group	Mean teeth/person Permanent	Primary	D_T	d_T	Percentage caries free Permanent	Primary
A	15·621	8·120	0·461	0·893	62%	64%
B	14·748	8·864	0·556	0·876	67%	56%
C	16·514	7·460	0·662	0·866	62%	69%
D	14·896	8·611	1·031	0·329	55%	82%
$\frac{A+B+C+D}{4}$	15·445	8·264	0·678	0·741	62%	67%

PROFILER'S NOTE: The study did not correlate the degree of fluorosis with the incidence of caries, only the incidence of caries with the fluoride concentration of the water.

Food and water sources

Dietary percentages of fish, salted fish and mussels consumed as main (protein) food items as well as drinking water consumed from individual wells for each village group were included in Table 4 of the study report. The fluoride content of the Banyu Putih River was reported to be 5.0 to 5.2 mg F/L (Rai 1980); this river passed by the study villages and was the source of locally consumed fish, etc. The river is also used as a source of irrigation water for crops.

The authors further note that individual wells located near the river exhibited a high fluoride content (2.07-3.25 mg F/L), while wells located at a greater distance from the river in a less heavily irrigated area exhibited relatively low F (0.41-0.90 mg F/L).

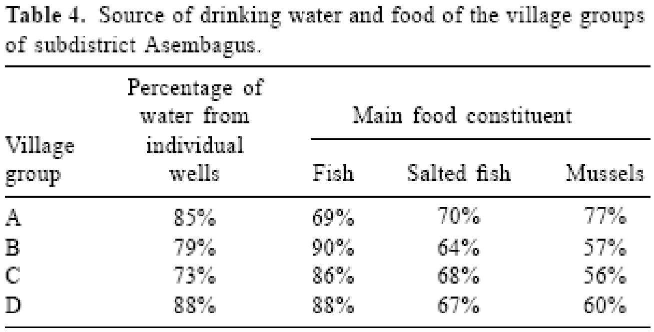


Table 4. Source of drinking water and food of the village groups of subdistrict Asembagus.

Village group	Percentage of water from individual wells	Main food constituent Fish	Salted fish	Mussels
A	85%	69%	70%	77%
B	79%	90%	64%	57%
C	73%	86%	68%	56%
D	88%	88%	67%	60%

PROFILER'S NOTE: The percentages stated in Table 4 (Budipramana et al. 2002) of the main food items do not correlate to the percentages stated in the summary at the beginning of the paper. The profiler is unsure why there is a discrepancy.

		REVIEWER'S NOTE: The Budipramana et al (2002) paper does not include a current measurement of the Banyu Putih River fluoride concentration, which is expected to fluctuate with time of year (drought, rainy season, etc.). The reported river water concentrations published by Rai (1980) were collected approximately 20 years before the time of the Budiprama et al (2002) study and may not be representative of conditions at the time of the Budipramana et al (2002) study.
STUDY AUTHORS' CONCLUSIONS:		The principal findings from this study provided evidence that dietary sources other than drinking water should be taken into account in studies of fluorosis. There was no relationship between fluoride levels in drinking water and caries, despite significant differences in dental fluorosis. The study also indicated that dental caries in primary teeth of children exposed to high concentrations of drinking water fluoride was lower than for those living in localities with less fluoride. There was a positive correlation between CFI and fluoride concentration of drinking water. PROFILER'S NOTE: In the study summary at the beginning of the paper, the author states that caries prevalence in the subdistrict was 62% for permanent teeth and 68% for primary teeth when actually the data in Table 2 (Budipramana et al. 2002) indicates that 62 and 67% were the average percentages that were ***caries free*** in the permanent and primary teeth, respectively.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Bischoff, JL, EHM Van Der Merwe, DH Retief, FH Barbakow and PE Cleaton Jones. 1976. Relationship between fluoride concentration in enamel, DMF index and degree of fluorosis in a community residing in an area with a high level of fluoride. Journal of Dental Research. 1:37-42. Rai, IGN. 1980. The relation between prevalence of endemic hypoplasia teeth in children with fluoride content in the drinking water, urine and carious teeth. PhD thesis. Surabaya, Indonesia: Airlangga University, 62-84. World Health Organization (WHO). 1997. Oral health survey, basic methods. 4th edn, Geneva: WHO: 35-35, 41-6.
PROFILER'S REMARKS	***DFG/12-06***	The profiler finds this study unacceptable due to a confounder identified and data that are stated incorrectly. While it is possible that the study summary was added at a later date and/or there was a problem with translation, the data do not reflect what is stated in the body of the report. Therefore, a dose-response could not be derived. The study also did not correlate the degree of fluorosis with the incidence of caries, only the incidence of caries with the fluoride concentration of the water. Noted fluctuations in the F concentrations of individual drinking water wells due to local climate variations (drought vs rainy conditions) and proximity to irrigation channels containing river water generate uncertainty when attempting to compare the amount of F to which subjects' teeth were exposed during enamel production and tooth eruption. The authors are aware of this and point out that F concentrations in well water fluctuate, with high concentrations during drought and lower concentrations after heavy rains; and that there is "large variation" in F concentrations between individual wells within a single community. It is thus doubtful that the reported well-water fluoride concentrations per village are representative. The above is further evidence that the Budipraman et al (2002) data are likely compromised. The reviewer concurs with the profiler's findings. Profile is approved for project officer review.
PROFILER'S ESTIM.		Not suitable for development of a NOAEL.

NOEL/NOAEL	
PROFILER’S ESTIM. LOEL/ LOAEL	Not suitable for development of a LOAEL.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (X), Poor ( ), Medium ( ), Strong ( )
CRITICAL EFFECT(S):	Dental fluorosis and caries

Chen, B.C. 1989. Epidemiological study on dental fluorosis and dental caries prevalence in communities with negligible, optimal, and above-optimal fluoride concentrations in drinking water supplies. Zhonghua Ya Yi Xue Hui Za Zhi. 8(3):117-127.

ENDPOINT STUDIED:	Dental fluorosis and dental caries
TYPE OF STUDY:	Cross-sectional survey (conducted August, 1987 to July, 1988) of dental caries and dental fluorosis.
POPULATION STUDIED:	Taiwan, Shenkang Hsiang Province: children (2,669 boys and 1438 girls) aged 6 to 16 yr old and lifelong residents of 14 communities.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	6 to 16 yrs, and beginning in1971-72 (for 16 yr olds), and beginning in1981-82 (for 6 yr olds).
EXPOSURE GROUPS:	Fourteen study sites were divided into six exposure categories based on water fluoride levels; negligible, optimal, 2 x optimal, 4 x optimal, 5 x optimal and 7 x optimal. Negligible fluoride levels were considered to be <0.4 ppm and optimal levels >0.4<0.7 ppm. The study author notes that the great majority of the population acquire their drinking water from shallow wells, and the rest from deep-wells. However, it was reported that beginning in June 1981 a communal water supply (non-fluoridated with a fluoride level of 0.09 ppm) was available to the population and was supplied to all the schools in the province. Other exposure factors, such as dietary contributions to fluoride intake and the use of fluoride dentifrice and supplements were not evaluated.
ANALYTICAL METHODS:	Fluoride levels were determined with an Orion SA 270 Ion Specific Electrode. Well water from 98 sampling sites was collected during the four seasons, and the annual average of four readings from each location was determined. Other water quality parameters, such as calcium levels, were not reported for any of the water supplies.
STUDY DESIGN	Dental fluorosis and caries incidence were evaluated in children 6 to 16 yrs old (2,669 boys and 1438 girls) residing in 14 communities in Shenkang Hsiang province, Taiwan. The communities were divided into six exposure categories based on water fluoride levels as defined by Chen et al (1989); negligible, optimal, 2 x optimal, 4 x optimal, 5 x optimal and 7 x optimal. Negligible fluoride levels were considered to be <0.4 ppm and optimal levels >0.4<0.7 ppm. The recommended range of optimal water fluoride concentrations used in the study was 0.4-0.5 ppm for the tropical zones of Taiwan and 0.6-0.7 ppm for the subtropical zone, and is based on zone-specific water consumption rates. Dental fluorosis was scored using TSIF and the Dean Fluorosis Index. Caries incidence was scored using the DMFS index. Statistical analysis was carried out using Student's t-test, Chi-square, analysis of variance, and multiple regression.
PARAMETERS MONITORED:	Tooth surface index of fluorosis (TSIF) and the Dean Fluorosis Index (FI) were utilized in the examinations (see Section 2 for definitions and descriptions). Radiographs were not taken. Caries incidence was scored using the DMFT index (see List of Acronyms for definition). A Community Fluorosis Index (CFI) and the public health significance of the fluorosis problem were determined for each village using the methodology of Dean (1946)..
STATISTICAL METHODS:	Student's t-test, Chi-square, analysis of variance, and multiple regression. The level of significance used was p<0.05. Scheffe's method for multiple comparison was used to compare pairs of CFI scores and pairs of DMFT scores. No other specific information was provided on statistical methods.

RESULTS:

Results of the study are shown in Tables 1, 2 and 5 copied directly from Chen (1989):

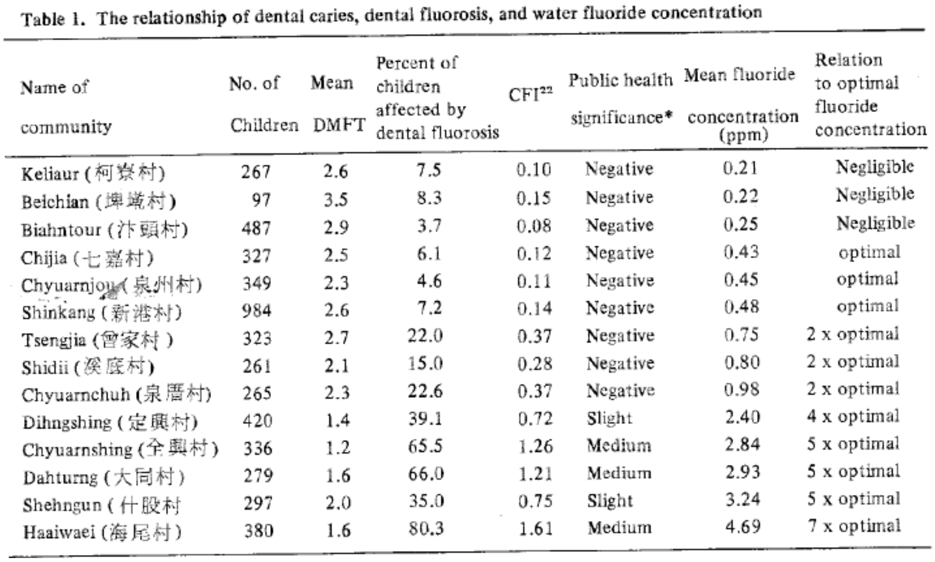


Table 1. The relationship of dental caries, dental fluorosis, and water fluoride concentration

Name of community	No. of Children	Mean DMFT	Percent of children affected by dental fluorosis	CFI[22]	Public health significance*	Mean fluoride concentration (ppm)	Relation to optimal fluoride concentration
Keliaur (柯寮村)	267	2.6	7.5	0.10	Negative	0.21	Negligible
Beichian (埤崁村)	97	3.5	8.3	0.15	Negative	0.22	Negligible
Biahntour (汴頭村)	487	2.9	3.7	0.08	Negative	0.25	Negligible
Chijia (七嘉村)	327	2.5	6.1	0.12	Negative	0.43	optimal
Chyuarnjou (泉州村)	349	2.3	4.6	0.11	Negative	0.45	optimal
Shinkang (新港村)	984	2.6	7.2	0.14	Negative	0.48	optimal
Tsengjia (曾家村)	323	2.7	22.0	0.37	Negative	0.75	2 x optimal
Shidii (溪底村)	261	2.1	15.0	0.28	Negative	0.80	2 x optimal
Chyuarnchuh (泉厝村)	265	2.3	22.6	0.37	Negative	0.98	2 x optimal
Dihngshing (定興村)	420	1.4	39.1	0.72	Slight	2.40	4 x optimal
Chyuarnshing (全興村)	336	1.2	65.5	1.26	Medium	2.84	5 x optimal
Dahturng (大同村)	279	1.6	66.0	1.21	Medium	2.93	5 x optimal
Shehngun (什股村	297	2.0	35.0	0.75	Slight	3.24	5 x optimal
Haaiwaei (海尾村)	380	1.6	80.3	1.61	Medium	4.69	7 x optimal

DMFT = decayed, missing, filled permanent teeth index (Klein et al., 1938; Knutson et al., 1940); CFI = Community Fluorosis Index (Dean, 1942: 0-0.4, negative; 0.4-0.6 borderline; 0.6-1.0, slight; 1.0-2.0, medium; 2.0-3.0 marked; 3.0-4.0, very marked): Optimal fluoride concentration as defined by Chen et al (1989) = >0.4<0.7 ppm.

Information on the relationship between fluoride levels, fluorosis scores, and CFI are given in Table 2 copied directly from Chen (1989):

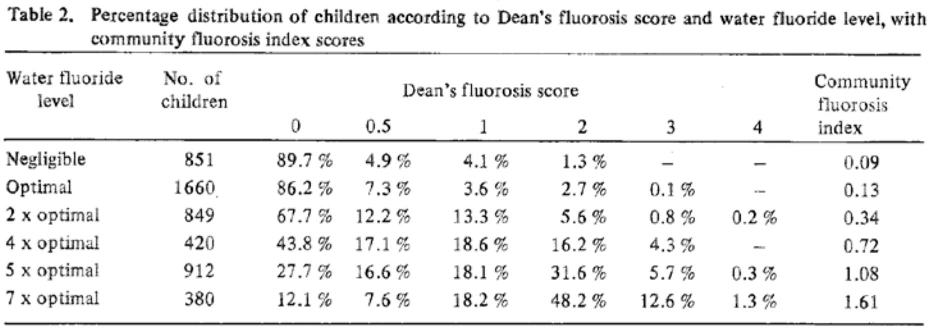


Table 2. Percentage distribution of children according to Dean's fluorosis score and water fluoride level, with community fluorosis index scores

Water fluoride level	No. of children	Dean's fluorosis score						Community fluorosis index
		0	0.5	1	2	3	4	
Negligible	851	89.7 %	4.9 %	4.1 %	1.3 %	–	–	0.09
Optimal	1660	86.2 %	7.3 %	3.6 %	2.7 %	0.1 %	–	0.13
2 x optimal	849	67.7 %	12.2 %	13.3 %	5.6 %	0.8 %	0.2 %	0.34
4 x optimal	420	43.8 %	17.1 %	18.6 %	16.2 %	4.3 %	–	0.72
5 x optimal	912	27.7 %	16.6 %	18.1 %	31.6 %	5.7 %	0.3 %	1.08
7 x optimal	380	12.1 %	7.6 %	18.2 %	48.2 %	12.6 %	1.3 %	1.61

A dash (—) equals 0%; Fluorosis scores: 0 = none, 0.5 = questionable; 1 = very mild; 2= mild; 3= moderate; 4 = severe.

The report indicates that compared with the negligible exposure group, DMFT scores were 10.7% lower in the optimal fluoride area, 14.3% lower in the 2 x optimal area, 50.0% lower in the 4 x optimal area, 42.9% lower in the 5 x optimal area, and 42.9% lower in the 7 x optimal area (statistically significant, p<0.05, only in the latter three groups).

Table 5 from Chen (1989) indicates that older children exhibit higher levels of fluorosis than younger children as indicated by the Tooth Surface Index of Fluorosis (TSIF, see Section 2); TSIF scores of 1-3 indicate parchment-white areas of enamel of gradually increasing size but no pitting or brown stain; a TSIF of 3 indicates white discoloration over ≥2/3 of the enamel surface). Chen et al do not speculate on the observed finding that "tooth surfaces of 13-16 year olds are more affected by fluorosis…irrespective of water fluoride level" (p. 122).

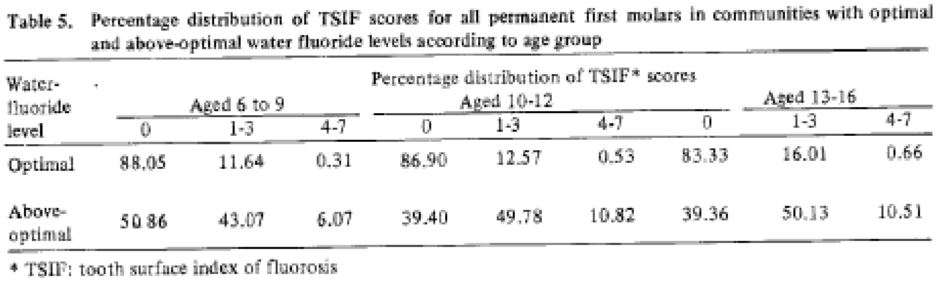


Table 5. Percentage distribution of TSIF scores for all permanent first molars in communities with optimal and above-optimal water fluoride levels according to age group

Water-fluoride level	Percentage distribution of TSIF* scores								
	Aged 6 to 9			Aged 10-12			Aged 13-16		
	0	1-3	4-7	0	1-3	4-7	0	1-3	4-7
Optimal	88.05	11.64	0.31	86.90	12.57	0.53	83.33	16.01	0.66
Above-optimal	50 86	43.07	6.07	39.40	49.78	10.82	39.36	50.13	10.51

* TSIF: tooth surface index of fluorosis

In the TSIF scoring system, a score of 4 indicates brown staining; 5 indicates pitting, and 7 indicates confluent pitting with enamel missing (see Section 2 for a more complete description of the system)

STUDY AUTHORS' CONCLUSIONS:

The prevalence and severity of fluorosis are distinctly greater in all areas with higher than optimal fluoride levels. Severe fluorosis occurred in 0.2% of the children in the 2X optimal group, 0% in the 4X group, 0.3% in the 5X group, and in 1.3% in the 7X group. Data from children residing in the optimal and above optimal fluoride areas show that older children are affected more by fluorosis than younger children, according to the Tooth Surface Index of Fluorosis.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

Dean, H.T. 1946. Epidemiological studies in the United States. In: "Dental Caries and Fluorine". F.R. Moulton, ed., American Association for the Advancement of Science., Washington, DC.

Galagan , D.G., and G.G. Lamson. 1953. Climate and endemic dental fluorosis. Pub. Health. Rept. 68:496-508.

Klein, H., C.E. Palmer, and J.W. Knutson. 1938. Studies on the dental needs of elementary school children. Pub. Health Report 53:751-765.

Knutson, J.W., H. Klein, and C.E. Palmer. 1940. Dental needs of grade school children of Hagerstown, Maryland. J. Amer. Dent. Assoc. 27:579-588.

PROFILER'S REMARKS

Initials/Date
DMO 2/18/06 and 2/08/07

The study has several weaknesses that impact it suitability for application to US populations. Fluoride levels in the environment are high in certain areas of China because of fluoride presence in the coals used for fuel. Anthropogenic fluoride may be reflected in the water concentrations because of wet and/or dry deposition, or may not be if all the water sources are ground water. The authors also do not estimate other sources of exposure (ambient air, food). Tea, a beverage favoured by the Chinese, is a food with a relatively high level of fluoride. The data are further confounded by the introduction of a communal water supply of relatively low fluoride (0.09 ppm) which was used in the school system beginning in June of 1981).

The "optimal" F levels in this study (0.4-0.7 mg/L for tropical and subtropical climate zones) are different from those used by the US PHS, where "optimal" is defined as 0.7 mg/L for a "warm" climate and up to 1.2 mg/L for a cool climate. The user is cautioned to make allowance for these geographically different definitions of "optimal."

Chen (1989) notes that his results are supported by earlier studies by Dean (1942), and Galagan and Lamson (1953). The latter authors did show increasing fluorosis with increasing fluoride levels at concentrations similar to those reported by Chen (1989) [see profiles on the Dean (1942) and Galagan and Lamson (1953) studies]. Further, if communities with similar climates and drinking water fluoride levels are compared, the percentages of the population with fluorosis (Dean scores ≥ 1) are similar (i.e., in the Galagan and Lamson (1953) studies, 3-10% of the population in communities in the southwest US with 0.4-0.5 ppm fluoride in their water had fluorosis, compared to 4.6-7.2% reported in the Chen study.

Chen reported that children 12-13 yrs old had higher levels of fluorosis than 8-9 yr olds.

		Dean (1942) states that 12-14 yr olds were the preferred age group for fluorosis studies in areas with low fluoride water levels because “this permits the examination of a group in whom a high percentage (approximately 94%) of the permanent teeth have erupted”. Dean further states that inclusion of children as young as 9 years old “seemingly makes little material difference when the group has been exposed to relatively high water fluoride levels (e.g., over 2.0 ppm of F)”, but would introduce an “error of considerable magnitude” if included in studies where fluoride levels were lower, because fluorosis in non-erupted teeth would not be included in the analysis.
PROFILER’s ESTIM. NOAEL		Could be possible with further statistical assessment.
PROFILER’S ESTIM. LOAEL		A low incidence of severe fluorosis was found in the 0.8-1.4 ppm F (2X optimal), 2-3.5 ppm F (5X) and 2.8-4.9 ppm F (7X) groups, but not in the 1.6-2.8 ppm F (4X) group. Therefore the data need to be examined statistically to determine whether the incidence in the 2X group is significant.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor (X), Medium (_), Strong (_) Severe fluorosis (DFI of 4) was reported in three of the six exposure groups (see Table 2 above); however, a dose response was not seen across the 2X and 4X optimal groups; therefore, modeling may not provide a statistically reliable result.

Chibole, Opati. 1987. Epidemiology of dental fluorosis in Kenya. J.R.S.H., p. 242-243

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Cross-sectional survey of native inhabitants within specific provinces/districts of Kenya, Africa. There were eight provinces evaluated and they included: Central, Coast, Eastern, North Eastern, Nyanza, Rift Valley, Western and Nairobi. The provinces were further divided into districts (see Table 2 below in Results section).
POPULATION STUDIED:	Over 34,000 people (ages or gender not specified) native (born and raised) to each specific region were examined.
CONTROL POPULATION:	none
EXPOSURE PERIOD:	Individuals were examined from 1979-1982 to determine the prevalence of dental fluorosis.
EXPOSURE GROUPS:	Individuals from each specific Kenyan region were examined separately for evidence of dental fluorosis occurring from exposure to the ground water. There were eight (8) different provinces in the study with a further breakdown to districts within each province (See Tables 1 and 2 below under Results section).
EXPOSURE ASSESSMENT:	Study participants underwent a mouth examination with dental probes and mirrors using natural light as the source of illumination.
ANALYTICAL METHODS:	Analytical methods for measuring fluoride concentrations in the water were not provided in this study.
STUDY DESIGN	Over 34,000 people from different areas in Kenya were examined at various schools, hospitals and the Dental School of the University of Nairobi with mouth mirrors and dental probes using natural daylight. These surveys took place during 1979-1982 and included only those native to the regions listed. Individuals were examined for evidence of dental fluorosis.
PARAMETERS MONITORED:	The following scale was developed by Chibole (1987) to be used to assess the degree of fluorosis; however, no data on the prevalence of study participants exhibiting each score were reported. Degree 0: no mottling Degree 1: white or light brown patches on parts of the coronal surfaces of teeth Degree 2: dark brown patches on parts of the coronal surfaces of teeth Degree 3: brown discolouration of the entire crown Degree 4: brown discolouration associated with fracture of the enamel and presence of pitting or cracks on enamel.
STATISTICAL METHODS:	Chibole (1987) stated that data were used from an earlier report (Gitonga and Nair, 1982) that compared the population with fluorosis to the proportion of those ingesting borehole water having fluoride levels greater than 1 ppm. A positive correlation was made with the Pearson's "r" value being 0.65, and the probability that this correlation occurred by chance was less than once in a hundred ($p<0.01$). However, no data specifically characterizing the water fluoride levels by province or district were provided.
RESULTS:	Results for the incidence of fluorosis are provided in Tables 1 and 2 copied directly from Chibole (1987). The author did not provide data characterizing the observed fluorosis prevalence by score (i.e. Degrees 0-4). Table 1 shows the % fluorosis present in each province with the total incidence of fluorosis in Kenya being 32.2%. Table 2

indicates a further breakdown of data by providing the incidence of the population with fluorosis from the districts within each province.

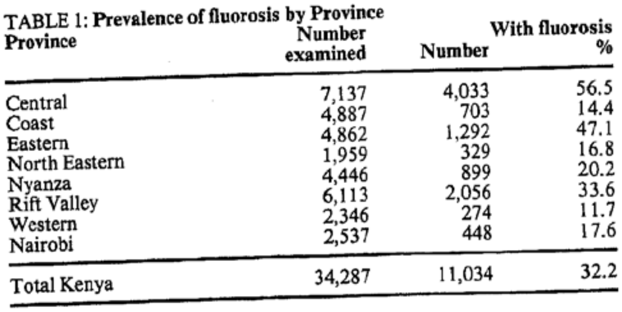


TABLE 1: Prevalence of fluorosis by Province

Province	Number examined	With fluorosis Number	%
Central	7,137	4,033	56.5
Coast	4,887	703	14.4
Eastern	4,862	1,292	47.1
North Eastern	1,959	329	16.8
Nyanza	4,446	899	20.2
Rift Valley	6,113	2,056	33.6
Western	2,346	274	11.7
Nairobi	2,537	448	17.6
Total Kenya	34,287	11,034	32.2

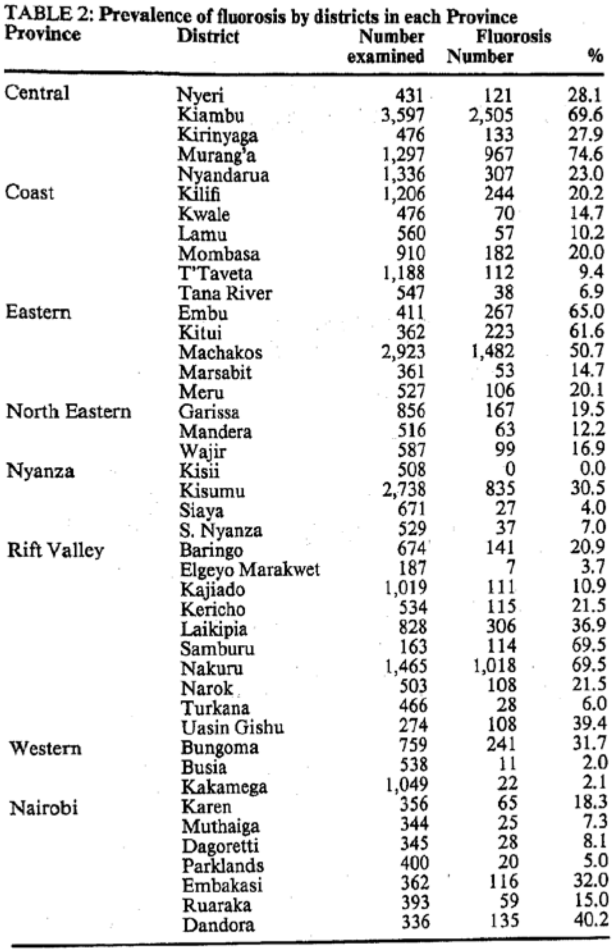


TABLE 2: Prevalence of fluorosis by districts in each Province

Province	District	Number examined	Fluorosis Number	%
Central	Nyeri	431	121	28.1
	Kiambu	3,597	2,505	69.6
	Kirinyaga	476	133	27.9
	Murang'a	1,297	967	74.6
	Nyandarua	1,336	307	23.0
Coast	Kilifi	1,206	244	20.2
	Kwale	476	70	14.7
	Lamu	560	57	10.2
	Mombasa	910	182	20.0
	T'Taveta	1,188	112	9.4
	Tana River	547	38	6.9
Eastern	Embu	411	267	65.0
	Kitui	362	223	61.6
	Machakos	2,923	1,482	50.7
	Marsabit	361	53	14.7
	Meru	527	106	20.1
North Eastern	Garissa	856	167	19.5
	Mandera	516	63	12.2
	Wajir	587	99	16.9
Nyanza	Kisii	508	0	0.0
	Kisumu	2,738	835	30.5
	Siaya	671	27	4.0
	S. Nyanza	529	37	7.0
Rift Valley	Baringo	674	141	20.9
	Elgeyo Marakwet	187	7	3.7
	Kajiado	1,019	111	10.9
	Kericho	534	115	21.5
	Laikipia	828	306	36.9
	Samburu	163	114	69.5
	Nakuru	1,465	1,018	69.5
	Narok	503	108	21.5
	Turkana	466	28	6.0
	Uasin Gishu	274	108	39.4
Western	Bungoma	759	241	31.7
	Busia	538	11	2.0
	Kakamega	1,049	22	2.1
Nairobi	Karen	356	65	18.3
	Muthaiga	344	25	7.3
	Dagoretti	345	28	8.1
	Parklands	400	20	5.0
	Embakasi	362	116	32.0
	Ruaraka	393	59	15.0
	Dandora	336	135	40.2

PROFILER'S NOTE: Based on the data provided, it is unclear as to what score characterizes "fluorosis". Chibole (1987) does not indicate whether the number considered having fluorosis are those with a degree of ≥ 1 or some other criteria.

STUDY AUTHORS' CONCLUSIONS:

Although the national level for the prevalence of dental fluorosis in Kenya is about 32%, the prevalence was observed to be higher in areas where the population is totally dependant on ground water (i.e. Rift Valley; see Table 2 of report). The author states the need for more frequent monitoring of the ground water for fluoride levels and for effective methods of defluoridation of water to stop endemic cases of fluorosis.

DEFINITIONS AND

Gitonga, J.N. and K.R. Nair. 1982. The rural water fluorides project technical report.

REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		IDRC/University of Nairobi and Ministry of Water Development, Kenya.
PROFILER'S REMARKS	***DFG/11-06 and 12/14/06***	The study is not suitable for development of dose response for fluoride. Although the author provides an assessment on how the degree of fluorosis was evaluated, neither these data nor results were included. The degree of fluorosis present in the population examined would have been extremely helpful for evaluation of this study. Further, actual measured values for the groundwater fluoride concentration from a specific province were not included. As a consequence the profiler is unable to determine a correlation between fluoride exposure levels and the incidence of fluorosis. The data showed wide variation in the incidence of fluorosis between districts within the same Province. The profiler is unsure if other sources of fluoride could be causing these variations because no fluoride concentration levels were included.
PROFILER'S ESTIM. NOEL/NOAEL		The profiler is unable to derive any values from the study due to insufficient data reported.
PROFILER'S ESTIM. LOEL/ LOAEL		The profiler is unable to derive any values from the study due to insufficient data reported.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( )
CRITICAL EFFECT(S):		Dental fluorosis

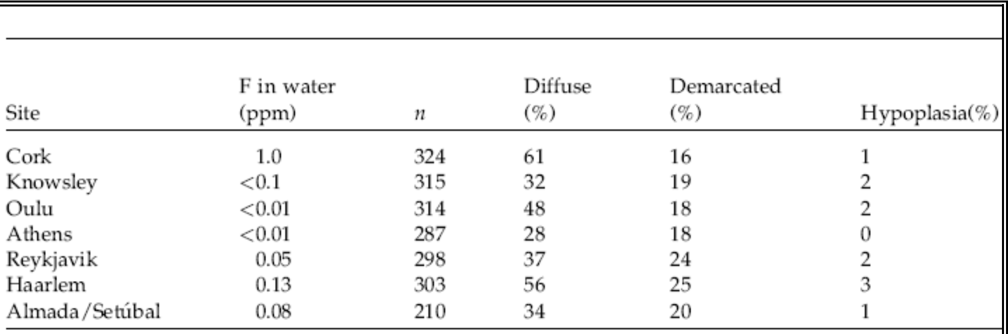
Cochran, J.A., C.E. Ketley, I.B. Árnadóttir, B. Fernandes, H. Koletsi-Kounari, A-M. Oila, C. van Loveren, H.P. Whelton and D.M. O’Mullane. 2004a. A comparison of the prevalence of fluorosis in 8-year-old children from seven European study sites using a standardized methodology. Community Dent. Oral Epidemiol, 32 (Suppl. 1): 28-33.

Cochran, J.A., C.E. Ketley, L. Sanches, E. Mamai-Homata, A-M. Oila, I.B. Árnadóttir, C. van Loveren, H.P. Whelton and D.M. O’Mullane. 2004b. A standardized photographic method for evaluating enamel opacities including fluorosis. Community Dent. Oral Epidemiol, 32 (Suppl. 1): 19-27.

PROFILER’S NOTE: Both articles were published in the same journal and will be evaluated in the same profile. The 2004a article presents the study details and the 2004b article more thoroughly describes the photographic method used for standardizing study data.

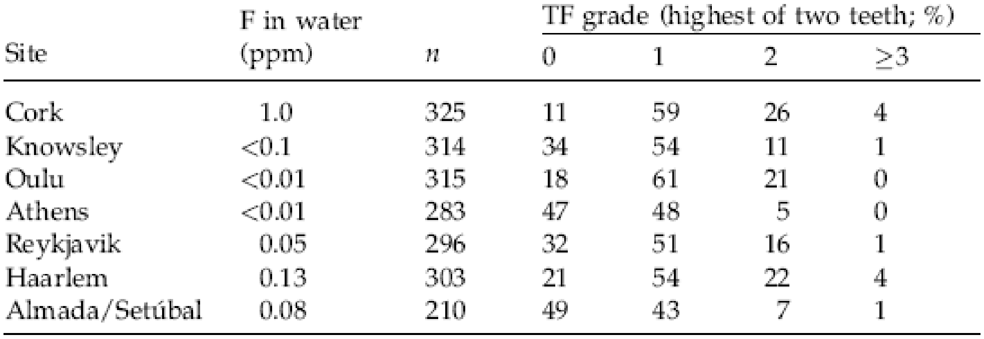
<table>
<tr><td colspan="2"></td></tr>
<tr><td>ENDPOINT STUDIED:</td><td>Dental fluorosis (enamel opacities)</td></tr>
<tr><td></td><td></td></tr>
<tr><td>TYPE OF STUDY:</td><td>Cross-sectional survey</td></tr>
<tr><td></td><td></td></tr>
<tr><td>POPULATION STUDIED:</td><td>Europe: Cork, Ireland; Knowsley, a suburb of Liverpool, England; a suburb (name not given) in Athens, Greece; Haarlem, a town near Amsterdam in the Netherlands; Oulu in the north of Finland; Reykjavik, capital of Iceland; and Almada and Setúbal, both suburbs of Lisbon in Portugal. Approximately 300 eight-year-old schoolchildren were randomly selected from each of these seven European sites.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>CONTROL POPULATION:</td><td>None</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE PERIOD:</td><td>Fluoride levels from water sources were obtained for a 10-year period (1988-1998) including the 8 years the children were exposed. The children were asked about their residential history but the residential data were not included.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE GROUPS:</td><td>The following table shows the concentration (ppm) of fluoride in the water and the number of participants at each specific site. Only the water in Cork, Ireland was artificially fluoridated (to a concentration between 0.8 and 1.0 ppm); fluoride in drinking water occurred naturally at the other sites.
<table>
<tr><th>Site</th><th>No. of children</th><th>Fluoride concentration (ppm)</th></tr>
<tr><td>Cork (Ireland)</td><td>324</td><td>1.0</td></tr>
<tr><td>Knowsley (England)*</td><td>315</td><td><0.1</td></tr>
<tr><td>Oulu (Finland)*</td><td>314</td><td><0.01</td></tr>
<tr><td>Athens (Greece)*</td><td>287</td><td><0.01</td></tr>
<tr><td>Reykjavik (Iceland)*</td><td>298</td><td>0.05</td></tr>
<tr><td>Haarlem (Netherlands)**</td><td>303</td><td>0.13</td></tr>
<tr><td>Almada/ Setúbal (Portugal)*</td><td>210</td><td>0.08</td></tr>
</table>
*Fluoride concentrations reported annually.
**Fluoride levels fluctuated between 0.1 and 0.15 ppm for the 10-year period.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE ASSESSMENT:</td><td>Only fluoride in the tap water from each area was measured. Parents of the participants were given a questionnaire to inquire about use of fluoride supplements, history of living in area, age when toothpaste was first used, and the amount and type of toothpaste used. Care was taken to ensure the same concepts were expressed in the different languages on all of the questionnaires.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>ANALYTICAL METHODS:</td><td>Fluoride levels in the local drinking water were obtained for 10 years, 1988-1998, including the period the study children were exposed. How the water was analyzed for fluoride was not included in the study report. No other water parameters were reported.</td></tr>
</table>

STUDY DESIGN	Data were collected from Fall 1997 to February 1998. Several schools in each area representing a wide socioeconomic basis were chosen. From these schools, children in the 8-year-old range were invited to participate. Cochran, the study lead author, was responsible for teaching one dentist in each area the photographic technique that was used in the study. All seven dentists used the same camera with an identical set-up (i.e. lenses/flashes). Film used was bought at the same location and originated from the same production batch. The study author had several “training” sessions with dentists from each location to ensure the photographic technique was similar. This involved a training session at Cork and also two “pilot” studies at each location. After each pilot session, discussions were held and technical problems addressed and corrected prior to the actual study. Before being photographed, each child cleaned their teeth without water or toothpaste using a new toothbrush. For the photograph, each child was positioned against a wall, a cheek retractor placed and the incisors kept closed with edge-to-edge contact. A piece of damp cotton wool was used to keep teeth damp. Two timed photographs were taken of the permanent, maxillary incisors, one after 8 seconds for a wet photograph and one after 105 seconds for a dry photograph. While taking the photographs, the camera was held at a 45° angle to minimize reflections and lip shadows. All film was then sent to London and developed in one laboratory. The resulting transparencies were then randomized, viewed blindly and scored for fluorosis by Cochran. Questionnaires were also completed to determine if fluoride supplements had been used, residential history, age when started using toothpaste and the type and amount of toothpaste used. From the total of 5250 transparencies taken, 114 (2.2%) were not suitable for analysis. During the study, the intra-examiner reproducibility of each photographer was measured by taking a repeat photo for 15% of the transparencies; inter-examiner reproducibility was measured by the study author visiting each study site and repeating 15% of the photographs.
PARAMETERS MONITORED:	The photographs taken after 8 seconds, when the teeth were still wet, were examined for fluorosis based on the Developmental Defects of Enamel (DDE) index (FDI Commission on Oral Health 1982), and those taken after 105 seconds, when teeth were dry, used the Thylstrup and Fejerskov (TF) index (Thylstrup and Fejerskov 1978). PROFILER’S NOTE: The DDE index (FDI Commission on Oral Health 1982) used in the study is not recognized in the NRC document (2006) as a true measure of fluorosis as it emphasizes aesthetic concerns and is not based on etiologic considerations. The TF index is described in Section 2 of the report.
STATISTICAL METHODS:	Logistic regression was used to determine which variables to which the children were exposed were most important in relationship to fluorosis. To summarize the variability in the data for the range of time periods when the photographs were taken, box-and-whisker charts were plotted. The level of agreement between pairs of grades was determined using Cohen’s kappa statistic (Cohen 1960).
RESULTS:	
Dental fluorosis	Tables 1 and 2 are copied directly from the study report (Cochran et al. 2004a) and show the prevalence of fluorosis in both wet and dry teeth. With the DDE index, Cork had the greatest percentage of diffuse lesions with Haarlem having the greatest overall prevalence. In the TF index, Cork and Haalem had the greatest number of children (4) with the most severe TF score (≥3); although most children exhibited only mild fluorosis. Table 1. Percentage of subjects with at least one permanent maxillary central incisor affected by diffuse or demarcated opacities or hypoplasia and overall prevalence of enamel defects as graded by one examiner from transparencies taken of “wet” teeth measured using the DDE index.



Site	F in water (ppm)	*n*	Diffuse (%)	Demarcated (%)	Hypoplasia(%)
Cork	1.0	324	61	16	1
Knowsley	<0.1	315	32	19	2
Oulu	<0.01	314	48	18	2
Athens	<0.01	287	28	18	0
Reykjavik	0.05	298	37	24	2
Haarlem	0.13	303	56	25	3
Almada/Setúbal	0.08	210	34	20	1

Table 2. Percentage of subjects with each grade of the TF index (highest grade of 2 teeth) as graded by one examiner from transparencies taken of ‘dry’ teeth.



Site	F in water (ppm)	*n*	TF grade (highest of two teeth; %)			
			0	1	2	≥3
Cork	1.0	325	11	59	26	4
Knowsley	<0.1	314	34	54	11	1
Oulu	<0.01	315	18	61	21	0
Athens	<0.01	283	47	48	5	0
Reykjavik	0.05	296	32	51	16	1
Haarlem	0.13	303	21	54	22	4
Almada/Setúbal	0.08	210	49	43	7	1

PROFILER’S NOTE: For consistency, the same scoring technique should have been applied for both the wet and dry teeth. The study stated that Cochran (study author) had examined the two transparencies using either just the TF or just the DDE index but did not report why the final decision to combine the two different scoring indices was made. The upper endpoint for the TF index should have been included as it is unclear when stated as greater than or equal to 3.

Reproducibility for the DDE and TF indices

Table 1 is copied directly from Cochran et al. (2004b) and shows the kappa score and percent agreement for inter- and intra-examiner agreement. Most agreements ranked as good and the scale used was Cohen’s kappa statistic (Cohen 1960).

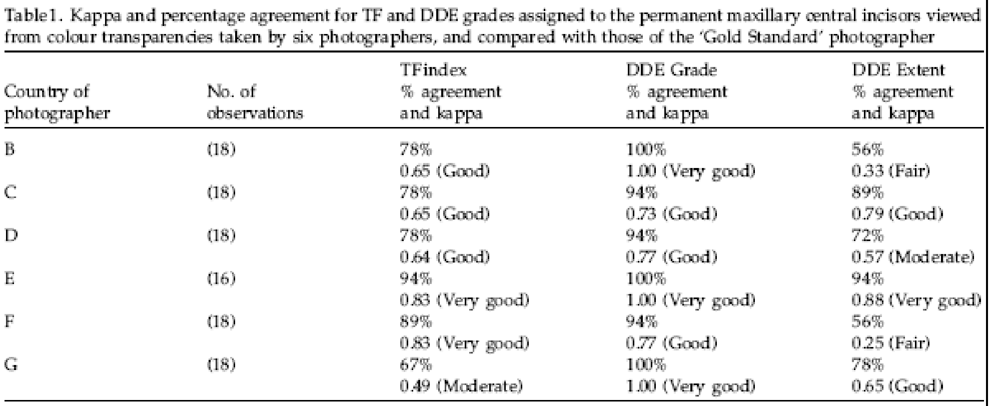


Table1. Kappa and percentage agreement for TF and DDE grades assigned to the permanent maxillary central incisors viewed from colour transparencies taken by six photographers, and compared with those of the ‘Gold Standard’ photographer

Country of photographer	No. of observations	TFindex % agreement and kappa	DDE Grade % agreement and kappa	DDE Extent % agreement and kappa
B	(18)	78% 0.65 (Good)	100% 1.00 (Very good)	56% 0.33 (Fair)
C	(18)	78% 0.65 (Good)	94% 0.73 (Good)	89% 0.79 (Good)
D	(18)	78% 0.64 (Good)	94% 0.77 (Good)	72% 0.57 (Moderate)
E	(16)	94% 0.83 (Very good)	100% 1.00 (Very good)	94% 0.88 (Very good)
F	(18)	89% 0.83 (Very good)	94% 0.77 (Good)	56% 0.25 (Fair)
G	(18)	67% 0.49 (Moderate)	100% 1.00 (Very good)	78% 0.65 (Good)

Variables in fluoride exposure

The variables found to be the most statistically important were artificial water fluoridation (odds ratio of 3.53 (95% CI of 2.52 to 4.93) and the prolonged use (> 2 years) of fluoride tablets (odds ratio of 2.17, with 95% CI of 1.60 to 2.95). Cork had the most diffuse opacities due to the artificially fluoridated water; however, Haarlem (0.13 ppm F) and Oulu (<0.01 ppm F) also had comparable numbers to Cork. When investigating the use of fluoride supplements, no children had used them in Cork, but 44 % of the children had fluoride supplementation for

		> 2 years in Haarlam and 58% had in Oulu. In the report, children exposed to water fluoride levels of 0.8 to 1.0 ppm were 3.53 times more likely to have a TF index grade 2 or more and those exposed to fluoride supplements for > 2 years were 2 times more likely to have enamel fluorosis. PROFILER'S NOTE: The amount of fluoride in the supplementations used were not reported.
STUDY AUTHORS' CONCLUSIONS:		In the article presenting the data on the study (Cochran et al. 2004a), the report found the prevalence of fluorosis to be highest in Cork, Ireland (artificially fluoridated water supply). Prolonged use of fluoridated supplements (tablets) was also associated with a significantly increased risk of dental fluorosis. For the second article describing in detail the photographic technique (Cochran et al. 2004b), the conclusion was the photographic method was robust and reproducible when used in seven European sites.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Cohen, J.A. 1960. A coefficient of agreement for nominal scales. Educational Psychol. Measurement, 20:37-46.
PROFILER'S REMARKS	***Initials/date: DFG/1-07***	While the study adequately convinces the profiler that the photographic method for assessing fluorosis could be a viable method to collect and compare data from several regions, the study was not designed to be used as a dose-response study. Some deficiencies were the use of a DDE index that the NRC (2006) does not endorse as a valid method for assessing fluorosis. Also, most of the children examined had TF scores of ≤3 which indicates only a mild fluorosis. The data indicated similar results in the TF scores and fluorosis prevalence in the area of highest community water fluoridation (Cork, 1.0 ppm F) and some of the lower water fluoride concentrations such as Haarlem (0.13 ppm) and Oulu (<0.01ppm). When investigated, it was found that use of fluoride supplements in Haarlem and Oulu had contributed to the observed dental fluorosis.
PROFILER'S ESTIM. NOEL/NOAEL		Data were not suitable for developing a NOAEL.
PROFILER'S ESTIM. LOEL/ LOAEL		Data were not suitable for developing a LOAEL.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( )
CRITICAL EFFECT(S):		Dental fluorosis (enamel opacities).

Cortes, D.F., R.P. Ellwood, D.M. O'Mullane and J.R. de Magalhaes Bastos. 1996. Drinking water fluoride levels, dental fluorosis and caries experience in Brazil. Journal of Public Health Dentistry, Vol. 56 (4): 226-228.

ENDPOINT STUDIED:	Dental fluorosis and dental caries
TYPE OF STUDY:	Cross sectional survey
POPULATION STUDIED:	Brazil: Olho D'Agua (Ceara), Vitoria (Espirito Santo) and Maceio (Alagoas) communities; 457 local schoolchildren aged 6-12 years old (47% males and 53% females). Participating schools selected for similarities in socioeconomic profiles.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	The children were required to be life-time residents of the area to be included in the study.
EXPOSURE GROUPS:	Children were chosen from these specific three areas because of the known differences in water fluoride content. Olho D'Agua had water fluoride levels of 2-3 ppm F, Vitoria 0.7 ppm F and Maceio less than 0.01 ppm F. While the areas had similar socioeconomic status, Olho D'Agua was a more rural community while Maceio and Vitoria were more urban. Water in Vitoria was artificially fluoridated since 1982 to a level of 0.7 ppm; water in Olho D'Agua came from bore holes and/or shallow or deep wells and it was known that the F content varied depending on local rainfall. No additional information about water in Maceio was reported.
EXPOSURE ASSESSMENT:	Only exposure to fluoride in the drinking water was considered in the study; no consumption rate or dose estimates were reported.
ANALYTICAL METHODS:	Analytical methods on how the fluoride (F) levels were determined were not reported. The study stated that water was regularly monitored in Vitoria with the majority of the samples reported between 0.6 and 0.7 ppm F. The level of F in Olho D'Agua supplies was stated to be between 2-3 ppm but would vary depending on the rainfall levels. The study did not indicate how often the wells were monitored. No information on how the levels of F in Maceio were determined or data on any other parameters measured were provided.
STUDY DESIGN	Children were chosen from a low, medium and high fluoride level region in Brazil. The population of children were chosen from participating schools having similar socioeconomic backgrounds. Parental consent was obtained for the children chosen for the study and a questionnaire was included to provide residential history. All examinations were done by the same person under natural light using plane dental mirrors. Dental caries was recorded at the level of cavitation. In the permanent dentition examination, caries was recorded for six teeth (the upper central incisors and first molars). For the primary dentition examination, all teeth were examined. Photographs were then taken and used for assessment of the degree of fluorosis of the upper central incisors. The TF index (Thylstrup and Fejerskov 1978) was used. Color scale cards were photographed with each film to ensure consistency of film development. Slides were scored blindly in random order using a graphics light box without magnification.
PARAMETERS MONITORED:	For permanent dentition, dental caries was scored with the DMF notation; for primary dentition, dental caries was scored with the dmft notation. The TF index (Thylstrup and Fejerskov 1978) was used to record any enamel hypomineralization with scores ranging from 1 to 4 with the higher scores indicating gradually increasing quantitative loss of

enamel (pitting). The TF scores were determined by photographs that were taken following the method of Ellwood and O'Mullane (1995).

PROFILER'S NOTE: Although the study states it uses the TF index (Thylstrup and Fejerskov 1978), a table in the study ranked the fluorosis based on the following TF scores: 0, 1-2, 3-4 and ≥ 5 so the profiler is unsure if ≥5 actually means 5-9, as 9 is the upper limit of the TF index.

STATISTICAL METHODS:

Kappa scores were developed for the reproducibility of recording dental caries and for tooth TF scores. Comparisons of caries levels were done by using multiple analysis of variance. No other information on statistics used was reported.

Repeat examinations were performed on 24 subjects to reproduce the recording of dental caries. Kappa scores were greater than 0.95. Also, re-examination of 25% of the photographs was performed to ensure the same TF scores were obtained. The Kappa score for this exercise was 0.85.

RESULTS:

Dental fluorosis

Tables 1 and 2 are copied directly from Cortes et al. (1996) and show the mean caries experience as compared with the TF scores. Caries experience for the six permanent teeth (DMFT) and for primary (dmft) scores presented in the tables were adjusted for the mean age of the total participants (10 years). In the primary dentition, there was a statistically significant (p<0.001) decrease in caries with increasing levels of fluoride. In the permanent dentition, the incidence of caries in Vitoria was statistically significantly (p<0.01) less than the other two regions. In Olho D'Agua, there was a statistically significant (p<0.05) increase in the mean caries DMFT in those children with TF scores of 3 or greater when compared to those with TF scores less than 3.

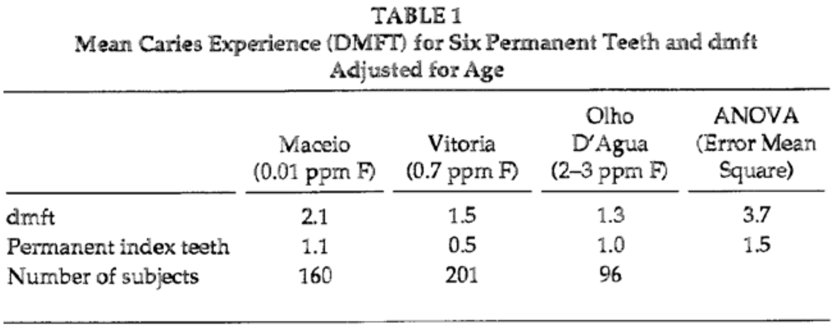


TABLE 1
Mean Caries Experience (DMFT) for Six Permanent Teeth and dmft Adjusted for Age

	Maceio (0.01 ppm F)	Vitoria (0.7 ppm F)	Olho D'Agua (2–3 ppm F)	ANOVA (Error Mean Square)
dmft	2.1	1.5	1.3	3.7
Permanent index teeth	1.1	0.5	1.0	1.5
Number of subjects	160	201	96	

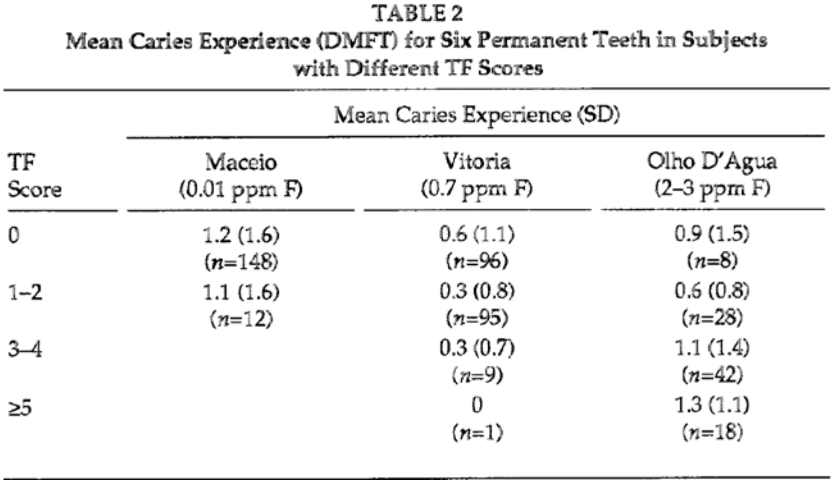


TABLE 2
Mean Caries Experience (DMFT) for Six Permanent Teeth in Subjects with Different TF Scores

	Mean Caries Experience (SD)		
TF Score	Maceio (0.01 ppm F)	Vitoria (0.7 ppm F)	Olho D'Agua (2–3 ppm F)
0	1.2 (1.6) (*n*=148)	0.6 (1.1) (*n*=96)	0.9 (1.5) (*n*=8)
1–2	1.1 (1.6) (*n*=12)	0.3 (0.8) (*n*=95)	0.6 (0.8) (*n*=28)
3–4		0.3 (0.7) (*n*=9)	1.1 (1.4) (*n*=42)
≥5		0 (*n*=1)	1.3 (1.1) (*n*=18)

PROFILER'S NOTE: Statistical significance is not clearly shown especially on Table 2. The study report did not provide any reference that the examiner used for deriving the

	DMFT and dmft scores for evaluation of caries. The high limit for the TF score was not established. The TF index usually goes to 9 while this report only states it as ≥5.
STUDY AUTHORS' CONCLUSIONS:	Cortes et al. (1996) concluded that the overall caries prevalence in these children was lower than expected but felt that it was because only six teeth were examined in the permanent dentition, making comparisons easier but underestimating the caries incidence. The authors also stated that increasing the fluoride levels above 0.7 ppm was beneficial in reducing caries prevalence for primary dentition but did not appear to be beneficial to the permanent dentition. **In the study, children in the high fluoride areas with a TF score of 3 or greater had higher levels of dental caries suggesting that if fluoride intake is too high, severe enamel hypomineralization takes place increasing the risk of caries.**
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Ellwood, R.P. and D.M. O'Mullane. 1995. Dental enamel opacities in three groups with varying levels of fluoride in their drinking water. Caries Res., 29:137-42.
PROFILER'S REMARKS ***Initials/date: DFG/12-06***	The study needs more information about statistical analysis performed to allow more definitive trends to be stated. There does appear to be an increase in caries in Olho D'Agua when the TF score was greater than or equal to 3. Cortes et al. (1996) does state, however, that this was a more rural community and some socioeconomic factors (i.e. limited access to fluoridated toothpaste) may have been additional factors beside water fluoride levels. The study did not state on how the fluoride levels were measured in the water and did not provide insight to the reference or method used to score for dmft or DMFT. Table 3 compares level of fluorosis in 6 permanent teeth (TF index) with caries (DMFT).
PROFILER'S ESTIM. NOEL/NOAEL	Not suitable for development of a NOAEL for fluorosis or caries prevalence due to incomplete data.
PROFILER'S ESTIM. LOEL/ LOAEL	Not suitable for development of a LOAEL for fluorosis or caries prevalence due to incomplete data.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable ( ), Poor (X), Medium ( ), Strong ( ) Nevertheless, observed associations between the TF index score and DMFT are summarized (Table 3).
CRITICAL EFFECT(S):	Caries experience and TF scores as related to levels of fluoride in water and as related to each other.

Dean, H.T. 1938. Endemic fluorosis and its relation to dental caries. Public Health Rep 53(33) (Republished in Public Health Rep, 2006 Supplement 1, 121: 213-19.

ENDPOINT STUDIED:	Dental caries and fluorosis
TYPE OF STUDY:	Cross sectional survey PROFILER'S NOTE: The paper by Dean (1938) is a conglomeration of several studies in which Dean was either a participant in or principal investigator of and combines data from these to make conclusions of the relationship between mottled enamel, prevalence of caries and the amount of fluoride in the water.
POPULATION STUDIED:	U.S.: A 1933-1934 study conducted by the U. S. Public Health Service (PHS) performed a dental survey of school children ages 6-14 years from 26 states and included a total of 34,283 examinations of white children in South Dakota, 15,465 in Colorado and 48,628 in Wisconsin. US/ South Dakota: During April-May 1938, Dean examined 3,300 school children in 51 communities for mottled enamel. All South Dakota counties listed in the earlier PHS study in which 35% or more of the estimated population of ages 6-14 years had been examined, were selected for the study. Dean also used the PHS study data to analyze the percentages of caries-free children in 6 cities but limited this analysis to 9 year olds.
CONTROL POPULATION:	None.
EXPOSURE PERIOD:	Children in the U.S. Public Health Service survey were 6-14 years old, were born and had always resided in their respective communities, and had continuous access to a common water supply used for both drinking and cooking. The PHS Study was conducted from 1933 to 1934 and the Dean study April-May, 1938.
EXPOSURE GROUPS:	PHS study: 34,283 children ages 6-14 years old from 26 states were included and the fluoride level in the water was measured. Dean's 1938 study: All South Dakota counties listed in the PHS study in which 35% or more of the estimated population of ages 6-14 years had been examined, were selected for the study. On the basis of the mottled enamel data, these counties were divided into three groups: a) counties where mottled enamel was prevalent; b) counties where mottled enamel distribution was uneven; and c) counties which were entirely free from mottled enamel.
EXPOSURE ASSESSMENT	Fluoride in water only was measured.
ANALYTICAL METHODS:	None provided. Consecutive monthly water samples were received from each of the cities surveyed in the PHS study, which permitted the computation of an arithmetic mean annual fluoride content of the communal water supply.
STUDY DESIGN	PHS study: The study was begun to determine the minimal threshold of toxicity of chronic endemic dental fluorosis. In some cites, in addition to recording the degree of severity of mottled enamel, the children were examined by Dean for other enamel defects such as present caries, past caries, pits and fissures and hypoplasias. These examinations were made in natural light with the children facing a window using mouth mirrors and new explorers. Residence and continual uses of the community water were verified by interviewing the child's parents. Dean 1938 study: A survey of mottled enamel was conducted in 1938 on school children in

51 communities of South Dakota. Mouth mirrors and new explorers were used in all examinations and children were examined in natural light. The amount of caries was determined by combining the data associated with the following items: “caries, permanent teeth”, “extraction indicated, permanent teeth”, “filled permanent teeth” and “extracted permanent teeth”. For each of these terms, the PHS study provided the number of carious permanent teeth per 100 children. Adjustment was made for sex, and the amount of caries for each county was expressed in terms of the number of carious permanent teeth per 100 children.

PARAMETERS MONITORED:

Dean 1938 study: In addition to definite cavitation, defects in the enamel on caries-susceptible surfaces showing either a discoloration or an opacity around the edges and in which the explorer would cling were counted as caries, making the amount of caries appear higher than usual. To compute an index to show differences in caries in the counties, the amount of caries (severity) was presented in terms of the number of carious permanent teeth per 100 children using the 12-14 year old age group.

PROFILER’S NOTE: Because these studies were performed prior to the developed standards used today for evaluating degrees of fluorosis and caries, there are no exact measurements for assessment.

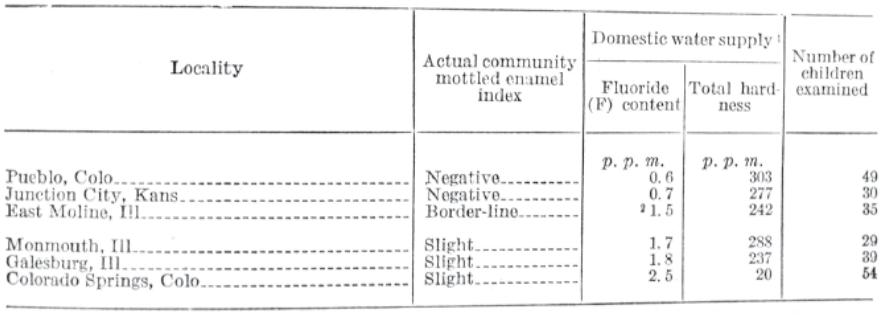
STATISTICAL METHODS:

Statistical analysis was not provided.

RESULTS:

Because the study interchanged data from all of the analyses, the conclusions will be presented together. The prevalence of caries was determined using a selected group of 9-year-olds (see Table 2 copied directly from Dean, 1938). The article indicated that observations showed that a high percentage of children were caries-free in the places with appreciable amounts of fluoride.

Table 2. – Percentages of caries-free children, 9 years of age in 6 selected cities classified according to their continuous use of water of different fluoride (F) concentration



Locality	Actual community mottled enamel index	Domestic water supply [1]		Number of children examined
		Fluoride (F) content	Total hardness	
		p. p. m.	*p. p. m.*	
Pueblo, Colo	Negative	0.6	303	49
Junction City, Kans	Negative	0.7	277	30
East Moline, Ill	Border-line	[2] 1.5	242	35
Monmouth, Ill	Slight	1.7	288	29
Galesburg, Ill	Slight	1.8	237	39
Colorado Springs, Colo	Slight	2.5	20	54

[1] For detailed mineral analyses of these waters, see ref. *(8) (10)*

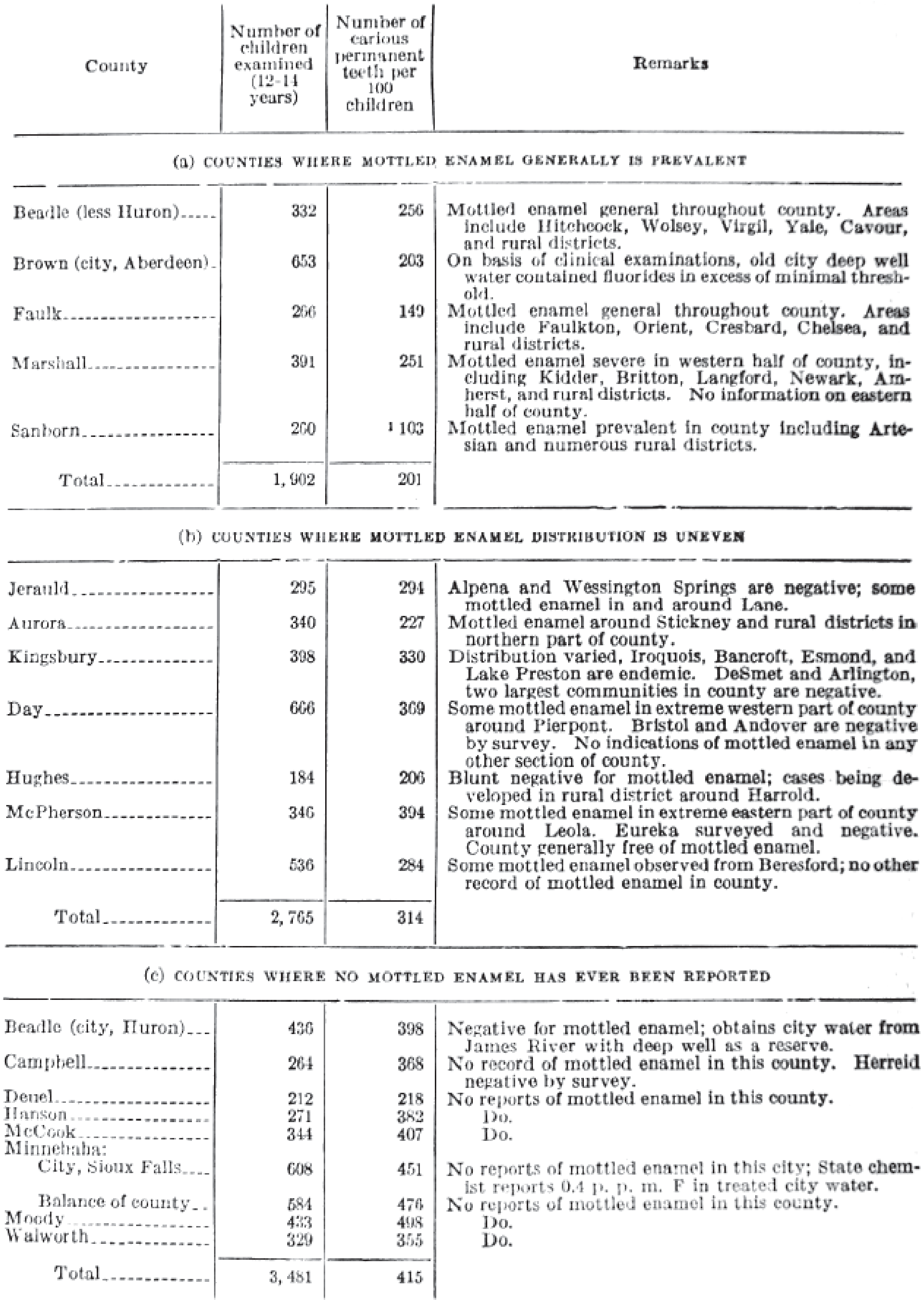
[2] Subject to possible correction to 1.3 p.p.m.

PROFILER’S NOTE: Although the title of Table 2 indicates that it contains information on the percentages of caries-free teeth, these data are not included in the table, and additional information from the text must be used to verify Dean’s conclusions.

In one part of the text Dean states that of the 114 children exposed continuously to water with fluoride concentrations of 0.6 to 1.5 ppm, only 5% were caries free, and of the 122 children exposed to water with fluoride concentrations of 1.7 to 2.5 ppm, 22 (27%) were caries free. However, in another part of the text, Dean states that for permanent teeth, 60 of the 122 children (49%) were caries free, and the incidence of mottled enamel was 53%. It is unclear which of these statements is correct.

Evidence of the relation of dental caries to endemic fluorosis was provided by using a computation of the dental caries attack rate on permanent teeth of 12-14 year olds using the data from the PHS study correlated with the data obtained on the geographical distribution of mottled enamel in South Dakota (Dean, 1938). In the group of counties where mottled enamel was generally prevalent, there were 201 carious permanent teeth per 100 children out of 1,902 12-14 year olds. In the intermediate counties, the examination of 2,765 children showed 314 permanent teeth affected per 100 children and finally in the counties where no mottled enamel was found, the examination of 3,481 children indicated 415 carious permanent teeth per 100 children. Table 3, copied directly from Dean (1938), shows these results.

Table 3. - Dental Caries attack rates in permanent teeth of 12-14 year old white children in selected South Dakota counties and cities classified according to the prevalence of mottled enamel.



County	Number of children examined (12-14 years)	Number of carious permanent teeth per 100 children	Remarks
(a) COUNTIES WHERE MOTTLED ENAMEL GENERALLY IS PREVALENT			
Beadle (less Huron)	332	256	Mottled enamel general throughout county. Areas include Hitchcock, Wolsey, Virgil, Yale, Cavour, and rural districts.
Brown (city, Aberdeen)	653	203	On basis of clinical examinations, old city deep well water contained fluorides in excess of minimal threshold.
Faulk	266	149	Mottled enamel general throughout county. Areas include Faulkton, Orient, Cresbard, Chelsea, and rural districts.
Marshall	391	251	Mottled enamel severe in western half of county, including Kidder, Britton, Langford, Newark, Amherst, and rural districts. No information on eastern half of county.
Sanborn	260	[1] 103	Mottled enamel prevalent in county including Artesian and numerous rural districts.
Total	1, 902	201	
(b) COUNTIES WHERE MOTTLED ENAMEL DISTRIBUTION IS UNEVEN			
Jerauld	295	294	Alpena and Wessington Springs are negative; some mottled enamel in and around Lane.
Aurora	340	227	Mottled enamel around Stickney and rural districts in northern part of county.
Kingsbury	398	330	Distribution varied, Iroquois, Bancroft, Esmond, and Lake Preston are endemic. DeSmet and Arlington, two largest communities in county are negative.
Day	666	369	Some mottled enamel in extreme western part of county around Pierpont. Bristol and Andover are negative by survey. No indications of mottled enamel in any other section of county.
Hughes	184	206	Blunt negative for mottled enamel; cases being developed in rural district around Harrold.
McPherson	346	394	Some mottled enamel in extreme eastern part of county around Leola. Eureka surveyed and negative. County generally free of mottled enamel.
Lincoln	536	284	Some mottled enamel observed from Beresford; no other record of mottled enamel in county.
Total	2, 765	314	
(c) COUNTIES WHERE NO MOTTLED ENAMEL HAS EVER BEEN REPORTED			
Beadle (city, Huron)	436	398	Negative for mottled enamel; obtains city water from James River with deep well as a reserve.
Campbell	264	368	No record of mottled enamel in this county. Herreid negative by survey.
Deuel	212	218	No reports of mottled enamel in this county.
Hanson	271	382	Do.
McCook	344	407	Do.
Minnehaha:			
City, Sioux Falls	608	451	No reports of mottled enamel in this city; State chemist reports 0.4 p. p. m. F in treated city water.
Balance of county	584	476	No reports of mottled enamel in this county.
Moody	433	498	Do.
Walworth	329	355	Do.
Total	3, 481	415	

PROFILER'S NOTE: While the trend toward less carious permanent teeth with increasing incidence of mottled enamel was observed with this data, listing the actual fluoride content of the water in these areas would have been useful.

A similar comparison was performed with data from four cities in Colorado and eight

	Wisconsin cities. These data showed less caries in the areas with the higher fluoride concentration in the water and more mottled enamel. In Colorado, the non-endemic areas for mottled enamel, Pueblo, Fort Collins and Denver, the incidence of caries in permanent teeth per 100 children were 194, 296 and 343, respectively and in the endemic area, it was 163 per 100 children. In Wisconsin, the non-endemic areas for mottled enamel with lower water fluoride levels incidence of caries in permanent teeth per 100 children ranged from 646 to 917 while and in the endemic area, it was 275 per 100 children. Table 4 is copied directly from Dean (1938) to provide this information.

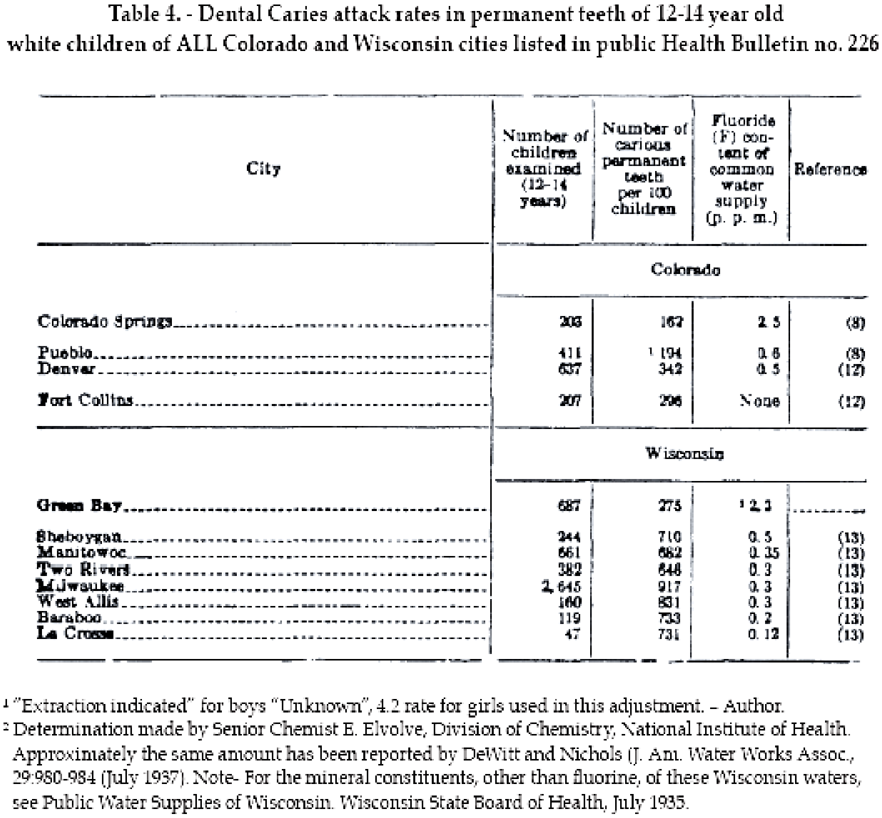


Table 4. - Dental Caries attack rates in permanent teeth of 12-14 year old white children of ALL Colorado and Wisconsin cities listed in public Health Bulletin no. 226

City	Number of children examined (12-14 years)	Number of carious permanent teeth per 100 children	Fluoride (F) content of common water supply (p. p. m.)	Reference
	Colorado			
Colorado Springs	206	167	2.5	(8)
Pueblo	411	[1] 194	0.6	(8)
Denver	637	342	0.5	(12)
Fort Collins	207	296	None	(12)
	Wisconsin			
Green Bay	687	275	[2] 2.3	....
Sheboygan	244	710	0.5	(13)
Manitowoc	661	682	0.35	(13)
Two Rivers	382	648	0.3	(13)
Milwaukee	2,645	917	0.3	(13)
West Allis	160	831	0.3	(13)
Baraboo	119	733	0.2	(13)
La Crosse	47	731	0.12	(13)

[1] "Extraction indicated" for boys "Unknown", 4.2 rate for girls used in this adjustment. – Author.

[2] Determination made by Senior Chemist E. Elvolve, Division of Chemistry, National Institute of Health. Approximately the same amount has been reported by DeWitt and Nichols (J. Am. Water Works Assoc., 29:980-984 (July 1937). Note- For the mineral constituents, other than fluorine, of these Wisconsin waters, see Public Water Supplies of Wisconsin. Wisconsin State Board of Health, July 1935.

PROFILER'S NOTE: While the data above does indicate the carious incidence as related to the fluoride content in the water, the data on the incidence of mottled enamel were not provided.

STUDY AUTHORS' CONCLUSIONS:		The study author concluded there was evidence to support the hypothesis that a limited immunity from dental caries was operative among school children residing in endemic mottled enamel areas. Also, examinations of 9-year olds showed that a higher percentage of children were caries free in the communities with a higher water fluoride content.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Dean, H.T. and E. Elvove. 1935. Studies on the minimal threshold of the dental sign of chronic endemic fluorosis (mottled enamel). Pub Health Rep 50:1719-1729 (Dec. 6, 1935). (Reprint No. 1721). Dean, H.T. and E. Elvove. 1936. Some epidemiological aspects of chronic endemic dental fluorosis. Am J Pub Health 26:567-575 (June 1936). Dean, H.T. and E. Elvove. 1937. Further studied on the minimal threshold of chronic endemic dental fluorosis. Pub Health Rep 52:1249-1264 (Sept. 10, 1937) (Reprint No. 1857). U.S. Public Health Service. 1936. Dental survey of school children, ages 6-14 years, made in 1933-34 in 26 States. Public Health Bulletin No. 226, Washington, D.C., May 1936.
PROFILER'S REMARKS	***Initials/Date*** VAD/01-09-	Details on the study conduct, including methods and standards used to assess fluorosis, were not provided; therefore, evaluation of the results and conclusions is difficult.

	07	The technical reviewer agrees with the conclusions of the profiler. The article provided a lot of data that were important to set the basis for developing standards in regards to fluorosis and caries as related to fluoride exposure; however, the reviewer found the information presented in an unorganized manner making interpretation of the article difficult to follow. Some of the conclusions made by Dean could not be verified based on the data provided.
PROFILER's ESTIM. NOAEL		The study design did not estimate a NOAEL.
PROFILER'S ESTIM. LOAEL		The study design did not estimate a LOAEL.
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable,(X_); Poor (_); Medium (_); Strong ( ) Although not suitable for a dose-response and interpretation of the data were difficult, the study does serve as a relative source contribution to the inverse relationship between water fluoride concentration, the incidence of mottled enamel and the incidence of caries.
CRITICAL EFFECTS:		Dental fluorosis and caries

Dean, H.T. 1942. The investigation of physiological effects by the epidemiology method. in Fluoride and Dental Health, Publ. Amer. Assoc Advanc. Sci., No. 19. pp 23-31.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Cross-sectional study of fluorosis and retrospective study of fluoride levels in drinking water.
POPULATION STUDIED:	US, 5824 Caucasian children in 22 cities in 10 states in several geographic regions; age 9-14 yrs old or in grades 2-12 (see Table 1 below in Results section)
CONTROL POPULATION:	None
EXPOSURE PERIOD:	Not stated when the individual examinations were conducted.
EXPOSURE GROUPS:	The exposure groups are described in Table 1 below in the “Results Section)” copied directly from Dean (1942).)
EXPOSURE ASSESSMENT:	Drinking water was the only exposure route evaluated. The study author notes, however, that other factors such as amount of water consumed, dietary and culinary habits, and probable climatological influences would also influence fluoride intake.
ANALYTICAL METHODS:	The Elvove (1933) method was used to determine the fluoride concentrations in drinking water; the sensitivity of the method was reported to be about 0.1 ppm.
STUDY DESIGN	The incidence and severity of dental fluorosis was evaluated in Caucasian children approximately 9-16 yrs of age in 22 US cites. Fluorosis was evaluated using Dean’s Index of Fluorosis (see Section 2). The fluorosis classification for each child was based on the degree of fluorosis recorded for two or more teeth. A community Index of Fluorosis was calculated as the sum of the products of the frequency and fluorosis score divided by the total size of the study population. The Community Indices of Fluorosis (CIF) were plotted graphically against fluoride concentration in drinking water.
PARAMETERS MONITORED:	Dean’s fluorosis index was used to evaluate each tooth in the mouth of each study participant. An Index of fluorosis was calculated for each community; the Index was computed as the sum of the products of the frequency times each fluorosis score divided by the total size of the study population.
STATISTICAL METHODS:	Community drinking water concentration was calculated as the arithmetic mean of 12 monthly samples.
RESULTS:	
Dental fluorosis	The size and age (or grade level) of the study populations, the community drinking water fluoride concentration, the Community Index of Fluorosis, and the incidence and severity of fluorosis are presented in Table 1, copied directly from Dean (1942).

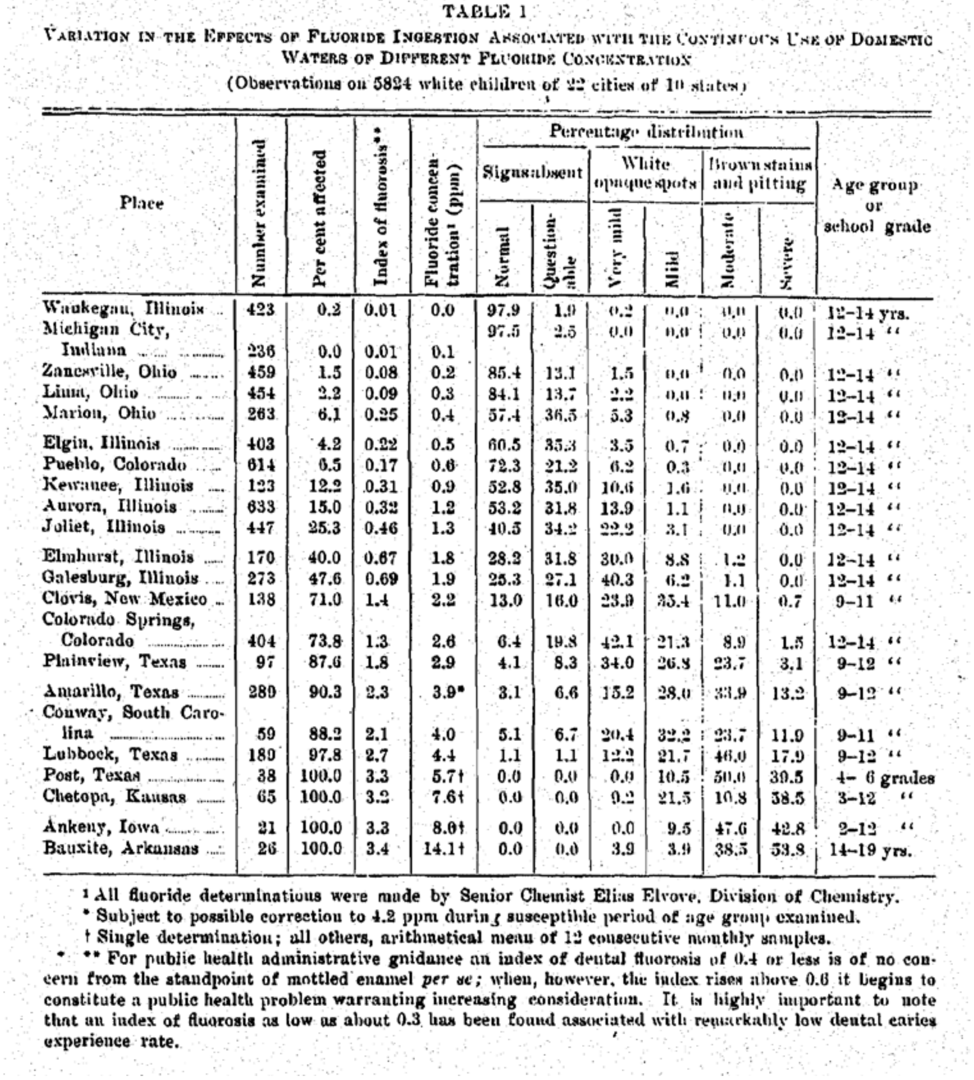


TABLE 1

VARIATION IN THE EFFECTS OF FLUORIDE INGESTION ASSOCIATED WITH THE CONTINUOUS USE OF DOMESTIC WATERS OF DIFFERENT FLUORIDE CONCENTRATION

(Observations on 5824 white children of 22 cities of 10 states)

Place	Number examined	Per cent affected	Index of fluorosis**	Fluoride concentration[1] (ppm)	Percentage distribution						Age group or school grade
					Signs absent		White opaque spots		Brown stains and pitting		
					Normal	Questionable	Very mild	Mild	Moderate	Severe	
Waukegan, Illinois	423	0.2	0.01	0.0	97.9	1.9	0.2	0.0	0.0	0.0	12–14 yrs.
Michigan City, Indiana	236	0.0	0.01	0.1	97.5	2.5	0.0	0.0	0.0	0.0	12–14 "
Zanesville, Ohio	459	1.5	0.08	0.2	85.4	13.1	1.5	0.0	0.0	0.0	12–14 "
Lima, Ohio	454	2.2	0.09	0.3	84.1	13.7	2.2	0.0	0.0	0.0	12–14 "
Marion, Ohio	263	6.1	0.25	0.4	57.4	36.5	5.3	0.8	0.0	0.0	12–14 "
Elgin, Illinois	403	4.2	0.22	0.5	60.5	35.3	3.5	0.7	0.0	0.0	12–14 "
Pueblo, Colorado	614	6.5	0.17	0.6	72.3	21.2	6.2	0.3	0.0	0.0	12–14 "
Kewanee, Illinois	123	12.2	0.31	0.9	52.8	35.0	10.6	1.6	0.0	0.0	12–14 "
Aurora, Illinois	633	15.0	0.32	1.2	53.2	31.8	13.9	1.1	0.0	0.0	12–14 "
Joliet, Illinois	447	25.3	0.46	1.3	40.5	34.2	22.2	3.1	0.0	0.0	12–14 "
Elmhurst, Illinois	170	40.0	0.67	1.8	28.2	31.8	30.0	8.8	1.2	0.0	12–14 "
Galesburg, Illinois	273	47.6	0.69	1.9	25.3	27.1	40.3	6.2	1.1	0.0	12–14 "
Clovis, New Mexico	138	71.0	1.4	2.2	13.0	16.0	23.9	35.4	11.0	0.7	9–11 "
Colorado Springs, Colorado	404	73.8	1.3	2.6	6.4	19.8	42.1	21.3	8.9	1.5	12–14 "
Plainview, Texas	97	87.6	1.8	2.9	4.1	8.3	34.0	26.8	23.7	3.1	9–12 "
Amarillo, Texas	289	90.3	2.3	3.9*	3.1	6.6	15.2	28.0	33.9	13.2	9–12 "
Conway, South Carolina	59	88.2	2.1	4.0	5.1	6.7	20.4	32.2	23.7	11.9	9–11 "
Lubbock, Texas	189	97.8	2.7	4.4	1.1	1.1	12.2	21.7	46.0	17.9	9–12 "
Post, Texas	38	100.0	3.3	5.7†	0.0	0.0	0.0	10.5	50.0	39.5	4– 6 grades
Chetopa, Kansas	65	100.0	3.2	7.6†	0.0	0.0	9.2	21.5	10.8	58.5	3–12 "
Ankeny, Iowa	21	100.0	3.3	8.0†	0.0	0.0	0.0	9.5	47.6	42.8	2–12 "
Bauxite, Arkansas	26	100.0	3.4	14.1†	0.0	0.0	3.9	3.9	38.5	53.8	14–19 yrs.

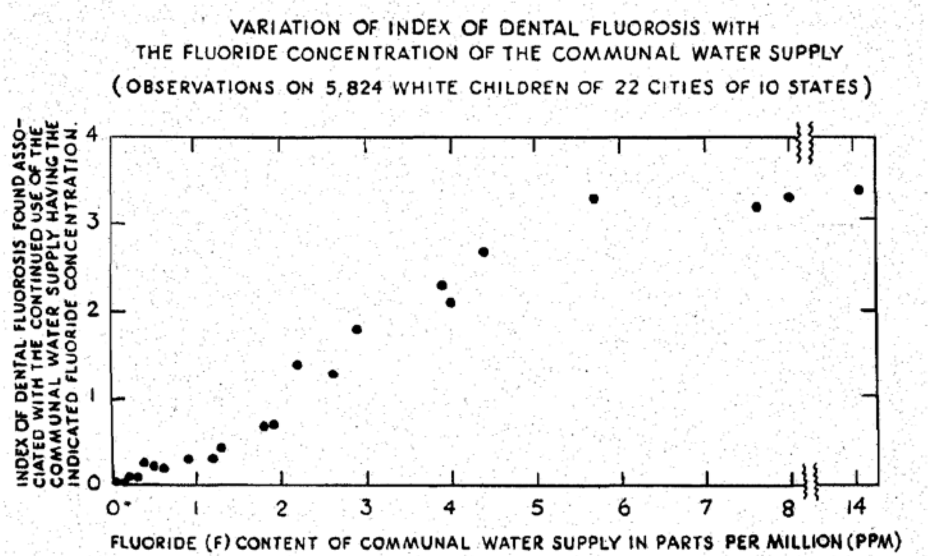
[1] All fluoride determinations were made by Senior Chemist Elias Elvove, Division of Chemistry.

* Subject to possible correction to 4.2 ppm during susceptible period of age group examined.

† Single determination; all others, arithmetical mean of 12 consecutive monthly samples.

** For public health administrative guidance an index of dental fluorosis of 0.4 or less is of no concern from the standpoint of mottled enamel *per se*; when, however, the index rises above 0.6 it begins to constitute a public health problem warranting increasing consideration. It is highly important to note that an index of fluorosis as low as about 0.3 has been found associated with remarkably low dental caries experience rate.

The correlation of the CFI with the fluoride concentration in drinking water is shown in figure below copied directly from Dean (1942).

	 FIG. 2.
STUDY AUTHORS' CONCLUSIONS:	Dean (1942) concluded that there was a correlation between the prevalence of endemic fluorosis in a community and fluoride levels in the public water supply, and that the marked differences in the severity of fluorosis among the groups studied could be demonstrated by comparing the CFI. The association between the CFI and fluoride drinking water concentration followed, with "reasonably precision, a rough S-shaped curve.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Elvove, E. 1933. Estimation of fluorides in waters. Pub. Health Rept. 48:1219-1222.
PROFILER'S REMARKS ***Initials/date DMO 2/14/07***	Although the study did not take into account other sources of fluoride exposure, the study occurred prior to the widespread use of fluoride supplements and dentifrices. The study populations only included Caucasian children, so it was not broadly representative of the entire U.S. population. The study did include populations from many geographic areas in the U.S., however, not all regions were included such as the desert Southwest and the cold temperate regions of New England or the upper Midwest.
PROFILER'S ESTIM. NOEL/NOAEL	Based on the data presented in Table 1, the NOAEL/LOAEL boundary for severe fluorosis (score of 4 in Dean's fluorosis classification) appears to fall between 1.8 and 2.2 ppm.
PROFILER'S ESTIM. LOEL/ LOAEL	Based on the data presented in Table 1, the NOAEL/LOAEL boundary for severe fluorosis (score of 4 in Dean's fluorosis classification) appears to fall between 1.8 and 2.2 ppm.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (_), Poor (_), Medium (_), Strong (X) An adequate number of populations were surveyed and an adequate number of individuals were studied within each population to provide sufficient data for statistical analysis. The CFI followed the same trend as that for dental fluorosis.
CRITICAL EFFECT(S):	Dental fluorosis

Den Besten, P.K. 1999. Mechanism and timing of fluoride effects on developing enamel. Journal of Public Health Dentistry. Vol. 59, No. 4: 247-251.

ENDPOINT STUDIED:	Effects of fluoride exposure on developing enamel
TYPE OF STUDY:	Assimilation of data- not true survey or study
POPULATION STUDIED:	Data summary drawn from human, animal and cellular studies.
CONTROL POPULATION:	Not applicable
EXPOSURE PERIOD:	Not applicable
EXPOSURE GROUPS:	Not applicable
EXPOSURE ASSESSMENT:	The report states that most animal studies evaluated fluoride exposure through either the drinking water or food, but at higher levels than humans normally ingest through drinking water and diet. Cell culture studies were also described.
ANALYTICAL METHODS:	Not applicable
STUDY DESIGN	The article assimilated data from previous studies and used them to help make predictions as to the effect of fluoride exposure on the different stages of enamel development.
PARAMETERS MONITORED:	The report gave results from several studies that affected each stage of enamel development but did not use a standard index to describe fluorosis.
STATISTICAL METHODS:	Not applicable
RESULTS:	
Mechanisms proposed for the formation of fluorosis	Two mechanisms are proposed as being influential to the formation of fluorosis. The first is a systemic effect of fluoride on calcium homeostasis and second, an effect of fluoride on cell function either directly through interactions with developing ameloblasts or indirectly through interactions with the extracellular matrix. The first mechanism, effect on calcium homeostasis, is only applicable in fluoride exposure resulting in skeletal fluorosis and was not addressed in the Den Besten (1999) paper. The second mechanism was examined. The main stages of enamel development are the pre-secretory stage, the secretory stage and the maturation stage; this report tries to identify which stage(s) is most affected by fluoride exposure.
Pre-secretory stage	The pre-secretory stage is when differentiating ameloblasts acquire their phenotype and prepare to secrete the organic matrix of enamel. Data identified on both the effects of fluoride on the proliferation of epithelial cells for enamel (precursors to ameloblasts) and on cell differentiation found no effect at the levels of fluoride commonly found in human exposures.
Secretory stage	The secretory stage is where ameloblasts secrete amelogenin protein to form a protein matrix over the full thickness of enamel with mineralization quickly following. Histological changes have been observed in rat enamel after high levels of fluoride. Fluoride also appears to cause an inhibitory effect on the uptake of amino acids which in turn could cause a decrease in the amount of enamel matrix proteins secreted.
Maturation stage	The maturation stage starts when a rapid loss of amelogenin protein occurs from the enamel matrix with mineralization continuing until there is a fully mineralized tissue at the end. **The hypomineralization characteristic of fluorosis appears to be caused by a delay in the removal of amelogenin in the early maturation stage.** These effects are observed in animals at doses similar to those of humans. Studies also determined that the duration of exposure and dose of fluoride prior to the early

		maturation stage affected the severity of dental fluorosis.
STUDY AUTHORS' CONCLUSIONS:		The formation of dental fluorosis is highly dependent on the dose, duration and timing of fluoride exposure. The early-maturation stage of enamel development appears to be the most sensitive. Although the risk of fluorosis is less when exposure only occurs during the secretory stage, the risk greatly increases when exposure occurs in both the secretory and maturation stages. The risk of fluorosis also appears to be related to the total cumulative fluoride exposure in the development stages.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		The profiler recommends using pages 250-251 (references section) of the study report to identify references.
PROFILER'S REMARKS	***Initials/date: DFG/1-07***	This study is not suitable for a dose-response estimate, but does provide insight on the effect of fluoride exposure in each stage of enamel development. Timing and the duration of fluoride exposure both influence the degree of dental fluorosis.
PROFILER'S ESTIM. NOEL/NOAEL		Data are not suitable for development of a NOAEL.
PROFILER'S ESTIM. LOEL/ LOAEL		Data are not suitable for development of a LOAEL.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( ) Suitable for identifying the critical time of exposure.
CRITICAL EFFECT(S):		Dental fluorosis.

Driscoll et al. 1983. Prevalence of dental caries and dental fluorosis in areas with optimal and above-optimal water fluoride concentrations. J. Amer. Dent. Assoc. 107(1):42-47

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<tr><td>ENDPOINT STUDIED:</td><td>Dental caries and dental fluorosis</td></tr>
<tr><td> </td><td> </td></tr>
<tr><td>TYPE OF STUDY:</td><td>Cross-sectional study of dental fluorosis and caries and fluoride levels in drinking water</td></tr>
<tr><td> </td><td> </td></tr>
<tr><td>POPULATION STUDIED:</td><td>US/Illinois: 807 schoolchildren (ages 8-16), approximately 46% males and 54% females. Nonwhites were <5% of the population in all the communities.</td></tr>
<tr><td> </td><td> </td></tr>
<tr><td>CONTROL POPULATION:</td><td>None</td></tr>
<tr><td> </td><td> </td></tr>
<tr><td>EXPOSURE PERIOD:</td><td>From birth until age 8-16 yrs, in April 1980</td></tr>
<tr><td> </td><td> </td></tr>
<tr><td>EXPOSURE GROUPS:</td><td>The exposure groups are described in Table 1 copied directly from Driscoll et al. 1983. The mean fluoride concentrations for each community were obtained by averaging all available readings for the years 1964 through 1977.

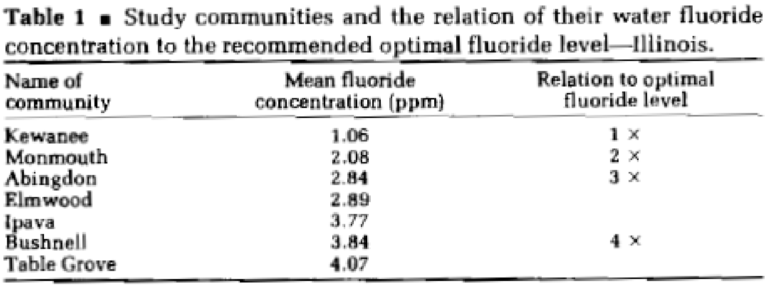



Table 1 ▪ Study communities and the relation of their water fluoride concentration to the recommended optimal fluoride level—Illinois.
<table>
<tr><th>Name of community</th><th>Mean fluoride concentration (ppm)</th><th>Relation to optimal fluoride level</th></tr>
<tr><td>Kewanee</td><td>1.06</td><td>1 ×</td></tr>
<tr><td>Monmouth</td><td>2.08</td><td>2 ×</td></tr>
<tr><td>Abingdon</td><td>2.84</td><td>3 ×</td></tr>
<tr><td>Elmwood</td><td>2.89</td><td></td></tr>
<tr><td>Ipava</td><td>3.77</td><td></td></tr>
<tr><td>Bushnell</td><td>3.84</td><td>4 ×</td></tr>
<tr><td>Table Grove</td><td>4.07</td><td></td></tr>
</table>
PROFILER’S NOTE: While the table indicates that the fluoride concentration for Ipava falls in the 3x optimal range, subsequent reports in this series of studies demonstrate that the data for Ipava were included in the 4x group.</td></tr>
<tr><td> </td><td> </td></tr>
<tr><td>EXPOSURE ASSESSMENT:</td><td>Drinking water was the only exposure route evaluated. However, a questionnaire was developed for parents of 8 children in one area who had moderate or severe fluorosis, asking questions about consumption of dietary fluoride supplements, consumption of high fluoride infant formulas, and ingestion of unusual amounts of fluoride dentifrice. The study authors state that the responses to the questionnaires “did not explain the clinical findings”. The responses were not reported.</td></tr>
<tr><td> </td><td> </td></tr>
<tr><td>ANALYTICAL METHODS:</td><td>Not stated</td></tr>
<tr><td> </td><td> </td></tr>
<tr><td>STUDY DESIGN</td><td>The prevalence of dental caries and dental fluorosis was assessed in U.S. children, ages 8-16, in 7 communities in Illinois where the water supplies contained natural fluoride at levels of 1, 2, 3, and 4 times the recommended optimal level of 1 ppm for the geographic area. Examinations for fluorosis and dental caries were carried out, with one examiner using Dean’s Index of Fluorosis (see Section 2) and the other two examiners using the Tooth Surface Index of Fluorosis, developed by the National Institute of Dental Research. (Note that the results using this index were still being analyzed by the authors and were not included in this paper). The DMF surface index was used to determine the incidence of dental caries and diagnostic criteria corresponded to those established in 1968 at the American Dental Association’s Conference on Clinical Testing of Cariostatic Agents. The percentage distribution of children with Dean’s fluorosis scores of 0 to 4 was assessed for each water fluoride level, and Community Fluorosis Index (CFI) scores were also developed, according to water fluoride levels. For dental caries, the mean decayed, missing, and filled (DMF) surface scores were examined based on the water fluoride levels.</td></tr>
<tr><td> </td><td> </td></tr>
</table>

PARAMETERS MONITORED: Dental caries was measured using the DMF surface index and dental fluorosis using Dean's Index of Fluorosis (see Section 2).

STATISTICAL METHODS: Not stated

RESULTS:

Caries: See Table 3 for mean DMF scores according to the water fluoride levels

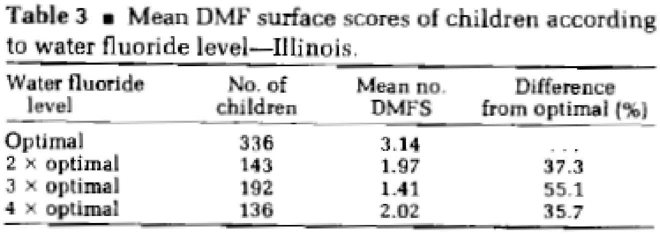


Table 3 ■ Mean DMF surface scores of children according to water fluoride level—Illinois.

Water fluoride level	No. of children	Mean no. DMFS	Difference from optimal (%)
Optimal	336	3.14	. . .
2 × optimal	143	1.97	37.3
3 × optimal	192	1.41	55.1
4 × optimal	136	2.02	35.7

Dental fluorosis: See Table 2 for the distribution of children according to Dean's Index of Fluorosis and water fluoride level

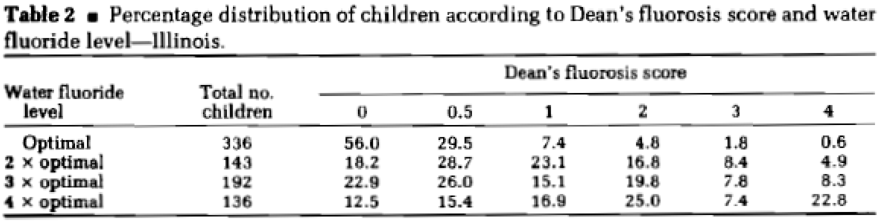


Table 2 ■ Percentage distribution of children according to Dean's fluorosis score and water fluoride level—Illinois.

Water fluoride level	Total no. children	Dean's fluorosis score					
		0	0.5	1	2	3	4
Optimal	336	56.0	29.5	7.4	4.8	1.8	0.6
2 × optimal	143	18.2	28.7	23.1	16.8	8.4	4.9
3 × optimal	192	22.9	26.0	15.1	19.8	7.8	8.3
4 × optimal	136	12.5	15.4	16.9	25.0	7.4	22.8

STUDY AUTHORS' CONCLUSIONS: The mean caries scores in all three above-optimal fluoride areas were significantly lower than in the optimal area. The prevalence of dental fluorosis was characteristically low in the optimal fluoride area. Substantial increases in fluorosis occurred in the above-optimal fluoride areas, with the condition being most pronounced in the 4x optimal area.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006) None

PROFILER'S REMARKS ***Initials/date SBG 3/28/07***

The study did not take into account other sources of fluoride exposure and no statistics were done on the data. In addition, the study only included one Midwest state, with primarily a white population, and so it is not broadly representative of the entire U.S. population.

There is a clear dose-response for severe fluorosis progressing from a 0.6% at the optimal fluoride level to 22.6% at the 4x fluoride level. The data may be helpful in determining the magnitude of the increase in severe fluorosis that has resulted from increased fluoride exposure through non-drinking water sources.

The mean DMFS scores for the 4x fluoride group was substantially less than that for the optimal fluoride group (2.02 vs. 3.14); however, statistical significance of the difference was not reported.

PROFILER'S ESTIM. NOEL/NOAEL Based on the data presented in Table 2, the NOAEL for severe dental fluorosis (Dean's Index of 4) is below 1.06 ppm, because 0.6% of the study population exhibited severe fluorosis at this fluoride level.

PROFILER'S ESTIM. LOEL/ LOAEL	Based on the data presented in Table 2, the LOAEL for severe dental fluorosis (Dean's Index of 4) is 1.06 ppm because 0.6% of the study population exhibited severe fluorosis at this fluoride level.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (_), Poor (_), Medium (x), Strong (_) Statistics were not done on the data.
CRITICAL EFFECT(S):	Dental caries, dental fluorosis

Driscoll, W.S., S.B.Heifetz, H.S.Horowitz, A. Kingman, R.J Meyers, and E.R. Zimmerman. 1986. Prevalence of dental caries and dental fluorosis in areas with negligible, optimal, and above-optimal fluoride concentrations in drinking water. J. Amer. Dental Assoc. 113: 29-33. [NOTE: Two reports have been published on this survey prior to the present report (Driscoll et al. 1983; Horowitz et al. 1984)].

ENDPOINT STUDIED:	Dental fluorosis and dental caries
TYPE OF STUDY:	Case control, retrospective
POPULATION STUDIED:	US/Illinois, Kewanee, Monmouth, Abingdon, Elmwood, Ipava, Bushnell, and Table Grove + US/Iowa, Belle Plaine, Durant, Marengo, and Missouri Valley: 1,123 children aged 8-16 who were lifelong residents of small rural towns in the same climatic zone with negligible, optimal, or above-optimal natural fluoride levels in their drinking water. The towns with optimal or higher fluoride levels (807 children) were in western Illinois, within 75 miles of each other (Kewanee, Monmouth, Abingdon, Elmwood, Ipava, Bushnell, and Table Grove). The towns with negligible fluoride levels (316 children) were in Iowa (Belle Plaine, Durant, Marengo, and Missouri Valley).
CONTROL POPULATION:	Several comparisons were made after sub-grouping the 1,123 children based on the fluoride content of their drinking water (negligible, optimal, or 2x, 3x, 4x optimal), or on their dental fluorosis score (0-4, per Dean's classification). Thus, the control groups were (1) children with negligible fluoride in their drinking water, who were compared to those with optimal and/or above-optimal drinking water fluoride [DMFS/child, community fluoride index, and distribution of fluorosis scores among children and for all teeth and tooth surfaces]; (2) children with a fluorosis score of zero*, who were compared to children with fluorosis scores of 0.5-4 [DMFS/child and percent sound, filled, and decayed teeth]; and (3) children exposed to optimal drinking water fluoride, who were compared to children exposed to above-optimal drinking water fluoride (TSIF scores for permanent first molars). *Included only children exposed to above-optimal drinking water fluoride levels
EXPOSURE PERIOD:	Lifetime, which was 8-16 years
EXPOSURE GROUPS:	Schoolchildren aged 8-16 (grades 3-10); mean age =11.48, ~46% male and 54% female, who lived their entire life in one of the 11 small rural communities in western Illinois or in Iowa, and whose primary drinking water source was the public water system. The current paper (Driscoll et al. 1986) did not identify the 7 Illinois towns in which 807 of the children lived, and only provided their drinking water concentrations as optimal, or 2x, 3x, 4x optimal. The identity of the towns [and their mean water fluoride concentration] were obtained from a previous publication by the same authors (Driscoll et al. 1983), as follows: Kewanee [1.06 ppm], Monmouth [2.08 ppm], Abingdon [2.84 ppm], Elmwood [2.89 ppm, Ipava [3.77 ppm], Bushnell [3.84 ppm], and Table Grove [4.07 ppm]. Based on the geographic location, the study authors considered 1 ppm to be the optimal water fluoride concentration, and thus classified water supply for the towns studied as optimal (~1 ppm), 2x optimal (~2 ppm), 3x optimal (~3 ppm), and 4x optimal (~4 ppm). The 316 children in the four Iowa towns (Belle Plaine, Durant, Marengo, and Missouri Valley) were also 8-16 years old, with a similar age distribution as the Illinois children (no further details provided). The children's drinking water fluoride concentrations were classified as "negligible," and were only quantified as being <0.3 ppm.
EXPOSURE ASSESSMENT:	No information was provided on other possible sources of fluoride exposure (e.g. toothpaste, mouth rinses, etc.)
ANALYTICAL METHODS:	The study did not indicate the method used for measuring the water fluoride concentrations, or report data on any other water quality parameters.

STUDY DESIGN

In April 1980, teeth were examined from 807 children aged 8-16 who lived in 7 small rural towns within 75 miles of each other in western Illinois. These children had lived their whole lives in their respective towns, per a questionnaire completed by their parents. Informed consent was obtained. The towns had varying levels of fluoride naturally in their drinking water, which came from deep wells. Based on the geographic location, the study authors considered 1 ppm to be the optimal water fluoride concentration, and thus classified water supply for the towns studied as optimal (~1 ppm), 2x optimal (~2 ppm), 3x optimal (~3 ppm), and 4x optimal (~4 ppm).

Teeth were examined in April of 1980 at the children's schools using portable dental chairs, artificial lights, plane dental mirrors, and #23 explorers, but radiographs were not made. Fluorosis was assessed in all children by one dentist using Dean's classification system, and by two other dentists using TSIF and the criteria of Russell (1962) to distinguish between fluorosis and nonfluoride enamel opacities. Another dentist examined each child for dental caries using the DMFS index.

Two years later (April 1982), 316 children aged 8-16, of comparable age and gender distribution, were similarly examined in four small rural towns in Iowa. The towns were in the same climatic zone as the Illinois towns, but had negligible (i.e., <0.3 ppm) water fluoride concentrations (towns unavailable in Illinois).

PARAMETERS MONITORED:

Dental fluorosis was assessed in all children by one dentist using Dean's classification system, and by two other dentists using TSIF (tooth surface index of fluorosis) and the criteria of Russell (1962) to distinguish between fluorosis and nonfluoride enamel opacities. Another dentist examined each child for dental caries using the DMFS (decayed, missing, and filled permanent surfaces) index. The Community Fluorosis Index (CFI) was determined by the method of Dean (1942).

STATISTICAL METHODS:

Scheffe's method for multiple comparisons was used to compare the mean DMFS scores of children according to water fluoride levels (negligible and 1x, 2x, 3x, or 4x optimal), and according to fluorosis classification (0, 0.5, 1-3, and 4). The Community Fluorosis Index (CFI) of areas with negligible or with optimal water fluoride levels were compared by the t-test.

RESULTS:

Dental caries (DMFS)

The mean DMFS score per child was inversely correlated with their drinking water fluoride concentration, as shown in Table 1. DMFS scores were statistically significantly higher in children with negligible drinking water fluoride than in children with optimal water fluoride, and both of these groups had higher mean DMFS scores than children from areas with 2x, 3x, or 4x optimal drinking water fluoride. DMFS scores of the 2x, 3x, and 4x exposure groups were not significantly different from one another.

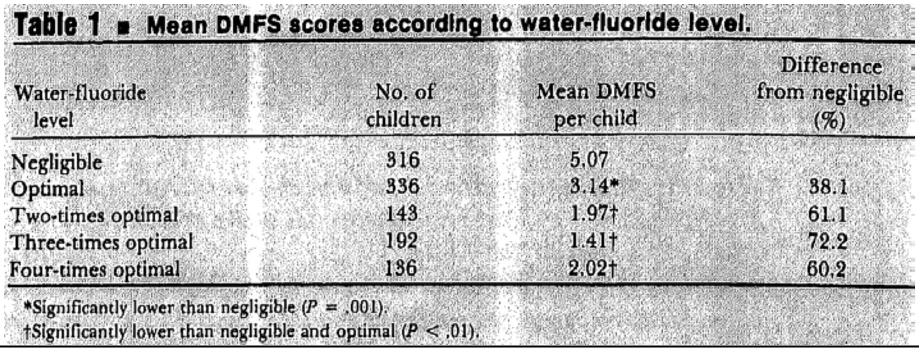


Table 1 ▪ Mean DMFS scores according to water-fluoride level.

Water-fluoride level	No. of children	Mean DMFS per child	Difference from negligible (%)
Negligible	316	5.07	
Optimal	336	3.14*	38.1
Two-times optimal	143	1.97†	61.1
Three-times optimal	192	1.41†	72.2
Four-times optimal	136	2.02†	60.2

*Significantly lower than negligible (P = .001).
†Significantly lower than negligible and optimal (P < .01).

Effect of dental fluorosis on dental caries

A comparison of the mean DMFS scores with the Dean's fluorosis classification of children from areas with above-optimal water fluoride showed that children with a fluorosis classification of 4 had statistically significantly greater DMFS scores/child than children with fluorosis classifications of 0.5-3, but the DMFS scores did not differ significantly among the latter groups (Table 2). Although children living in areas with negligible or optimal water fluoride concentrations were not included in this comparison, the DMFS score/child for areas with negligible water fluoride (5.07) was greater than the DMFS score/child of children with category 4 fluorosis (2.96), suggesting that even 4x optimal water fluoride protects against dental caries.

Table 2. Mean DMFS scores for children according to fluorosis classifications*

Classification of fluorosis	Number of children	Mean DMFS per child
0	87	1.89
0.5	112	1.40
1 to 3	218	1.58
4	54	2.96[#]

* Data limited to children residing in above-optimal fluoride areas.

[#] Significantly higher than scores for fluorosis classifications of 0.5 and 1 to 3 (P<0.05). All other differences are not significant.

A comparison of tooth fluorosis scores (Dean's index) with the percentage of teeth that were sound, decayed, or filled in children from areas with above-optimal water fluoride concentrations showed that children with a fluorosis classification of 4 had markedly (2.5 to 7.3-fold) greater percent decayed or filled teeth than children with fluorosis classifications of 0.5-3, but there was little difference among the latter groups (Table 3).

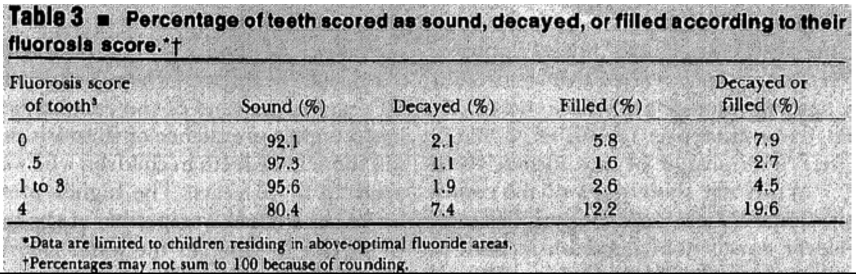


Table 3 ■ Percentage of teeth scored as sound, decayed, or filled according to their fluorosis score.*†

Fluorosis score of tooth[3]	Sound (%)	Decayed (%)	Filled (%)	Decayed or filled (%)
0	92.1	2.1	5.8	7.9
.5	97.3	1.1	1.6	2.7
1 to 3	95.6	1.9	2.6	4.5
4	80.4	7.4	12.2	19.6

*Data are limited to children residing in above-optimal fluoride areas.

†Percentages may not sum to 100 because of rounding.

Dental fluorosis

Definite signs of fluorosis (Dean's score of 1-4) were seen in 2.9% of children from areas with negligible drinking water fluoride, compared to 14.6% of children from areas with optimal water fluoride. The distribution of Dean's fluorosis scores of the two groups is shown in Table 4. Analogously, the CFI for communities with optimal drinking water fluoride levels was significantly greater than of communities with negligible water fluoride concentrations.

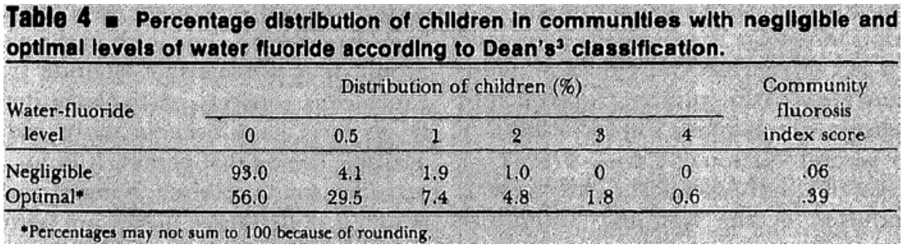


Table 4 ■ Percentage distribution of children in communities with negligible and optimal levels of water fluoride according to Dean's[3] classification.

Water-fluoride level	Distribution of children (%)						Community fluorosis index score
	0	0.5	1	2	3	4	
Negligible	93.0	4.1	1.9	1.0	0	0	.06
Optimal*	56.0	29.5	7.4	4.8	1.8	0.6	.39

*Percentages may not sum to 100 because of rounding.

A similar pattern was seen for the distribution of fluorosis scores on a per tooth basis (Dean's index) or on a per tooth surface basis (TSIF). Fluorosis was somewhat more prevalent in teeth from children living in areas of optimal than in areas of negligible water fluoride concentrations, as shown in Table 5.

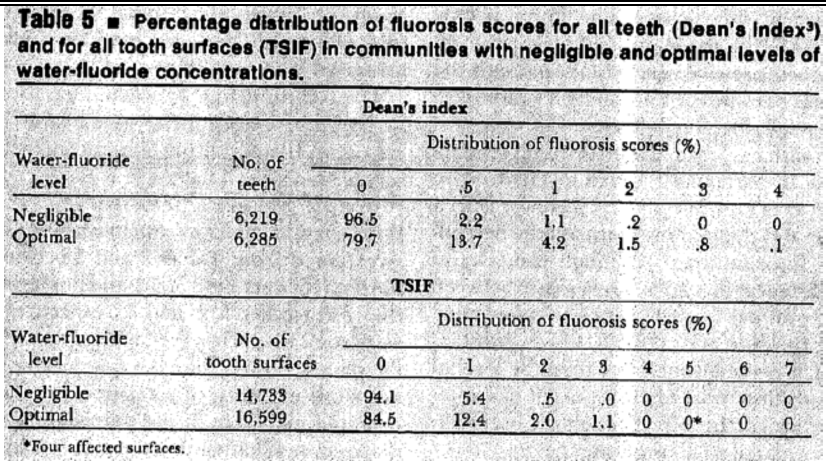


Table 5 ■ Percentage distribution of fluorosis scores for all teeth (Dean's index[3]) and for all tooth surfaces (TSIF) in communities with negligible and optimal levels of water-fluoride concentrations.

Dean's index

Water-fluoride level	No. of teeth	Distribution of fluorosis scores (%) 0	.5	1	2	3	4
Negligible	6,219	96.5	2.2	1.1	.2	0	0
Optimal	6,285	79.7	13.7	4.2	1.5	.8	.1

TSIF

Water-fluoride level	No. of tooth surfaces	Distribution of fluorosis scores (%) 0	1	2	3	4	5	6	7
Negligible	14,733	94.1	5.4	.5	.0	0	0	0	0
Optimal	16,599	84.5	12.4	2.0	1.1	0	0*	0	0

*Four affected surfaces.

A comparison of the distribution of TSIF scores of permanent first molars of children aged 8-10 and 13-16 was made according to type of tooth surface (occlusal, buccal, or lingual) and water fluoride level (optimal vs. above-optimal) (Table 6). TSIF scores were greater in molars exposed to above-optimal fluoride levels than molars exposed to optimal fluoride levels for all tooth surface types, for both age groups. However, TSIF scores were lower for the 13-16 year olds than for the 8-10 year olds at both water fluoride levels, suggesting to the study authors that the older children's molars were less affected by fluorosis.

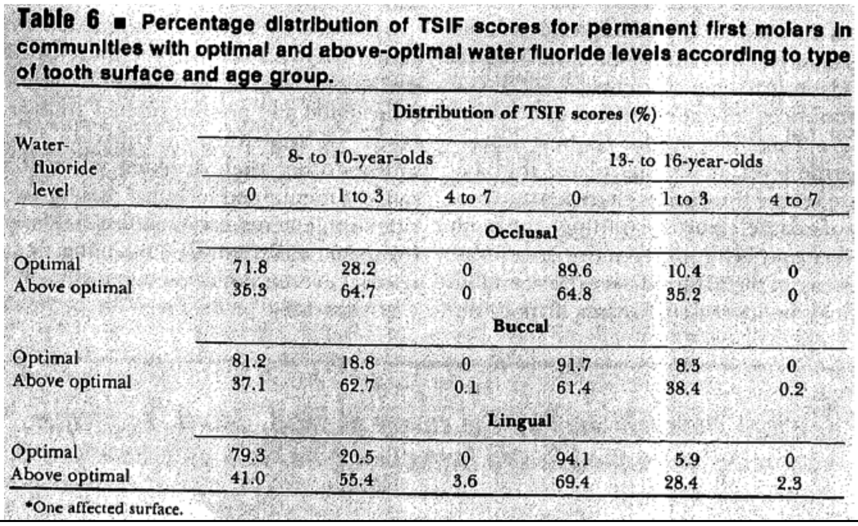


Table 6 ■ Percentage distribution of TSIF scores for permanent first molars in communities with optimal and above-optimal water fluoride levels according to type of tooth surface and age group.

Water-fluoride level	Distribution of TSIF scores (%) 8- to 10-year-olds 0	1 to 3	4 to 7	13- to 16-year-olds 0	1 to 3	4 to 7
			Occlusal			
Optimal	71.8	28.2	0	89.6	10.4	0
Above optimal	35.3	64.7	0	64.8	35.2	0
			Buccal			
Optimal	81.2	18.8	0	91.7	8.3	0
Above optimal	37.1	62.7	0.1	61.4	38.4	0.2
			Lingual			
Optimal	79.3	20.5	0	94.1	5.9	0
Above optimal	41.0	55.4	3.6	69.4	28.4	2.3

*One affected surface.

STUDY AUTHORS' CONCLUSIONS:

Children from above-optimal fluoride areas had fewer dental caries (i.e., mean DMFS/child) than those from optimal fluoride areas, who in turn had fewer dental caries than children from negligible fluoride areas. Children from above-optimal fluoride areas with severe fluorosis (Dean's index 4) had an increased the prevalence of dental caries relative to mild and moderate fluorosis (Dean's index 0.5-3); the study authors speculate that this finding may be due to food, debris, or plaque becoming trapped in the defective enamel.

The study authors speculated that the reason for the higher fluorosis scores of the molars of the 8-10 year old group, relative to the 13-16 year old group, could have been due to higher ingestion of fluoride from dentifrices by the younger group, or to greater enamel abrasion from more years of tooth brushing, and subsequent remineralisation of mild fluorosis, by the older group.

The authors countered the findings of Leverett (1982), who proposed that dental fluorosis has become overly prevalent in the U.S. due to ingestion of fluoride from sources other than drinking water, particularly in areas with optimal water fluoridation.

		In contrast to Leverett's finding that 28% of children from fluoridated communities had mild fluorosis, Driscoll et al. (1986) found that only 14.6% of children in optimal fluoride areas had definite signs of fluorosis, which was only slightly greater than the 10% estimated by Dean in 1936.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Driscoll et al. 1983. Prevalence of dental caries and dental fluorosis in areas with optimal and above-optimal water fluoride concentrations. J. Amer. Dental Assoc. 107: 42-47. Leverett, D.H. 1982. Fluorides and the changing prevalences of dental caries. Science 217: 26-30. Russell, A.L. 1962. The differential diagnosis of fluoride and nonfluoride enamel opacities. Public Health Dent. 21: 143-146.
PROFILER'S REMARKS	***Initials/date: SM 1/8/07 DMO/3/29/07***	This was a well conducted study showing that fluoridated water protects against dental caries, but also increases the prevalence of dental fluorosis. Mean DMFS scores per child were found to be significantly lower at higher fluoride drinking water levels; however, at the same time children residing in above optimal fluoride areas and who also had severe fluorosis had a significantly higher mean DMFS score than those with lower fluorosis scores (NOTE: the mean DMFS difference between children with a Dean score of 0 and that of 4 was not statistically significant (p=16), but it was still substantial, i.e., 1.89 vs. 2.96). NOTE: the mean DMFS score for the severe fluorosis group (2.96) was still below the mean score for the optimal fluoride area (3.14) and substantially lower than the score for the negligible fluoride area (5.07). These differences were not analyzed statistically. Information on fluorosis was provided by comparing the percentage distribution of children (Dean's index) or teeth (Dean's index and TSIF) for the negligible and optimal fluoride areas. The results indicate that even in the optimal fluoride areas (1 ppm) severe fluorosis occurred in a small percentage of children and teeth. The same information was not provided for the above optimal areas; therefore an overall evaluation of the dose response relationship for severe fluorosis is not possible. The study revealed greater fluorosis in first molars of 8-10 year old children than 13-16 year old children, but the reasons for this, as stated by the study authors, were not conclusively determined.
PROFILER'S ESTIM. NOEL/NOAEL for fluorosis and for fluorosis –induced caries		A NOAEL for minimal fluorosis could not be determined from the study data because fluorosis occurred even in the negligible fluoride area (in about 7% of the study population). The NOAEL for severe fluorosis appears to fall between the negligible fluoride concentration (<0.3 ppm) and the optimal concentration (1 ppm), as no individuals in the former group had a Dean index of 3 or 4. Based on the data collected, fluoride appears to have an anti-carries properties even at levels exceeding optimal. However, when the children from the negligible and optimal fluoride areas were excluded from the analysis, the lowest DF tooth incidence (was found among the children with a 0.5 score for fluorosis (2.7%) not the children with no fluorosis. The highest (19.6%) was found among the children with a fluorosis score of 4. Children having scores of 1-3 had an intermediate incidence of DF teeth (4.5%). All of the children included in this compilation of the data received water from a source that was classified as 2x optimal or greater. The mean DMFS value for the children with a fluorosis score of 4 was significantly higher than those with fluorosis scores of 0.5 or 1-3 but not those with no fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL for fluorosis		A LOAEL was not identified for a minimal level of fluorosis. The LOAEL for severe fluorosis appears to correspond to the optimal fluoride level of 1 ppm because a small percentage of children in this group had severe fluorosis (data not analyzed statistically).

POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (_), Poor (_), Medium (X), Strong (_) The percentage distribution of children (or teeth) with fluorosis was not documented for all drinking water fluoride levels; therefore, an overall dose-response relationship can not be established (although this information might be available in earlier or subsequent studies in this series, i.e., Driscoll et al., 1983). Nevertheless, the distributional data given for the negligible and optimal fluoride areas might be used in conjunction with that from earlier studies to assess the relative increase in fluorosis due to the increase in fluoride exposure from non-drinking water sources.
CRITICAL EFFECT(S):	Dental fluorosis

Ekanayake, L. and W. van der Hoek. 2002. Dental caries and developmental defects of enamel in relation to fluoride levels in drinking water in an arid area of Sri Lanka. Caries Res., 36: 398-404.

Ekanayake, L. and W. van der Hoek. 2003. Prevalence and distribution of enamel defects and dental caries in a region with different concentrations of fluoride in drinking water in Sri Lanka. International Dental Journal. 53: 243-248.

[PROFILER'S NOTE: Two sources for the same study were identified; data from both sources were used to develop the assessment and the tables provided are referenced].

ENDPOINT STUDIED:	Dental caries and defects of enamel
TYPE OF STUDY:	Cross-sectional survey
POPULATION STUDIED:	Asia/Sri Lanka/Uda Walawe: 486 (236 boys and 250 girls) schoolchildren aged 14 years old from Uda Walawe, a rural area in Sri Lanka, were used in the study. PROFILER'S NOTE: The exposure groups in Sri Lanka may not be representative of similar aged groups in the Unites States due to the arid climate of the area (average rainfall less than 2000 mm per year).
CONTROL POPULATION:	None
EXPOSURE PERIOD:	1987-2001; Only children that were life-time (14 years) residents of the area were used in the study.
EXPOSURE GROUPS:	Water samples from the children's homes were obtained and sampled for fluoride. Most of the drinking water to the individual homes came from wells. The children were then divided into 4 groups: <0.3 mg/L; 0.31-0.49 mg/L; 0.5-0.7 mg/L or > 0.7 mg/L. In Uda Walawe, the fluoride content of the water was reported to be 0.05 to 6.10 mg/L (unpublished data from the International Water Management Institute in Colombo, Sri Lanka). PROFILER'S NOTE: The profiler notes that the highest group of fluoride in the study was presented as > 0.7 mg/L with no limit to the upper boundary making interpretation more difficult as to the actual fluoride exposure.
EXPOSURE ASSESSMENT:	Only exposure to the fluoride in drinking water was assessed in this study. The children were questioned about tooth brushing frequencies and the type of materials used when brushing teeth.
ANALYTICAL METHODS:	Fluoride samples of the water were determined by an Orion ion-specific electrode within 4-5 weeks of obtaining the sample. TISAB buffer controlled the ionic strength of the water samples and the instrument was standardized using 1 and 10 mg/L fluoride standards. No other water parameters were measured.
STUDY DESIGN	Names of children in Uda Walawe that were 14 years old were obtained from six government schools. All children within the age group present in school on the day of the examination were included in the study. Examinations of the children were performed by one examiner during January and February 2001 and took place outside under natural light at the children's school. After any debris was removed using a piece of cotton wool, the teeth were examined for caries and defects in the enamel. Other information gathered at the examination was: name of child, date of birth, gender, name of school and home address. Intra-examiner reliability was assessed by re-examining 10% of the students.

	In April and July 2001, research assistants went to the homes of the children that had participated and an interview was performed with the mother, father and/or guardian. The following information was obtained: materials used to brush teeth, age when first started brushing teeth, source of drinking water and duration of residence. A sample of drinking water was collected from each home for measurement of fluoride concentration. PROFILER'S NOTE: While 518 children were examined at the schools, in the follow-up visits, drinking water samples were only collected from 486 homes; therefore, the data presented are only for the 486 children.
PARAMETERS MONITORED:	Caries were determined by using the methods of WHO (1997). Developmental defects of enamel were determined using the modified DDE index (Clarkson and O'Mullane 1989) on buccal and labial surfaces of 10 teeth. PROFILER'S NOTE: The NRC (2006) stated that the DDE index by Clarkson and O'Mullane emphasizes only aesthetic concerns and is not technically an index of enamel fluorosis.
STATISTICAL METHODS:	Data were analyzed using the Stata Release 6 (1997) software package. Non-parametric tests were used: Mann-Whitney U test to compare mean DMFS values in 2 samples and Kruskal-Wallis test to compare mean DMFS values in more than 2 samples. The differences between proportions were determined by chi-square test and Fisher's exact two-tail test. The association between the different categories of diffuse opacities in the DDE index and DMFS values was determined by Spearman's rank correlation. Cohen's kappa statistic was used to determine the intra-examiner reliability.
RESULTS:	
Dental effects of enamel	Table 1 and 2 are copied directly from Ekanayake and van der Hoek (2003) and show the enamel defect and diffuse opacities when compared to the level of fluoride in the water, and also the mean number of teeth affected. Table 1 shows a statistically significant ($p<0.001$) increase in the percentage of children with enamel defects and diffuse opacities with the increase in the fluoride concentration of the water. Fifty seven percent of the children exposed to fluoride levels of >0.70 mg/L had enamel defects as compared to only 29% of those exposed to ≤ 0.30 mg/L. Table 2 also shows a statistically significant ($p< 0.0001$) increase in the number of teeth affected with enamel defects in each child as the fluoride levels went up. The study also identified the maxillary first premolar as the tooth most often affected. Data for the study were combined for both genders as no differences were identified. Also, over 75% of the children had used fluoridated toothpaste from the ages of 9-12 months on.

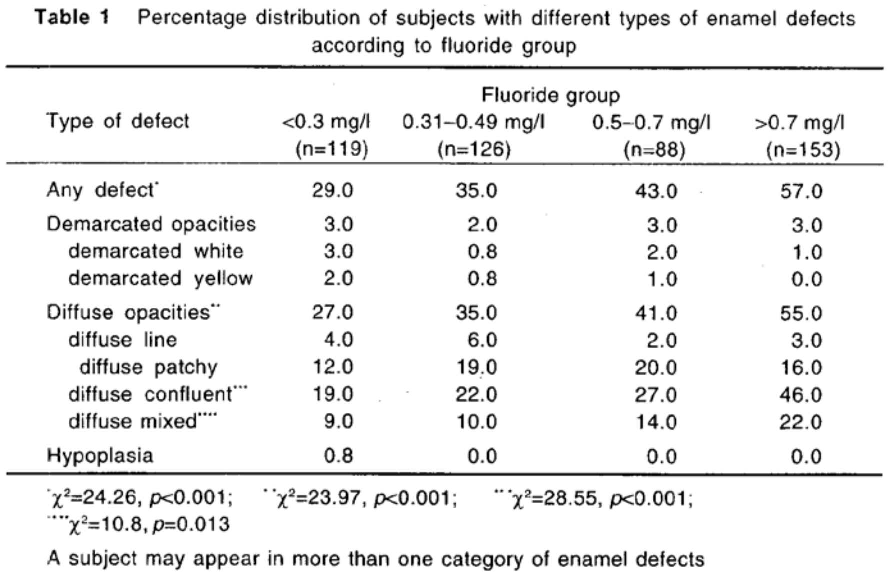


Table 1 Percentage distribution of subjects with different types of enamel defects according to fluoride group

Type of defect	Fluoride group <0.3 mg/l (n=119)	 0.31–0.49 mg/l (n=126)	 0.5–0.7 mg/l (n=88)	 >0.7 mg/l (n=153)
Any defect*	29.0	35.0	43.0	57.0
Demarcated opacities	3.0	2.0	3.0	3.0
demarcated white	3.0	0.8	2.0	1.0
demarcated yellow	2.0	0.8	1.0	0.0
Diffuse opacities**	27.0	35.0	41.0	55.0
diffuse line	4.0	6.0	2.0	3.0
diffuse patchy	12.0	19.0	20.0	16.0
diffuse confluent***	19.0	22.0	27.0	46.0
diffuse mixed****	9.0	10.0	14.0	22.0
Hypoplasia	0.8	0.0	0.0	0.0

*χ^2=24.26, p<0.001; **χ^2=23.97, p<0.001; ***χ^2=28.55, p<0.001; ****χ^2=10.8, p=0.013

A subject may appear in more than one category of enamel defects

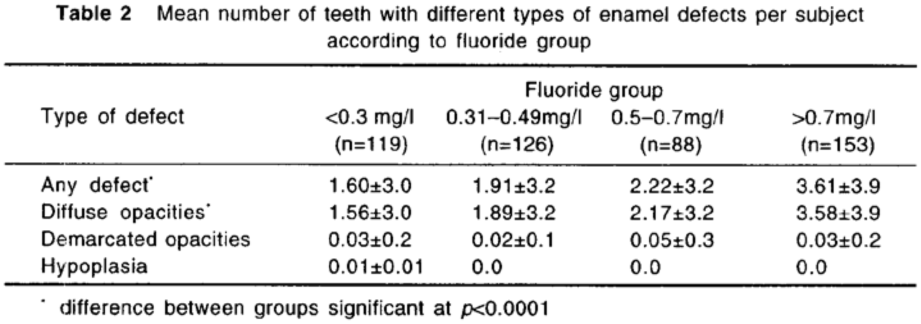


Table 2 Mean number of teeth with different types of enamel defects per subject according to fluoride group

Type of defect	Fluoride group <0.3 mg/l (n=119)	 0.31–0.49mg/l (n=126)	 0.5–0.7mg/l (n=88)	 >0.7mg/l (n=153)
Any defect*	1.60±3.0	1.91±3.2	2.22±3.2	3.61±3.9
Diffuse opacities*	1.56±3.0	1.89±3.2	2.17±3.2	3.58±3.9
Demarcated opacities	0.03±0.2	0.02±0.1	0.05±0.3	0.03±0.2
Hypoplasia	0.01±0.01	0.0	0.0	0.0

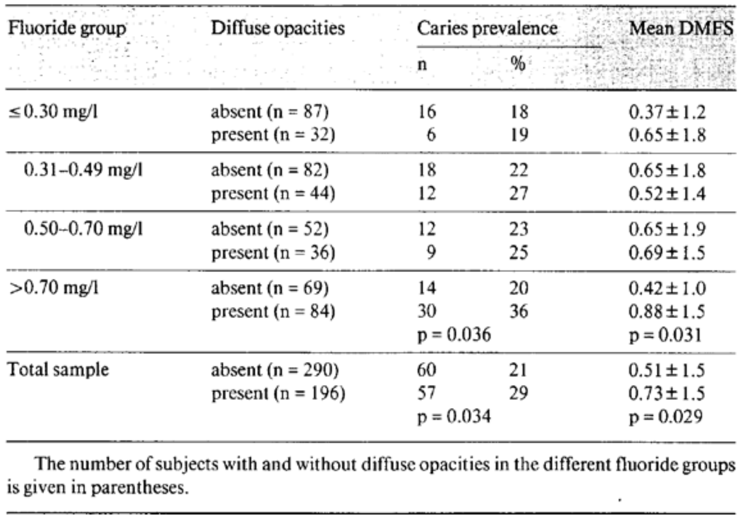
* difference between groups significant at p<0.0001

PROFILER'S NOTE: The study authors (Ekanayake and van der Hoek) used the DDE index by Clarkson and O'Mullane (1989) and the NRC (2006) does not endorse this method as a true indicator of fluorosis, although the number of defects and diffuse opacities did appear to increase with higher fluoride concentrations. The upper boundary to the fluoride exposure is not known as it is only presented at >0.7 mg/L.

Dental caries

The next two tables are provided and copied directly from Ekanayake and van der Hoek (2002) showing the caries prevalence and mean DMFS in regards to the number of diffuse opacities and DDE index score. Table 2 below shows the caries prevalence and the mean DMFS in children with and without diffuse opacities and indicates there was a higher incidence of caries in children with opacities but only statistically higher in the >0.7 mg/L group. In Table 3, pooled data indicate a significant increase in caries prevalence in those children as with the highest DDE score (6) and mean DMFS (1.04).

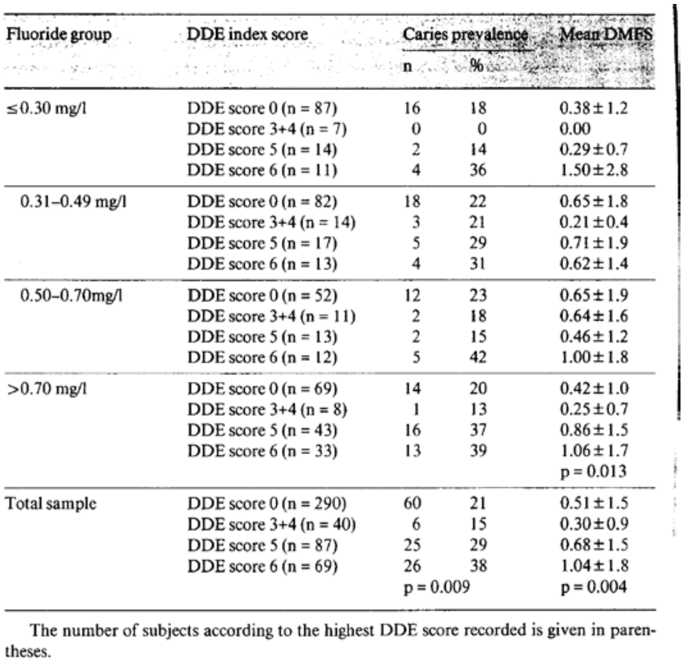
Table 2. Caries prevalence and mean DMFS in children with and without diffuse opacities by level of fluoride in drinking water



Fluoride group	Diffuse opacities	Caries prevalence		Mean DMFS
		n	%	
≤ 0.30 mg/l	absent (n = 87)	16	18	0.37 ± 1.2
	present (n = 32)	6	19	0.65 ± 1.8
0.31–0.49 mg/l	absent (n = 82)	18	22	0.65 ± 1.8
	present (n = 44)	12	27	0.52 ± 1.4
0.50–0.70 mg/l	absent (n = 52)	12	23	0.65 ± 1.9
	present (n = 36)	9	25	0.69 ± 1.5
>0.70 mg/l	absent (n = 69)	14	20	0.42 ± 1.0
	present (n = 84)	30	36	0.88 ± 1.5
		p = 0.036		p = 0.031
Total sample	absent (n = 290)	60	21	0.51 ± 1.5
	present (n = 196)	57	29	0.73 ± 1.5
		p = 0.034		p = 0.029

The number of subjects with and without diffuse opacities in the different fluoride groups is given in parentheses.

Table 3. Association between the severity of developmental defects of enamel, caries prevalence and mean DMFS in the different fluoride groups



Fluoride group	DDE index score	Caries prevalence		Mean DMFS
		n	%	
≤ 0.30 mg/l	DDE score 0 (n = 87)	16	18	0.38 ± 1.2
	DDE score 3+4 (n = 7)	0	0	0.00
	DDE score 5 (n = 14)	2	14	0.29 ± 0.7
	DDE score 6 (n = 11)	4	36	1.50 ± 2.8
0.31–0.49 mg/l	DDE score 0 (n = 82)	18	22	0.65 ± 1.8
	DDE score 3+4 (n = 14)	3	21	0.21 ± 0.4
	DDE score 5 (n = 17)	5	29	0.71 ± 1.9
	DDE score 6 (n = 13)	4	31	0.62 ± 1.4
0.50–0.70mg/l	DDE score 0 (n = 52)	12	23	0.65 ± 1.9
	DDE score 3+4 (n = 11)	2	18	0.64 ± 1.6
	DDE score 5 (n = 13)	2	15	0.46 ± 1.2
	DDE score 6 (n = 12)	5	42	1.00 ± 1.8
>0.70 mg/l	DDE score 0 (n = 69)	14	20	0.42 ± 1.0
	DDE score 3+4 (n = 8)	1	13	0.25 ± 0.7
	DDE score 5 (n = 43)	16	37	0.86 ± 1.5
	DDE score 6 (n = 33)	13	39	1.06 ± 1.7
				p = 0.013
Total sample	DDE score 0 (n = 290)	60	21	0.51 ± 1.5
	DDE score 3+4 (n = 40)	6	15	0.30 ± 0.9
	DDE score 5 (n = 87)	25	29	0.68 ± 1.5
	DDE score 6 (n = 69)	26	38	1.04 ± 1.8
		p = 0.009		p = 0.004

The number of subjects according to the highest DDE score recorded is given in parentheses.

Profiler's Note: If the concentration data are removed and one just looks at the incidence of cavities versus DDE score, the relationship is significant (p= 0.009) and shows the u-shape curve one would expect. The u-shape becomes even more pronounced if 5 and 6 scores are combined as were the scores of 3-4.

The next Table 3 is from Ekanyake and van der Hoek (2003) and shows caries prevalence and mean caries experience according to the fluoride groups but does not indicate any statistical significance between groups.

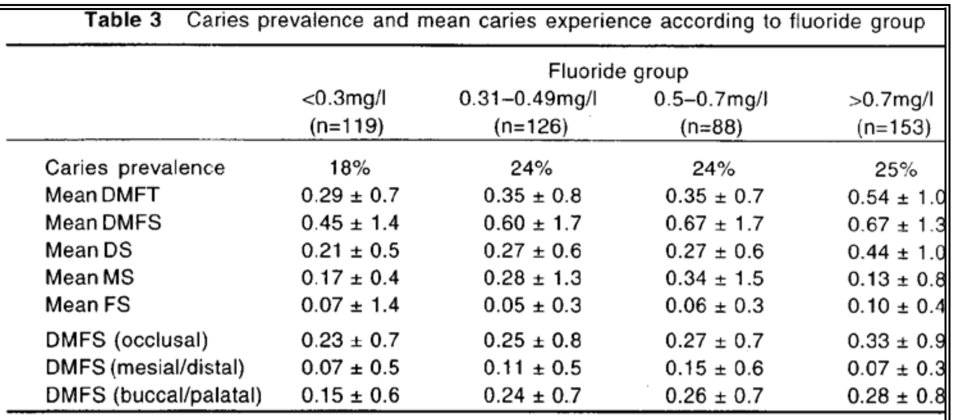


Table 3 Caries prevalence and mean caries experience according to fluoride group

	Fluoride group			
	<0.3mg/l (n=119)	0.31–0.49mg/l (n=126)	0.5–0.7mg/l (n=88)	>0.7mg/l (n=153)
Caries prevalence	18%	24%	24%	25%
Mean DMFT	0.29 ± 0.7	0.35 ± 0.8	0.35 ± 0.7	0.54 ± 1.0
Mean DMFS	0.45 ± 1.4	0.60 ± 1.7	0.67 ± 1.7	0.67 ± 1.3
Mean DS	0.21 ± 0.5	0.27 ± 0.6	0.27 ± 0.6	0.44 ± 1.0
Mean MS	0.17 ± 0.4	0.28 ± 1.3	0.34 ± 1.5	0.13 ± 0.8
Mean FS	0.07 ± 1.4	0.05 ± 0.3	0.06 ± 0.3	0.10 ± 0.4
DMFS (occlusal)	0.23 ± 0.7	0.25 ± 0.8	0.27 ± 0.7	0.33 ± 0.9
DMFS (mesial/distal)	0.07 ± 0.5	0.11 ± 0.5	0.15 ± 0.6	0.07 ± 0.3
DMFS (buccal/palatal)	0.15 ± 0.6	0.24 ± 0.7	0.26 ± 0.7	0.28 ± 0.8

PROFILER’S NOTE: Data provided from the earlier paper (Ekanayake and van der Hoek 2002) that used the DDE index indicated significance in caries prevalence when compared to the amount of fluorosis as seen in the first Table 3 listed, but the second chart (Table 3 in the 2003 article) indicates there was no significant increase in caries prevalence when it was evaluated by water fluoride group and mean DMFT and DMFS score.

STUDY AUTHORS’ CONCLUSIONS:

In the first paper (2002), Ekanayake and van der Hoek concluded that the relationship between fluoride levels in drinking water, diffuse opacities and caries suggested that the appropriate level of fluoride in drinking water in arid regions of Sri Lanka should be around 0.3 mg/L. Also, individuals with severe forms of enamel defects in high-flouride levels were susceptible to dental caries.

In the second paper (2003), Ekanayake and van der Hoek revealed that 29-57% of the children were affected by developmental defects of enamel and the caries prevalence ranged from 18-25% in the different fluoride groups indicating wide differences in the prevalence and severity of enamel defects and wide variations in the individual responses to high fluoride levels in the water. They also stated that the study demonstrated a need to look at other factors that contribute to enamel defects. .

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

PROFILER’S REMARKS ***DFG/12-06***

There were some deficiencies in this study. The study (Ekanayake and van der Hoek 2002 and 2003) used the DDE index according to Clarkson and O’Mullane (1989) for determination of fluorosis which the NRC (2006) felt was not an appropriate index to be used. The study did not account for any other types of fluoride besides the usage of fluoridated toothpaste that could have added to the fluoride exposure. Because of the higher temperatures and arid conditions of this area, the profiler questions the applicability of this data for use in the United States. The study also did not give a limit to the highest exposed group and the profiler does not know what percentage of children could have been exposed to very high levels.

PROFILER’S ESTIM. NOEL/NOAEL

Data are not suitable to determine a NOAEL for fluorosis or caries prevalence.

PROFILER’S ESTIM. LOEL/ LOAEL

Data are not suitable to determine a LOAEL for fluorosis or caries prevalence.

POTENTIAL SUITABILITY FOR DOSE-RESPONSE

Not suitable (X), Poor ( ), Medium ( ), Strong ( )
However, the study contributes to the weight-of-evidence for the relationship between

MODELING:	fluorosis and cavities.
CRITICAL EFFECT(S):	Fluorosis and caries prevalence

Eklund, S.A., A.I. Isamil, B.A. Burt, and J.J. Calderone. 1987. High-fluoride drinking water, fluorosis, and dental caries in adults. J. Amer. Dental Assoc. 114: 324-328.

ENDPOINT STUDIED:	Dental fluorosis and cornonal caries characterized by DMFT (decayed, missing, and filled permanent teeth index)
TYPE OF STUDY:	Case control, retrospective
POPULATION STUDIED:	USA/New Mexico/Lordsburg: Lifelong adult residents (n=164) from Lordsburg, NM (60 miles from Deming, NM), which has naturally fluoridated drinking water containing 3.5 mg/L fluoride. The adults were whites of Hispanic or other origin (89.6% Hispanic); 43.2 years old; 67.1% female; had 11.4 years of education, 27.0 teeth (mean values). Income level was similar to the control population (N = 187 examined, which generated 164 subjects). Same water supply has been in use since early 1900s.
CONTROL POPULATION:	USA/New Mexico/Deming: Lifelong adult residents (n=151) from Deming, NM (60 miles from Lordsburg, NM), which has naturally fluoridated drinking water containing 0.7 mg/L fluoride. The adults were whites of Hispanic or other origin (74.2% Hispanic); 39.8 years old; 68.2% female; had 12.5 years of education, 27.1 teeth (mean values) (N = 189 examined, which generated 151 subjects). Same water supply has been in use since early 1900s.
EXPOSURE PERIOD:	From birth to age 6, and through adulthood, subjects consumed city water (subject age ranged from 27-65). Some subjects had left town temporarily for military service or higher education. However, these subjects were included in the study because they lived in their respective towns for the majority of their life, including the years during which their teeth were formed.
EXPOSURE GROUPS:	Adult lifelong residents of Lordsburg or Deming who consumed city water during the first 6 years of life, and had clearly documented water drinking history through adulthood. Some subjects had temporarily left town for military service or higher education.
EXPOSURE ASSESSMENT:	Based on public records, city water natural fluoride concentrations of 0.7 mg F/L (Deming) and 3.5 mg F/L (Lordsburg) had been constant since the turn of the century. Individual intake of fluoride was not measured; study protocol confirmed that the subjects consumed city water from birth through age six (i.e. did not have private wells) and through most or all of their adulthood. No information was provided characterizing other sources of fluoride exposure such as toothpaste, mouth rinses, etc.
ANALYTICAL METHODS:	The report did not state analytical procedures used to determine city water fluoride concentrations. No other water quality parameters were reported.
STUDY DESIGN	Populations from two nearby towns (60 miles apart) in New Mexico, which were similar on the basis of income, climate and demographics, but had 5-fold different concentrations of natural fluoride in their drinking water, were studied to determine the influence of water fluoride concentration on teeth (fluorosis and caries). Subjects selected were ~30-60 years old, had consumed city water during their first six years of life as well as through most or all of their adulthood, and had been born in the community. Those with a history of private well use were excluded. Short absences (undefined) during adulthood for military service or education were acceptable to the study protocol. All eligible adults were recruited (due to small community size). Authors estimate that 88-90% of those eligible to do so did participate.

All 32 teeth of each subject were examined for dental fluorosis and caries and scored. Fluorosis severity was reported using Dean's 1942 classification scheme, except that the category of "severe" was split into two categories, one used when the pitting was discrete (severe), and the other when pitting was confluent (very severe). To calculate the community fluorosis index, both severe and very severe cases were scored as category 4. The classification for a given person was based on the most severe fluorosis seen for two or more teeth. Duplicate scoring on 29 people showed 77% concurrence, and 92% were scored within one fluorosis category of each other.

Dental caries were examined using the criteria of Radike (1968) and the DMFT index. Teeth that had not erupted or were lost to trauma were not scored. Results were reported for ≤28 teeth/person and excluded the third molars and teeth with crowns. Agreement on diagnosis was 94% between examiners for all teeth, and 83% for teeth with caries (did not state if exams were made in duplicate, as for fluorosis), indicating reliability.

PARAMETERS MONITORED:

All teeth of each subject were examined for dental fluorosis and caries (DMFT, crowns). Fluorosis severity was evaluated using Dean's 1942 classification scheme, but the qualitative description of severe fluorosis specified if the pitting was discrete or confluent (latter considered very severe). Dental caries were examined using the criteria of Radike (1968) and the DMFT index.

STATISTICAL METHODS:

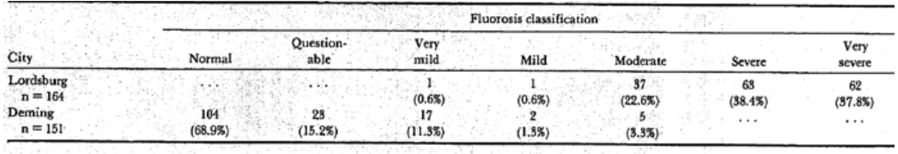
The number of decayed teeth, missing teeth, filled teeth, and the DMFT were compared in subjects of the two towns by the Student t-test or the Mann-Whitney U test. Comparisons were made for all subjects, and for age subgroups 27-40, 41-50, and 51-65. In addition, the results were analyzed by covariant linear regression, using the city of residence as the independent variable, and various dental conditions or the DMFT index as the dependent variables, with adjustments made for extraneous effects such as education, ethnic group, gender, age, and dental care.

RESULTS:

Dental fluorosis

Residents of Lordsburg had much more severe fluorosis (98.8% moderate to very severe) than residents of Deming (95.4% normal to very mild), as shown in study Table 2 (copied from p. 326 of study). The mean community fluorosis index (per Dean, 1942) was 3.74 for Lordsburg and 0.31 for Deming.

Table 2. Number and percent of subjects by city and fluorosis classification

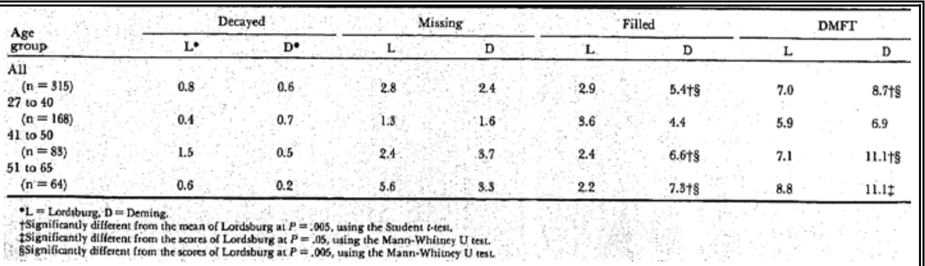


	Fluorosis classification						
City	Normal	Question-able	Very mild	Mild	Moderate	Severe	Very severe
Lordsburg n = 164	. . .	. . .	1 (0.6%)	1 (0.6%)	37 (22.6%)	63 (38.4%)	62 (37.8%)
Deming n = 151	104 (68.9%)	23 (15.2%)	17 (11.3%)	2 (1.3%)	5 (3.3%)	. . .	. . .

Dental caries

The overall DMFT score (per Radike 1968) was 7.0 for Lordsburg and 8.7 for Deming, suggesting that the Lordsburg residents had better protection against dental caries; these differences were significant (P = 0.0041). The difference in the DMFT was largely due to a higher value for the "filled" component, as shown in study Table 3 (copied from p. 326 of study). The DMFT also included rarely encountered components not shown in the table (e.g. restored teeth with recurrent caries or fractured enamel), which is why the DMFT score is in all cases greater than the sum of decayed, missing, and filled teeth. Covariant linear regression analysis indicated that the Lordsburg residents had 0.09 more decayed teeth, 0.24 fewer missing teeth, 1.71 fewer filled teeth, and 1.67 fewer DMFT per person than in Deming; only the differences in filled teeth and DMFT were statistically significant.

Table 3. Comparison of mean DMFT and selected components by city and age of lifelong resident adults.



Age group	Decayed		Missing		Filled		DMFT	
	L*	D*	L	D	L	D	L	D
All (n = 315)	0.8	0.6	2.8	2.4	2.9	5.4†§	7.0	8.7†§
27 to 40 (n = 168)	0.4	0.7	1.3	1.6	3.6	4.4	5.9	6.9
41 to 50 (n = 83)	1.5	0.5	2.4	3.7	2.4	6.6†§	7.1	11.1†§
51 to 65 (n = 64)	0.6	0.2	5.6	3.3	2.2	7.3†§	8.8	11.1‡

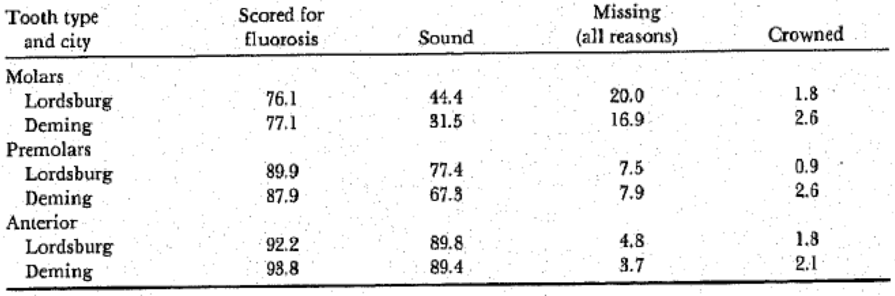
*L = Lordsburg, D = Deming.
†Significantly different from the mean of Lordsburg at $P = .005$, using the Student t-test.
‡Significantly different from the scores of Lordsburg at $P = .05$, using the Mann-Whitney U test.
§Significantly different from the scores of Lordsburg at $P = .005$, using the Mann-Whitney U test.

The authors state that adult participants in Deming possess nearly 2 more restored teeth than Lordsburg residents.

Effect of dental fluorosis on dental caries

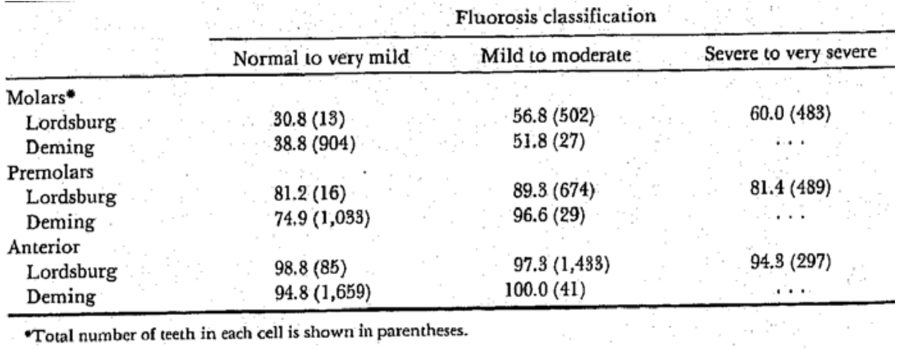
To determine whether fluorosis affected the incidence of dental caries in either town, the authors evaluated the percent of individual teeth that were sound (without caries) at three fluorosis severity categories for molars, premolars, and anterior teeth (see study Table 4). As shown in study Table 5, for a given fluorosis severity, the percent of sound teeth was similar for residents of the two towns. However, as the severity of fluorosis increased, so did the percent of sound molars, for residents of both towns. Fluorosis had less of an effect on anterior teeth or premolars, which were less prone to caries than molars (~75-99% sound vs. 31-39% sound for molars in either town); the most pronounced differences are observed in the molars. The correlation between the incidence of dental caries and fluorosis was not analyzed statistically due to the "complicated nature of the data" and because the teeth results were not independent observations, i.e. many teeth came from the same mouth. Further, there is only a small overlap in fluorosis levels between the 2 communities.

Table 4 ■ Percent of teeth scored for fluorosis, and as sound, missing, or crowned by tooth type and city of residence.



Tooth type and city	Scored for fluorosis	Sound	Missing (all reasons)	Crowned
Molars				
Lordsburg	76.1	44.4	20.0	1.8
Deming	77.1	31.5	16.9	2.6
Premolars				
Lordsburg	89.9	77.4	7.5	0.9
Deming	87.9	67.3	7.9	2.6
Anterior				
Lordsburg	92.2	89.8	4.8	1.8
Deming	93.8	89.4	3.7	2.1

Table 5. Percent of teeth that were sound in each fluorosis category, by tooth type and city of
residence



	Fluorosis classification		
	Normal to very mild	Mild to moderate	Severe to very severe
Molars*			
Lordsburg	30.8 (13)	56.8 (502)	60.0 (483)
Deming	38.8 (904)	51.8 (27)	. . .
Premolars			
Lordsburg	81.2 (16)	89.3 (674)	81.4 (489)
Deming	74.9 (1,033)	96.6 (29)	. . .
Anterior			
Lordsburg	98.8 (85)	97.3 (1,433)	94.3 (297)
Deming	94.8 (1,659)	100.0 (41)	. . .

*Total number of teeth in each cell is shown in parentheses.

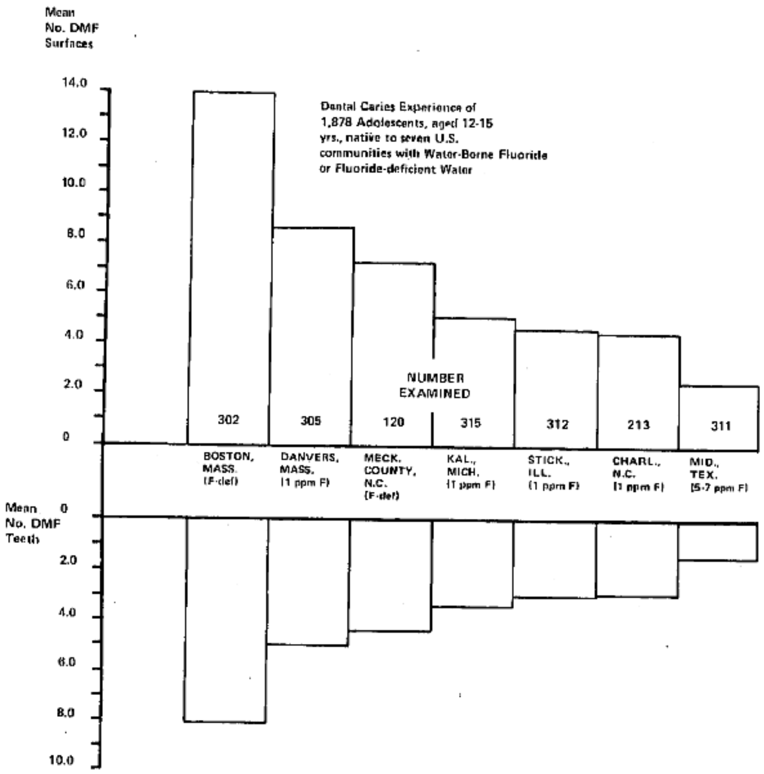
STUDY AUTHORS' CONCLUSIONS:

Eklund et al. (1987) concluded that (1) fluorosis was associated with an increased resistance to dental caries in the molars, which are the teeth most susceptible to dental caries (more so than premolars or anterior teeth), despite the lack of demonstrated statistical significance in the data; (2) **the data show no evidence that pitting seen in**

		teeth in severe dental fluorosis increases their susceptibility to caries; and (3) high fluoride levels (such as of 3.5 mg/L) are a cosmetic, and not a health-oriented, concern. The authors acknowledge that is it unknown whether or not the advantage is due to fluorosis per se or another parameter associated with fluorosis.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Radike, A.W. 1968. Criteria for diagnosis of dental caries. In: Proceedings of the Conference on the Clinical Testing of Cariostatic Agents. Chicago, American Dental Association.
PROFILER'S REMARKS	***Initials/date:SM 01/03/2007***	This was a well-conducted study from which logical conclusions were drawn. The demographic profiles of the two study populations were well matched. The study clearly showed an increased severity of fluorosis in the Lordsburg, NM, subjects, who were exposed to higher natural fluoride concentrations (3.5 mg F/L vs 0.7 mg F/L in Deming, NM) in the drinking water. The study was internally consistent in that for both populations, a given tooth type (molar, premolar, anterior) exhibited a similar susceptibility to caries, and a greater level of water fluoridation was associated with and increased resistance to caries. The primary study weaknesses were (1) a lack of quantitative individual cumulative exposure data from the drinking water, and from other possible sources such as toothpaste, mouth rinses, etc. and (2) no evaluation in individuals, but only in individual teeth, of the relationship between the percent of sound teeth and fluorosis severity (results of teeth within a given mouth are dependent variables). The study would have been more powerful if more people and an intermediate fluoride exposure level had been evaluated.
PROFILER'S ESTIM. NOEL/NOAEL		Based on absence of an increase in caries formation in the presence of fluorosis (approximately 38% of subject teeth in high-F community ranked as severe/very severe fluorosis), the NOAEL was ≥3.5 mg/L lifetime exposure. NOEL for severe fluorosis is >0.7 mg F/L lifetime drinking water exposure, but <3.5 mg F/L lifetime drinking water exposure.
PROFILER'S ESTIM. LOEL/ LOAEL		A LOAEL was not identified. Authors considered the effects of fluorosis on the teeth to be cosmetic, and that fluoride conferred protection against caries in molars of both populations (low-dose and high-dose).
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable ( ), Poor ( ), Medium (X), Strong ( ) The critical endpoint of **dental fluorosis** was clearly shown to be correlated with a higher intake of fluoride in the drinking water. Although individual exposures were not quantitated, intake could be estimated by using default or empirical values for water intake.
CRITICAL EFFECT(S):		Dental fluorosis and caries in molars, premolars and anterior teeth

Englander, H.R. and DePaola, P.F. 1979. Enhanced anticaries action from drinking water containing 5 ppm fluoride. JADA 98: 35-39.

ENDPOINT STUDIED:	Dental caries (permanent teeth)
TYPE OF STUDY:	USA: Prevalence study of dental caries in male and female children aged 12 to 15 years in seven communities in five states (MA, NC, MI, IL, and TX); dates of the study were not provided. All children included in the study were lifelong residents of their respective communities, and none had lived away for more than 30 consecutive days during any calendar year.
POPULATION STUDIED:	A total of 1,878 white adolescents (aged 12 to 15 years) were examined for caries on permanent teeth by one of two dentists. The children were examined in Boston, MA (<0.1 ppm fluoride); Danvers, MA (approximately 1 ppm fluoride); Mecklenburg County, NC (<0.1 ppm fluoride from well water); Kalamazoo, MI (approximately 1 ppm fluoride); Stickley, IL (approximately 1 ppm fluoride); Charlotte, NC (approximately 1 ppm fluoride); and Midland, TX (5 to 7 ppm fluoride). The mean age of the examined children ranged from 13.3 to 13.5 years depending on the community studied. The dates of the dental examinations were not provided in the study report. Subject children in each city were distributed similarly according to age, gender, race and socioeconomics factors. (The demographic data were not provided in the study report.) All children included in the study were lifelong residents of their respective communities, and none had lived away for more than 30 consecutive days during any calendar year. The geographic areas were chosen because, at the time, they presented few administrative difficulties. Data collected in each community were based on all the children who volunteered for the examinations.
CONTROL POPULATION:	None.
EXPOSURE PERIOD:	Children were lifelong residents of the communities so their exposure period was since birth to the age at which study examination took place (12-15 years' old).
EXPOSURE GROUPS:	Adolescents (aged 12 to 15 years) were exposed to different levels of fluoride in the water supply of seven communities in five states: Boston, MA (<0.1 ppm fluoride); Danvers, MA (approximately 1 ppm fluoride); Mecklenburg County, NC (<0.1 ppm fluoride from well water); Kalamazoo, MI (approximately 1 ppm fluoride); Stickley, IL (approximately 1 ppm fluoride); Charlotte, NC (approximately 1 ppm fluoride); and Midland, TX (5 to 7 ppm fluoride). The children were also categorized into three groups; those who consumed either fluoride-deficient drinking water, fluoridated water containing approximately 1 ppm fluoride or water containing 5 to 7 pm of naturally occurring fluoride.
EXPOSURE ASSESSMENT	Samples of fluoridated water obtained at the time of dental examination showed that the fluoride concentration in Danvers was 0.67 ppm. The previous high level of fluoride in the Midland (TX) water (5 to 7 ppm) had been reduced by dilution to 0.3 ppm fluoride ten months before the dental examinations were conducted because the concentration had exceeded the MCL of 1.6 ppm fluoride for this area as set by USEPA. Children in Mecklenburg County NC generally consumed fluoride-deficient water from shallow wells, but they frequently drank soft drinks and other beverages processed with fluoridated water from nearby Charlotte, NC; and many subjects also visited Charlotte often, and were herefore frequently exposed to Charlotte city water. The children from Danvers MA also drank beverages bottled and canned in nearby Boston MA, and many visited Boston often (and were assumed to consume "fluoride deficient" Boston city water).
ANALYTICAL METHODS:	None provided.
STUDY DESIGN	The objective of the study was to determine the prevalence of dental caries in adolescents who, since birth, have consumed either fluoride-deficient drinking water, fluoridated water containing approximately 1 ppm fluoride or water containing 5 to 7 pm of naturally

	occurring fluoride. One of two dentists conducted examinations according to the method of H.T. Dean (personal communication, 1953) on 1,876 adolescents (aged 12 to 15 years) exposed to different levels of fluoride in the water supply of seven communities in five states: Boston, MA (<0.1 ppm fluoride); Danvers, MA (approximately 1 ppm fluoride); Mecklenburg County, NC (<0.1 ppm fluoride from well water); Kalamazoo, MI (approximately 1 ppm fluoride); Stickley, IL (approximately 1 ppm fluoride); Charlotte, NC (approximately 1 ppm fluoride); and Midland, TX (5 to 7 ppm fluoride).
PARAMETERS MONITORED:	Monitored parameters included DMFT and DMFS. One of two dentists conducted examinations on the permanent teeth to determine the prevalence rate of dental caries in adolescents (aged 12 to 15 years) in seven communities of five states. All examinations were conducted according to the method of H.T. Dean (personal communication, 1953) with the use of mouth mirror, explorer and portable field equipment, including a dental light. Good agreement was found between the examiners with mean scores for decayed (D), missing (M), and filled (F) permanent teeth on the same group of 100 children in each of the communities consistently showing an insignificant difference of less than 0.2 DMFT between the examiners.
STATISTICAL METHODS:	Since there was good agreement between the examiners, data from all examinations were pooled for presentation, analysis and interpretation. Differences among means were tested by analysis of variance; the method of Scheffé was used for multiple comparisons.
RESULTS:	The number of children examined in each community and the caries experiences are illustrated below. REVIEWER'S NOTE: Due to the tight binding of the journal, the figure caption ("Dental caries experience of 1,878 adolescents who consumed water containing varying concentrations of fluoride") could not be captured in the image below.  Study results in Tables 1 and 2 are shown directly from Englander, 1979.

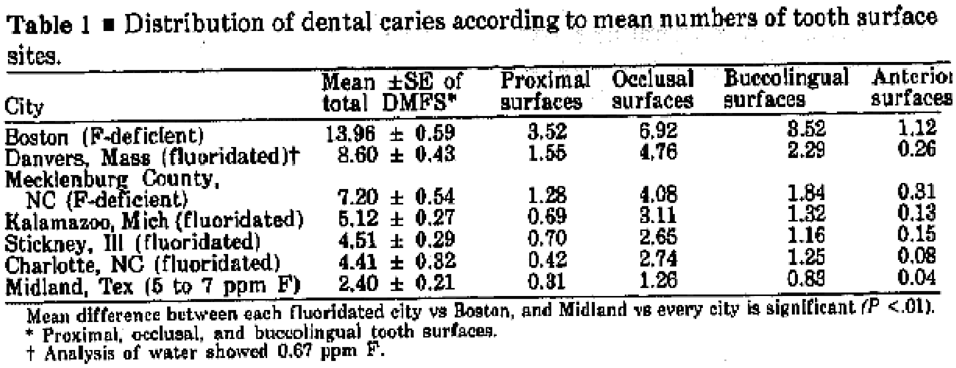


Table 1 ■ Distribution of dental caries according to mean numbers of tooth surface sites.

City	Mean ±SE of total DMFS*	Proximal surfaces	Occlusal surfaces	Buccolingual surfaces	Anterior surfaces
Boston (F-deficient)	13.96 ± 0.59	3.52	6.92	8.52	1.12
Danvers, Mass (fluoridated)†	8.60 ± 0.43	1.55	4.76	2.29	0.26
Mecklenburg County, NC (F-deficient)	7.20 ± 0.54	1.28	4.08	1.84	0.31
Kalamazoo, Mich (fluoridated)	5.12 ± 0.27	0.69	3.11	1.32	0.13
Stickney, Ill (fluoridated)	4.51 ± 0.29	0.70	2.65	1.16	0.15
Charlotte, NC (fluoridated)	4.41 ± 0.32	0.42	2.74	1.25	0.08
Midland, Tex (5 to 7 ppm F)	2.40 ± 0.21	0.31	1.26	0.83	0.04

Mean difference between each fluoridated city vs Boston, and Midland vs every city is significant ($P < .01$).

* Proximal, occlusal, and buccolingual tooth surfaces.

† Analysis of water showed 0.67 ppm F.

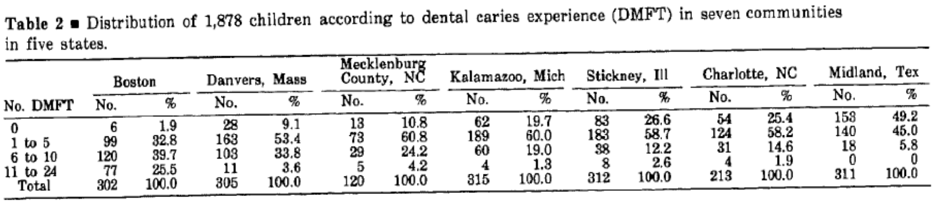


Table 2 ■ Distribution of 1,878 children according to dental caries experience (DMFT) in seven communities in five states.

	Boston		Danvers, Mass		Mecklenburg County, NC		Kalamazoo, Mich		Stickney, Ill		Charlotte, NC		Midland, Tex	
No. DMFT	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0	6	1.9	28	9.1	13	10.8	62	19.7	83	26.6	54	25.4	153	49.2
1 to 5	99	32.8	163	53.4	73	60.8	189	60.0	183	58.7	124	58.2	140	45.0
6 to 10	120	39.7	103	33.8	29	24.2	60	19.0	38	12.2	31	14.6	18	5.8
11 to 24	77	25.5	11	3.6	5	4.2	4	1.3	8	2.6	4	1.9	0	0
Total	302	100.0	305	100.0	120	100.0	315	100.0	312	100.0	213	100.0	311	100.0

STUDY AUTHORS' CONCLUSIONS:

The study authors concluded that the results of the study provide strong evidence that there can be much greater protection against dental caries from the almost continuous consumption, from birth, of a geologically fluoridated water supply that contains five to seven times the concentration of fluoride that is generally regarded as optimum for prevention of caries. The authors further conclude that the low caries activity observed in Midland, TX, should be corroborated with further study in high natural F areas to confirm this study's results. The authors do not recommend fluoridating community waters to concentrations higher than 1 or 2 ppm.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

None.

PROFILER'S REMARKS

Initials/Date
VAD
01-02-07
DMO
03/02/07

The dates and percentage of dental examinations conducted by each of the study authors were not provided. The study may have been biased by the following: 1) the study sites were chosen because they presented few administrative difficulties that could interfere with the arrangements and conduct of the examinations; and 2) the number of subjects in the exposure categories was unequal; there were 422, 1145 and 311 children with fluoride levels in the drinking water of <1 ppm, approximately 1 ppm and 5-7 ppm, respectively. The study group was 100% white and from a high socioeconomic status (as judged by their dental care) and therefore were not representative of the U.S. general population. The study didn't account for other sources of fluoride exposure in addition to the drinking water. Children from fluoride-deficient (<1ppm) communities may have had exposure to water and beverages containing fluoride when visiting nearby communities. Analytical testing data were not presented on samples of the fluoridated water obtained at the time of the dental examinations; however, fluctuations in the expected levels of fluoride apparently occurred.

In several subject cities (Danvers, MA and Midland, TX) the measured fluoride levels at the time of dental exam did not correspond to expected F concentrations incorporated into the study design. Further, many of the adolescents enrolled in the study were frequently exposed

		to water supplies from nearby communities with quite different fluoride concentrations (e.g., Danvers, MA and F-deficient Boston, MA). These observations tend to compromise interpretation of study results.
PROFILER's ESTIM. NOAEL		The study design did not estimate a NOAEL.
PROFILER'S ESTIM. LOAEL		The study design did not estimate a LOAEL.
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable,(_); Poor (X); Medium (_); Strong (_)
CRITICAL EFFECTS:		Dental caries (permanent teeth)

Ermis, R. B., F. Koray and B.G. Akdeniz. 2003. Dental caries and fluorosis in low- and high-fluoride areas in Turkey. Restorative Dentistry. Volume 34 (5): 354-360.

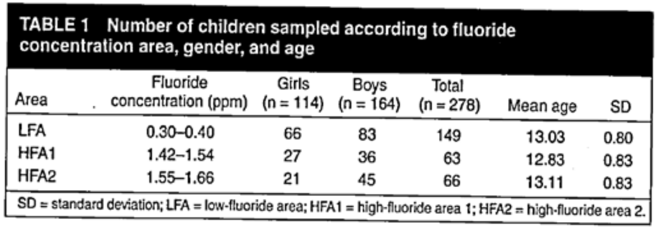
<table>
<tr><td colspan="2"></td></tr>
<tr><td>ENDPOINT STUDIED:</td><td>Dental fluorosis and prevalence of dental caries</td></tr>
<tr><td></td><td></td></tr>
<tr><td>TYPE OF STUDY:</td><td>Cross-sectional survey</td></tr>
<tr><td></td><td></td></tr>
<tr><td>POPULATION STUDIED:</td><td>Turkey/Izmir and Isparta. 278 (114 girls and 164 boys) schoolchildren, 12 to 14 years old, in Turkey. In the study, 149 children were from the city of Izmir, a low-fluoride area, and 129 children were from Isparta, a high-fluoride area. All children were required to have been residents of the study site.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>CONTROL POPULATION:</td><td>None</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE PERIOD:</td><td>Exact duration of exposure was not stated, although children were required to be a resident of the study site and using the public water supply continuously as their drinking water source. In addition, they were required to have no nutritional deficiencies; however, Ermis et al (2003) provide no data or protocol characterizing how nutritional status was determined. Data were collected in the Spring of 1999.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE GROUPS:</td><td>
TABLE 1 Number of children sampled according to fluoride concentration area, gender, and age
<table>
<tr><th>Area</th><th>Fluoride concentration (ppm)</th><th>Girls (n = 114)</th><th>Boys (n = 164)</th><th>Total (n = 278)</th><th>Mean age</th><th>SD</th></tr>
<tr><td>LFA</td><td>0.30–0.40</td><td>66</td><td>83</td><td>149</td><td>13.03</td><td>0.80</td></tr>
<tr><td>HFA1</td><td>1.42–1.54</td><td>27</td><td>36</td><td>63</td><td>12.83</td><td>0.83</td></tr>
<tr><td>HFA2</td><td>1.55–1.66</td><td>21</td><td>45</td><td>66</td><td>13.11</td><td>0.83</td></tr>
</table>
SD = standard deviation; LFA = low-fluoride area; HFA1 = high-fluoride area 1; HFA2 = high-fluoride area 2.

Table 1 was copied directly from the study report (Ermis et al., 2003) indicating the gender, number and ages of the participants and the levels of fluoride concentration (ppm) of the water supply.

PROFILER’S NOTE: The fluoride in the water supply occurred naturally as the water supplies in the study communities had not been deliberately fluoridated.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE ASSESSMENT:</td><td>Two examiners were used for the study. Prior to the study, the two examiners were involved in a 2-day training session to standardize how they rated the incidence of fluorosis and caries. At the end of the training, the two agreed on the scoring of fluorosis and caries greater than 90% of the time. Intra-examiner reliability was performed on 10% of the sample, and the results showed an agreement of 77% to 94% for scoring of the fluorosis and caries. The examiners used the Tooth Surface Index of Fluorosis (TSIF) by Horowitz et al. (1984) for scoring the fluorosis. Caries were diagnosed according to the World Health Organization (WHO, 1997) recommendations. Examinations were performed under natural daylight using plane mouth mirrors and explorer tools.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>ANALYTICAL METHODS:</td><td>The method of measuring the fluoride in the water supply was not provided. The cities of testing were Izmir, which was considered an area of low-fluoride and had a fluoride concentration ranging from 0.30 to 0.40 ppm in the drinking water; and Isparta, which was a high-fluoride area in which fluoride ranged from 1.42 to 1.66 ppm Both cities did not have fluoridation programs and the fluoride occurred naturally. Values of the fluoride concentrations were obtained by the Ministry of Health, Public Health Laboratories.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>STUDY DESIGN</td><td>The study subjects included 278 (114 girls and 164 boys) schoolchildren, 12 to 14 years old, in 2 Turkish cities. The subject population included 149 children from the city of Izmir, a low-fluoride area; and 129 children from Isparta, a high-fluoride area.</td></tr>
</table>

To initially select the participants in the study, four schools in both cities were selected by random sampling from a list of secondary schools. Then, 12-14 year old schoolchildren were randomly selected from each school.

Clinical dental examination of each child was performed once (Spring 1999) by two examiners using natural daylight, plane mouth mirrors and explorer's tools.
The examinations scored dental fluorosis (Tooth Surface Index of Fluorosis) and caries (WHO criteria). Children were also asked about their tooth-brushing frequency.

PARAMETERS MONITORED:

Fluorosis was assessed by using the Tooth Surface Index of Fluorosis (TSIF) (Horowitz et al., 1984) which is defined in the Section 2 of the report. Individuals having at least 2 different teeth with a TSIF ≥ 1 were defined as a case of fluorosis.

Caries was diagnosed according to the World Health Organization (WHO, 1997) recommendations. Diagnosis was made when a lesion in a pit or fissure or on a free smooth surface had a detectable softened area, or there was a temporary restoration. A separate score was given to each facial and lingual surface of anterior teeth and to each facial, lingual, and occlusal surface of posterior teeth. Indices used for evaluation of the caries were: (1) decayed, missing and filled permanent teeth (DMFT) and (2) decayed, missing and filled permanent surfaces (DMFS). Radiographs were not taken on any of the children.

Children were also questioned about the frequency of their tooth-brushing and allowed the following answers: didn't brush, brushed once a day, more than once a day, or brushed irregularly.

No information about exposure to any other sources of fluoride or the amount of water consumed was included in the study protocol description.

STATISTICAL METHODS:

TSIF fluorosis scores were statistically analyzed using the correlation analysis to determine any differences between fluoride exposure groups. Kruskal-Wallis and Mann-Whitney U test were used to compare the tooth-brushing frequencies between the low- and high-fluoride areas; the caries indices were compared to the tooth-brushing frequencies. The tooth-brushing frequency efficiency in DMFT and DMFS indices was evaluated using analysis of covariance. Spearman's correlation analysis was used to determine the association between severity of dental fluorosis and caries prevalence. The level of significance was $p< 0.05$.

RESULTS:

Dental fluorosis

Children in the low fluoride areas had no evidence of fluorosis. Table 3 is copied directly from Ermis et al. (2003) and indicates the TSIF scores for all the children examined in the high-fluoride areas. The scores indicated that the prevalence and severity of fluorosis increased as the fluoride levels increased. Figure 2 was also provided from Ermis et al. (2003) and indicated the cumulative distribution of the average TSIF score per child in the different fluoride groups. According to the report, the percentage of children with TSIF scores ≥ 1 was 29% and 77% in the HF area 1 and HF area 2, respectively. According to the TSIF scoring index employed by Ermis, et al, pitting occurs at TSIF ≥ 5, with initiation of brown staining at TSIF = 4.

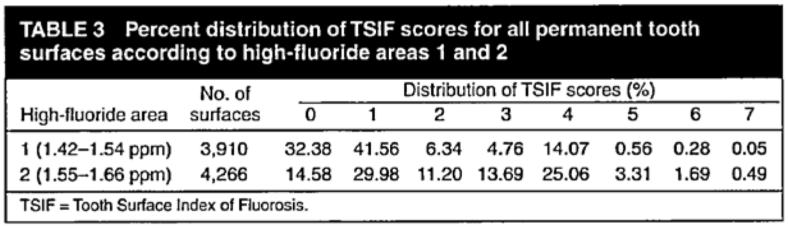
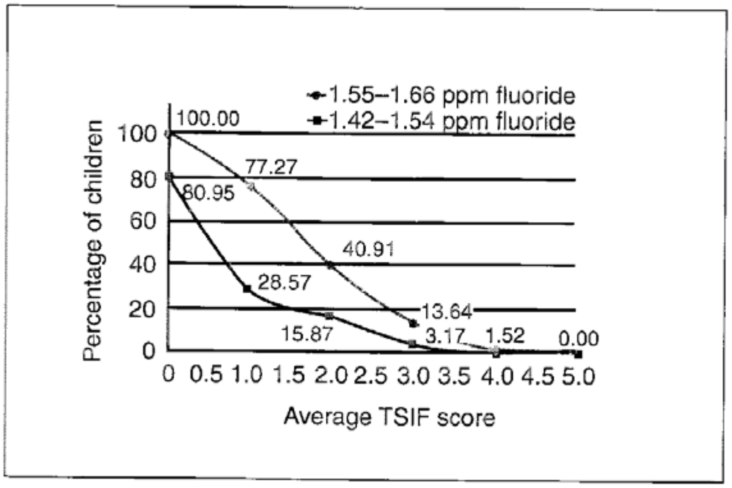


TABLE 3 Percent distribution of TSIF scores for all permanent tooth surfaces according to high-fluoride areas 1 and 2

High-fluoride area	No. of surfaces	Distribution of TSIF scores (%) 0	1	2	3	4	5	6	7
1 (1.42–1.54 ppm)	3,910	32.38	41.56	6.34	4.76	14.07	0.56	0.28	0.05
2 (1.55–1.66 ppm)	4,266	14.58	29.98	11.20	13.69	25.06	3.31	1.69	0.49

TSIF = Tooth Surface Index of Fluorosis.

	 **Fig 2** Cumulative distribution of TSIF fluorosis prevalence and severity for different fluoride-exposure groups. This figure is interesting because it does show dose response relative to the severity of fluorosis in two places where the differences in fluoride are small. It is unfortunate that the study authors did not provide information on differences regarding other sources of fluoride or water intake that could be examined. PROFILER'S NOTE: The profiler agrees with the study author that the prevalence and severity of fluorosis increased in the area with the higher amount of fluoride. However, the number of children with adverse TSIF scores (≥ 5, considered severe, was 0.89% in HF area 1 and 5.49% in HF area 2) were actually fairly low in both areas. The low-fluoride data in a comparable format should be provided even though it was stated that no fluorosis was identified. Further breakdown into gender was not needed but could have been helpful in determining any trends. Information on the methods used to test fluoride concentrations in the water and the frequency of the water testing was not included. The captions for Figure 2 do not readily indicate that the results illustrated are for high-fluoride communities only and that the X-axis unit is the average TSIF score *per child*; further, the distribution of TSIF scores/child cannot be determined from the high-fluoride community TSIF distribution (Table 3) presented.
Dental caries	Table 5 is copied directly from Ermis et al. (2003) to indicate the caries data in relation to the TSIF score. Another table, Table 4, was not copied as it just provided caries data. Ermis et al. (2003) states that the findings in the study indicate no significant difference in the prevalence of caries prevalence in the permanent teeth of children exposed to 0.30-0.40 ppm and 1.42-1.66 ppm fluoride in the drinking water. However, the relationship between DMFT and DMFS scores and the frequency of tooth-brushing was significant.

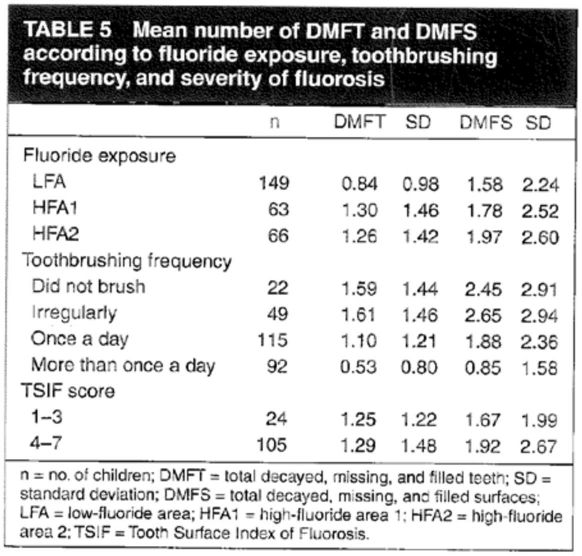


TABLE 5 Mean number of DMFT and DMFS according to fluoride exposure, toothbrushing frequency, and severity of fluorosis

	n	DMFT	SD	DMFS	SD
Fluoride exposure					
LFA	149	0.84	0.98	1.58	2.24
HFA1	63	1.30	1.46	1.78	2.52
HFA2	66	1.26	1.42	1.97	2.60
Toothbrushing frequency					
Did not brush	22	1.59	1.44	2.45	2.91
Irregularly	49	1.61	1.46	2.65	2.94
Once a day	115	1.10	1.21	1.88	2.36
More than once a day	92	0.53	0.80	0.85	1.58
TSIF score					
1–3	24	1.25	1.22	1.67	1.99
4–7	105	1.29	1.48	1.92	2.67

n = no. of children; DMFT = total decayed, missing, and filled teeth; SD = standard deviation; DMFS = total decayed, missing, and filled surfaces; LFA = low-fluoride area; HFA1 = high-fluoride area 1; HFA2 = high-fluoride area 2; TSIF = Tooth Surface Index of Fluorosis.

PROFILER'S NOTE: The profiler agrees that there was a lower DMFT and DMFS in the low-fluoride area compared to the high-fluoride areas but there was not much of a change between the two high-fluoride areas. The profiler also agrees that tooth brushing frequency does appear to help with the incidence of caries; however, without additional data, the profiler can not make any definite conclusions. The study author states that the lower fluoride area children had better oral hygiene (i.e. more frequent tooth brushing) but one cannot make that distinction from the data provided. Also, the instruments/cleaners used for tooth brushing were not characterized.

STUDY AUTHORS' CONCLUSIONS:

Findings of the study indicated that the significant difference in prevalence and severity of dental fluorosis was closely associated with fluoride concentration in the drinking water. While there was no significant difference found between the caries prevalence and fluoride concentration, poor oral hygiene had a significant effect on the higher risk of dental caries in the high-fluoride area.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

World Health Organization (WHO). 1997. Method of assessing dental caries. Oral Health Surveys: Basic Methods, ed. 4, Geneva, Switzerland. p. 39-44.

PROFILER'S REMARKS

Initials/date DFG/11-06 12/14/06

Adequate data were presented but the profiler could not determine how some conclusions were made with the data presented. Some of the percentages included in the paper were not consistent with the data provided (See Profiler's Note under Results section.). Also, there was a lack of confirmation about the subject's duration of exposure to the drinking water and if there was exposure to other sources of fluoride (i.e. supplements, food). Additional information on how the fluoride levels in the water were measured (i.e. analytical techniques) and how often the levels were measured to account for groundwater fluctuations would have added value to the study.

The study did try to minimize subjective differences by only having two examiners and having a "training" session with these two individuals to allow them to become consistent on their scoring techniques. The use of the TSIF scoring and the indices of dental caries by the WHO also helped in the study objectiveness. Statistical analysis appeared to be adequate although more data to support the conclusions are needed. The addition of the tooth brushing frequency added another variable that took away some of the study's objectiveness. The study did not address how tooth brushing was performed and if it involved the use of toothpaste containing NaF as most commonly do. Also, from the data provided, the profiler could not distinguish which children were the ones with the better oral hygiene.

PROFILER'S ESTIM. NOEL/NOAEL	Study design was not suitable for development of a NOAEL.
PROFILER'S ESTIM. LOEL/ LOAEL	Study design was not suitable for development of a LOAEL.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (_), Poor (X), Medium (_), Strong (_)
CRITICAL EFFECT(S):	Fluorosis and prevalence of dental caries

Forsman, B. 1974. Dental fluorosis and caries experience in high-fluoride districts in Sweden. Community Dent. Oral Epidemiol. 2:132-148.

ENDPOINT STUDIED:	Dental fluorosis; caries
TYPE OF STUDY:	Cohort
POPULATION STUDIED:	Sweden/ Gadderas (pop. 90): 39 individuals aged 2-35 years; 28 were born in Gadderas and 15 were less than 15 years old. Sweden/Paskallavik (pop. 900): 190 schoolchildren, born in the years 1955-1966, 61 pupils were born and raised in the area. Sweden/Billesholm (pop. 3000): 300 schoolchildren; 133 were born and raised in the district. All children received regular dental care at the district clinics from the time they were either 3 or 6 years of age.
CONTROL POPULATION:	Sweden/Eskilstuna (pop. 93,000) and Kronoberg county (pop. 168,000): Schoolchildren (data for 160 children from Kronoberg county were used in comparison studies).
EXPOSURE PERIOD:	No consistently set exposure periods existed. In Gadderas, exposure at ~ 10 ppm ranged up to a maximum of 27 years (from 1946 when a new water source was implemented to 1973, the year this study was submitted), with exposure initiating from birth or at intervals up to 14 years old. In Paskallavik, exposure at ~10 ppm ranged up to 9 years and was categorized into periods less than or more than 4 years. In Billesholm, exposure at ~ 5 ppm ranged up to 12 years.
EXPOSURE GROUPS:	The following exposure group designations were used in the study analysis: Gadderas: Starting in 1946, homes in the town were connected to a new water source and all homes were connected by 1950; mean fluoride concentration from 1969 to 1973 was 10.1 mg/l. For the purposes of this study, the fluoride level was considered to be ~ 10 ppm. Paskallavik: The water source had a fluoride level of 7-10 mg/l from mid-1956 to beginning 1965; prior to 1956, private wells with low fluoride content were used, and after 1965 the water source was changed, with a fluoride content of 2.0-2.5 mg/l. For the purposes of this study, the fluoride level was considered to be ~ 10 ppm. Billesholm: Water was obtained from two deep wells; from 1957 to 1969 fluoride level varied between 4 and 7 mg/l, but mostly was around 5.5 mg/l. From 1969 to 1973 the fluoride content was 1-3 mg/l or less. For purposes of this study, the fluoride level was considered to be ~ 5 ppm. Eskilstuna had a water fluoride level of 1.2 mg/l; the same ground filtration system has been in use since 1913. Two districts in Kronoberg county have 0.9-1.0 mg F/l in the water and the other two districts, 1.3-1.7 mg/l, at least since 1950. For the purposes of this study, the fluoride level was considered to be ~ 1 ppm.
EXPOSURE ASSESSMENT:	Factors influencing fluoride intake (e.g., diet, fluoridated dentifrices, etc.), other than drinking water, were not considered in the study report.
ANALYTICAL METHODS:	Water, enamel/dentin, saliva, and breast milk fluoride data were analyzed using the Orion F^- electrode. Water quality data were not included in the report. For teeth, the crowns were divided into an occlusal and a cervical half; enamel was separated from dentin by the floatation method of Manly and Hodge (1939). Fluoride content was determined in buffered solutions of the washed and dried enamel/dentin powder. After an overnight fast, parotid saliva was collected with Lashley cups under stimulation with 6% citric acid on the dorsum of the tongue. Breast milk samples were taken for three days in the hospital located in the county capital, where water

	fluoride level was <0.2 mg/l. After some weeks at home in Gadderas, samples were taken for 2 days: a morning sample after fasting and an afternoon sample, hours after ingestion of ~0.5 l of Gadderas water.
STUDY DESIGN	The study included residents from communities in southern Sweden, mostly school children, exposed to fluoride at levels of either ~1 ppm (n= not reported, Eskilstuna and Kronoberg county), ~ 5 ppm (n=300, Billesholm) or ~10 ppm (n=229, Gadderas and Paskallavik). Water fluoride data were often checked by personal analysis. The occurrence of fluorosis and caries in primary and permanent teeth was investigated either by examination or dental records, using Dean's index and DMFT or DMFS scores, respectively. Caries generally was obtained from dental records; in subjects from Gadderas whose primary teeth had not already exfoliated, caries registration was done at the same time as the fluorosis examination. Color photographs of typical cases were taken in every district. Examination details were not reported, including location where examinations occurred, lighting conditions, or equipment used. Case histories, including water supply data, places of birth, migrations, etc., were collected from different sources: waterworks records, school authorities, the vital statistics system, etc. Several data from Gadderas and Billesholm were collected from previous surveys. Factors influencing the incidence and degree of fluorosis were evaluated, including duration of breastfeeding and prenatal fluoride exposure. Information on feeding during the first year of life was obtained by questionnaire; a second questionnaire was used by mothers in Paskallavik and Billesholm to assess fluoride exposure before and during pregnancy, in addition to during of breastfeeding. The relationship between fluoride exposure and content in enamel and dentin was analysed, as well as the relationship between plasma and saliva fluoride. Fluoride content was determined in exfoliated primary and permanent teeth extracted for orthodontic reasons from individuals in the ~10 ppm and ~ 5 ppm areas. Saliva samples were taken from 21 subjects. Fluoride content in breast milk was determined from two patients residing in Gadderas for less than 2 years.
PARAMETERS MONITORED:	Dental fluorosis was recorded according to Dean's index; fluorosis was scaled as none (0), questionable (0.5), very mild (1), mild (2), moderate (3), or severe (4). Caries generally was obtained from dental records and covered both DMFT (decayed, missing, and filled permanent teeth) and DMFS (decayed, missing, and filled permanent tooth surfaces).
STATISTICAL METHODS:	Statistical methods were not detailed in the study report. From figure legends and brief text, it was concluded that regression analyses were used. Chi-square test was used to determine significance in bivariable analyses.
RESULTS:	
Dental fluorosis	Figures and Tables were copied directly from Forsman (1974). Figure 2 summarizes the percent distribution of fluorosis in permanent teeth according to severity and community; data from primary teeth is not shown. At ~10 ppm, all individuals born in Gadderas after 1950 had moderate to severe fluorosis in all permanent teeth. Most primary teeth had moderate to severe fluorosis for canines and molars and up to mild fluorosis for incisors. Children who moved to the district after the age of 18 months showed no fluorosis in the primary dentition. Severe fluorosis also was noted in Paskallavik. All but one child born between 1957 and 1961 (exposure > 4 years) had moderate to severe fluorosis; 27% (7/26) had severe fluorosis on all teeth. Children born 1962-1964 and who had less than 4 years of high fluoride exposure showed milder fluorosis (only 40% with moderate to severe fluorosis). There were 11 children born within the 1.5 years after the fluoride content was lowered to ~2 ppm (in 1965); 9 of the 11 had fluorosis of grade 1-4 in their primary teeth. Thus, a long period of exposure is necessary, even with very high water fluoride concentrations, for a severe degree of fluorosis to occur in permanent teeth (difference between exposure durations was significant at p<0.01). In primary teeth, degree of fluorosis was generally moderate to severe. At the ~5 ppm fluoride level, 28% showed moderate to severe fluorosis in the permanent teeth,

50% mild fluorosis, 25% very mild, 1.5% (2/133) had no fluorosis. In the primary teeth, all degrees of fluorosis were observed, generally mild; 20% (of n=67) had no fluorosis in the primary dentition.

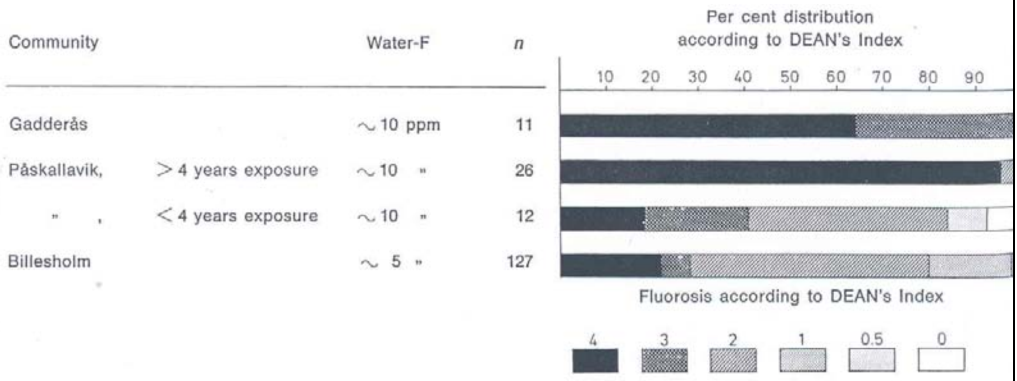


Fig. 2. Enamel fluorosis in permanent teeth of children born and reared in ~ 10 ppm and ~ 5 ppm areas.

Gender, duration of breast feeding, and prenatal exposure to fluoride were evaluated for their influence on the occurrence and degree of fluorosis. Table 2 shows that, there was a tendency for more severe fluorosis to occur in boys compared to girls at ~5 ppm fluoride (Chi-square test, p<0.05), but the sample size was small.

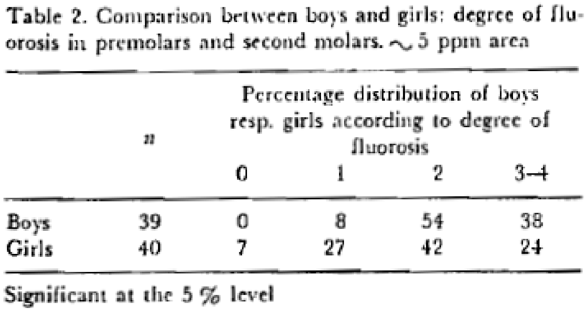


Table 2. Comparison between boys and girls: degree of fluorosis in premolars and second molars. ~ 5 ppm area

	n	Percentage distribution of boys resp. girls according to degree of fluorosis			
		0	1	2	3–4
Boys	39	0	8	54	38
Girls	40	7	27	42	24

Significant at the 5 % level

Figures 9-12 show the occurrence of fluorosis in permanent incisors and molars in relationship to duration of breastfeeding (up to 10-12 months) in areas with different water fluoride levels (data for primary teeth are not shown). Figure 12 shows that in the ~10 ppm areas, severe fluorosis occurred with a long duration of breastfeeding. Fluorosis in the primary dentition was milder in children breastfed for a longer period. In the other districts (Figures 9-11), increasingly severe fluorosis occurred with higher water fluoride levels for the same number of months of breastfeeding.

Fig. 9. Relationship breastfeeding – enamel fluorosis of permanent incisors and first molars. ~ 1 ppm area, 0.9–1.0 mg F/1.

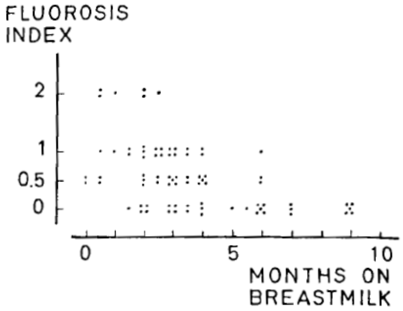


Fig. 10. Relationship breastfeeding – enamel fluorosis of permanent incisors and first molars. ~ 1 ppm area, 1.3–1.7 mg F/1.

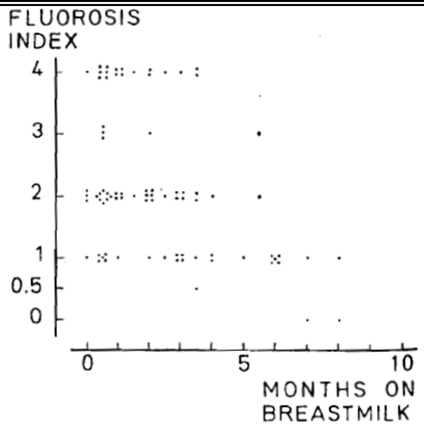


Fig. 11. Relationship breastfeeding – enamel fluorosis of permanent incisors and first molars. ~ 5 ppm area.

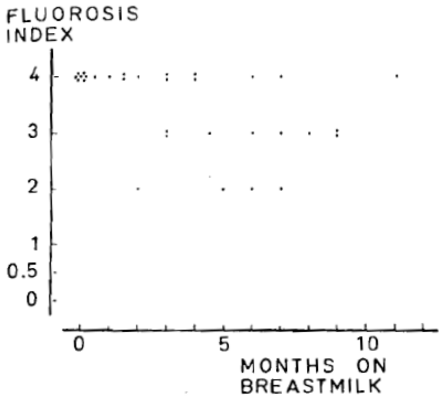


Fig. 12. Relationship breastfeeding – enamel fluorosis of permanent incisors and first molars. ~ 10 ppm area.

Table 3 summarizes the exposure of mothers to fluoride in the ~5 ppm area before and during pregnancy, combined with fluorosis data from primary teeth. The degree of fluorosis was higher in children whose mothers spent the pregnancy in a high (~5 ppm) fluoride area (75% with mild to severe fluorosis in ~5 ppm area vs. 50% in low fluoride area) and/or lived in a high fluoride district before pregnancy (85% mild to severe fluorosis with high exposure vs. 41% mild (0% moderate to severe) with low exposure) (Chi-square, p<0.01 and 0.001, respectively).

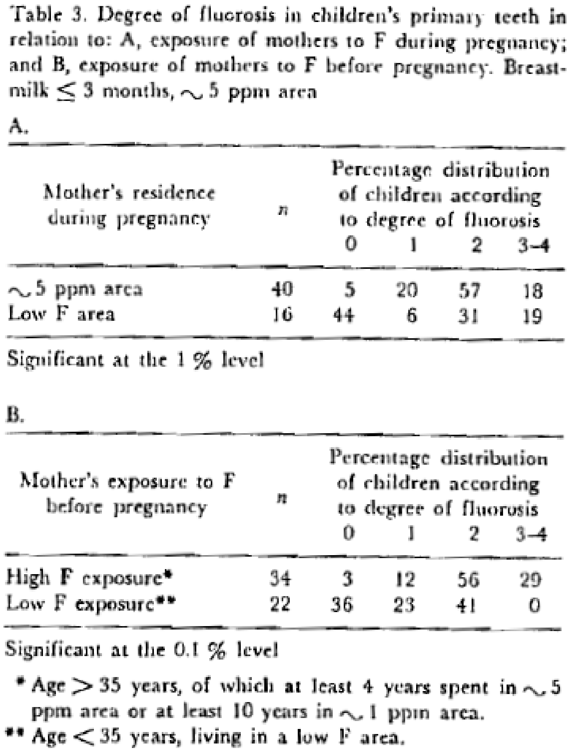


Table 3. Degree of fluorosis in children's primary teeth in relation to: A, exposure of mothers to F during pregnancy; and B, exposure of mothers to F before pregnancy. Breast-milk ≤ 3 months, ~ 5 ppm area

A.

Mother's residence during pregnancy	n	Percentage distribution of children according to degree of fluorosis 0	1	2	3–4
~ 5 ppm area	40	5	20	57	18
Low F area	16	44	6	31	19

Significant at the 1 % level

B.

Mother's exposure to F before pregnancy	n	Percentage distribution of children according to degree of fluorosis 0	1	2	3–4
High F exposure*	34	3	12	56	29
Low F exposure**	22	36	23	41	0

Significant at the 0.1 % level

* Age > 35 years, of which at least 4 years spent in ~ 5 ppm area or at least 10 years in ~ 1 ppm area.
** Age < 35 years, living in a low F area.

Three cases of 'delayed fluorosis' were found. One patient born in a ~10 ppm area moved to a district with a fluoride level <0.2 mg/l at 3.25 years of age and at age 17 years had moderate to severe fluorosis in all teeth except the second molars, which showed mild fluorosis. Two other patients, born in 1953, moved from a ~10 ppm area to a low fluoride area at age 7 years and had moderate to severe fluorosis in all teeth, but the third molars which had not yet erupted.

PROFILER'S NOTE: The profiler agrees that the occurrence of fluorosis was greater in subjects with a longer (>4 years) duration of high fluoride exposure (~10 ppm) compared to subjects with a shorter (<4 years) duration of high fluoride exposure or with mid-level (~5 ppm)

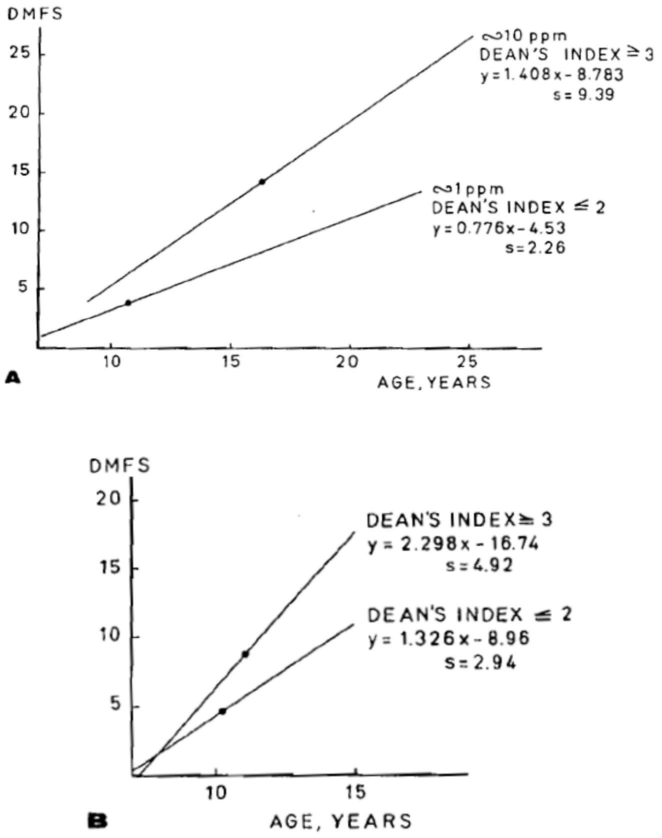
	fluoride exposure. However, it should be noted that the sample sizes were small in the ~10 ppm areas (n=11-26) and much different from that in the ~5 ppm area (n=127). Both the water fluoride level and the duration of breastfeeding impacted the occurrence and severity of fluorosis. Further, the mother's pre- and during pregnancy fluoride exposure seems to influence the severity of fluorosis in offspring, but the sample sizes were small and accurate history of actual fluoride exposure is difficult to confirm. A definitive conclusion regarding the cases of 'delayed fluorosis' can not be determined since the data were limited to only 3 cases and the two photographs included in the paper did not reproduce well.
Caries	In the ~10 ppm areas, the caries frequency in permanent teeth was unexpectedly high and extremely high in subjects in Gadderas who were over 20 year old; only one adult was caries-free. The caries frequency in primary teeth was low; in Gadderas, caries in primary teeth occurred only in children who moved into the area after 18 months of age. In the ~5 ppm area, the caries frequency in permanent teeth was less, except for about 20 teenagers, all of whom had >20 DMFS (data not shown). Previous investigations for caries and fluorosis with 160 children from ~1 ppm areas in Kronoberg county showed low caries frequency and, at most, mild fluorosis. Figure 14A demonstrates the comparison between this control data and data from individuals showing moderate to severe fluorosis following long (>4 years) and high (~10 ppm) fluoride exposure. There was a direct correlation between degree of fluorosis and caries frequency, as well as a direct correlation between age and DMFS count. The regression coefficients for both lines were not statistically significantly different from one another, but the difference in height between the lines (5.89) was significant (p<0.01). In the ~5 ppm area, the degree of fluorosis varied greatly among subjects so comparison for caries frequency was made between those with no to very mild (≤2) fluorosis and with moderate to severe (≥3) fluorosis. The results are presented in Figure 14B. The higher degree of fluorosis was associated with higher caries frequency (p<0.01). 

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Fig. 14. Age – caries regression lines for groups with different degrees of enamel fluorosis. The regression lines cover the respective age ranges, and the caries averages are marked by points on the lines.
s denotes standard deviations of the respective lines.
A. ~ 10 ppm, DEAN's index ≧ 3 versus ~ 1 ppm, DEAN's index ≦ 2.
Numbers of observation: ~ 10 ppm: 38, ~ 1 ppm: 160.
B. DEAN's index ≧ 3 versus ≦ 2, both in ~ 5 ppm area.
Numbers of observations: D. i ≧ 3:37, D. i ≦ 2:91.

Figure 15 shows a comparison between deft count (decayed, extracted, and filled teeth) at 6-7 years in areas with different fluoride levels. Increased water fluoride level significantly reduced caries frequency in the primary dentition even at ~10 ppm. No association between high degree of fluorosis and high caries frequency was demonstrated in the primary dentition.

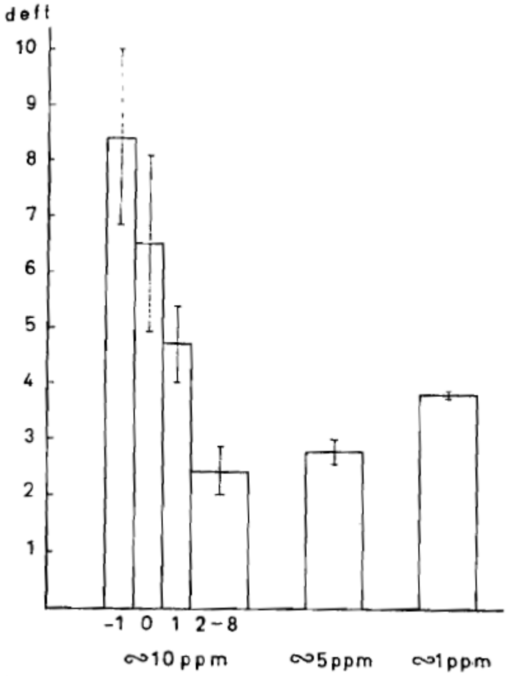

Fig. 15. Caries in the primary dentition of children born and reared in areas with different water F content.
~ 10 ppm = Påskallavik
-1 = children born the year before introducing ~ 10 ppm, $n = 5$
0 = children born the year of introducing ~ 10 ppm, $n = 6$
1 = children born the year after introducing ~ 10 ppm, $n = 7$
2–8 = children born 2–8 years after introducing ~ 10 ppm, $n = 40$
~ 5 ppm = Billesholm, $n = 124$
~ 1 ppm = Eskilstuna, $n = 2.170$
Påskallavik 2–8 children and Billesholm children significantly different from Eskilstuna children ($P < 0.1$ %).

PROFILER'S NOTE: The profiler agrees that higher degree of fluorosis was associated with higher caries frequency in both the ~5 ppm and ~ 10 ppm areas; caries frequency also tended to increase with age. Data for caries frequency was not included in the report, so results could not be confirmed.

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<tr><td>Fluoride content in enamel/dentin and saliva</td><td>The mean fluoride level in premolars (permanent teeth, n=3) from subjects in the ~ 5 ppm area was 447.2 ppm in enamel and 617.1 ppm in dentin, about 4 times greater than the values obtained from the ~1 ppm area. In the incisors (primary teeth, n=4) of children from the ~ 5</td></tr>
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ppm area, fluoride deposits in enamel (305.5 ppm in occlusal tissue, 582.1 ppm in cervical tissue) and dentin (688.2 ppm and 1200.2 ppm, respectively) also were high. For children who moved into the area, fluoride content was about ¼ of that of the children born there and about the same as for children in ~1 ppm areas (data not shown).

Figure 16 (A and B) shows fluoride deposition in the enamel and dentin of primary teeth in relation to fluoride exposure in the ~ 10 ppm areas, calculated as the number of post-mineralization months without breastfeeding. Fluoride level was high in teeth with zero months of exposure and some increase occurred with increased number of months. The correlation between estimated fluoride exposure and fluoride content of the dental tissues was strongest for occlusal tissue (Figure 16A, enamel r=0.73, dentin r=0.66, significant, but level of significance not indicated), but weak for cervical tissue (Figure 16B, r=0.32 and 0.18, respectively).

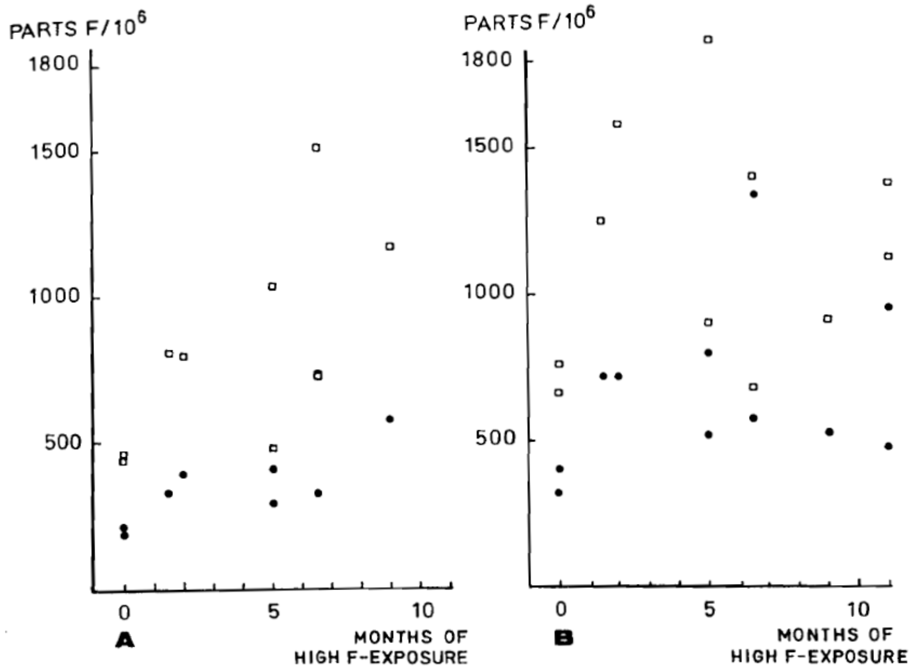

Fig. 16. Relationship F-exposure – F-content in decidous enamel and dentin. ~ 10 ppm areas. F-exposure = number of postnatal mineralization months without breastfeeding. A, occlusal tissue. B, cervical tissue. ● enamel, ☐ dentin.

The relationship between saliva and plasma fluoride levels was plotted in Figure 17 (r=0.40); the values for fluoride in saliva were lower than those for plasma.

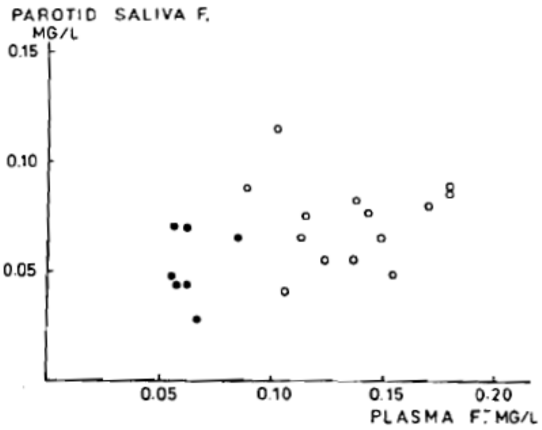

Fig. 17. Relationship plasma F⁻ – parotid saliva F. ● 6–18-year-old subjects. ○ 35–83-year-old subjects.

PROFILER'S NOTE: Data for fluoride content in enamel and dentin was not included in the report, so results could not be confirmed. The profiler agrees that there was a correlation

	between estimated fluoride exposure and fluoride content of the occlusal dental tissues. Data for fluoride content in saliva alone was not reported. Results for fluoride content in breast milk are not presented in the profile since data was of limited value, from only 2 subjects from the ~10 ppm area and inconsistent with each other.
STUDY AUTHORS' CONCLUSIONS:	In areas with ~ 10 ppm fluoride, virtually all subjects had moderate to severe fluorosis. In Paskallavik (~ 10 ppm), a greater percentage of moderate to severe fluorosis was observed in children with more than 4 years of fluoride exposure. The milder fluorosis seen in children with less than 4 years of fluoride exposure, due to a change in water supply to lower fluoride content, may be explained by the fact that the most recently formed layer of enamel was more completely mineralized because of the lower fluoride supply. The tendency for boys to in the ~ 5 ppm area to have higher degree of fluorosis compared to girls might be due to a larger intake of fluoride via water consumption by boys since they have a greater average body weight and are generally more physically active. In low F areas (including the ~1 ppm population studied here), the extra dosage may not be large enough to be of importance for incidence of fluorosis, and in the ~10 ppm areas the intake for both boys and girls is already so high that severe fluorosis results. In the ~5 ppm area, however, even a small increase in water consumption could weigh the balance. In the ~ 5 ppm area, and even more so in the ~10 ppm areas, both high fluoride deposition and severe fluorosis occurred in the permanent teeth even with long periods of breastfeeding. In the primary teeth, fluoride deposition was high but fluorosis milder. Thus, breastfeeding is important for the development of fluorosis and for the deposition of fluoride in the dental tissues. In permanent teeth, there was an increased frequency of caries in the ~ 10 ppm area, also partly noted in the ~ 5 ppm area; additionally, increased caries frequency was directly associated with more severe fluorosis. A reasonable hypothesis may be that teeth with severe fluorosis have hypoplastic enamel, allowing penetration of acid, sugar, and possibly bacteria such that the increased fluoride content is not sufficient to resist dissolution by acid. In primary teeth, caries frequency appears to decrease with higher fluoride level in the water supply, despite that fact that the degree of fluorosis in the ~ 10 ppm areas also was high in these teeth. The pattern of hypomineralization and/or the pattern of normal mineralization may be different from the permanent teeth. The successive improvement in deft count in the ~10 ppm area, Paskallavik, at the time of and immediately after the increase in fluoride level in the drinking water indicates that a combination of pre- and post-natal deposition may have the greatest effect. The high fluoride content in the early mineralized occlusal parts of enamel and dentin in primary teeth, even with long duration of breastfeeding, indicates prenatal deposition. Further indication is the relationship between the fluoride exposure of the mother before and during pregnancy and the degree of fluorosis of the child. The result must be assessed carefully since it is based on case history information. The significance of the relatively modest increase of fluoride content in saliva is somewhat obscure but calculations of the degree of saturation of fluorapatite in saliva indicate that even this small increase could have a cariostatic effect. In several aspects, the material presented here is too small to permit definite conclusions, particularly in regard to Gadderas.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Deft= decayed, extracted, and filled teeth Manly, R.S. and Hodge, H.C. 1939. Density and refrective index studies of dental hard tissues. I. Methods for separation and determination of purity. J. Dent. Res. 18: 133-141.
PROFILER' *Initials/dat*	Overall, the study was well-conducted and had adequate study design. The emphasis was on the

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REMARKS</td><td><i>e
SJG/
3/23/07</i></td><td>prevalence and severity of dental fluorosis and caries in individuals, mostly school children, in two areas with high fluoride in the water supply (~10 ppm or ~5 ppm) compared to areas with low (1 ppm) fluoride concentration. Gender, duration of breast feeding, and prenatal exposure to fluoride were evaluated for their influence on the occurrence and degree of fluorosis. Results from the study suggest that both fluoride level and exposure duration influence the prevalence and severity of fluorosis; further, duration of breastfeeding also influences fluorosis development. Increased caries frequency was directly associated with more severe fluorosis (in permanent teeth).

Limitations of the study include:
Data for caries frequency and for fluoride content in enamel, dentin and saliva was not included in the report, so results could not be confirmed. Results should be interpreted with caution since sample sizes were generally small, particularly in Gadderas (~10 ppm area) and some results are based on case history information (e.g., prenatal fluoride exposure), which is difficult to confirm. Further, the possible significance of drinking water factors other than high fluoride content for occurrence and degree of fluorosis is not known (e.g., water from the ~10 ppm areas contained high iron and manganese levels). Finally, other sources of fluoride intake are not considered (i.e., diet, fluoridated dentifrices).</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td colspan="2">PROFILER’S ESTIM. NOEL/ NOAEL</td><td>Based on the <u>prevalence of moderate to severe fluorosis</u>, the estimated LOAEL is 1 ppm fluoride (1 mg/L) in the drinking water.</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td colspan="2">PROFILER’S ESTIM. LOEL/ LOAEL</td><td>Based on the <u>prevalence of moderate to severe fluorosis</u>, the estimated LOAEL is 5 ppm fluoride (5 mg/L) in the drinking water.</td></tr>
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<tr><td colspan="2">POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:</td><td>Not suitable (_), Poor (x), Medium (_), Strong (_)

This was a well-conducted and designed study, with some important imitations, including small sample sizes. The study indicated that moderate to severe fluorosis occurred, generally in a dose-response manner, in subjects from ~5 ppm and ~ 10 ppm areas, but not in subjects from ~1 ppm areas. A longer duration of high fluoride exposure (e.g., >4 years) increased the prevalence of moderate to severe fluorosis, and a longer duration of breastfeeding reduced, but did not eliminate, the prevalence of fluorosis. Although increased caries frequency was directly associated with more severe fluorosis in permanent teeth, dose-response information for caries could not be determined from the study since stand alone data was not presented. The study did not address any issues of plaque or gingivitis.</td></tr>
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<tr><td colspan="2">CRITICAL EFFECT(S):</td><td>Dental fluorosis prevalence and severity and caries</td></tr>
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Franzman, M.R., S.M. Levy, J.J. Warren, and B. Broffitt. 2006. Fluoride dentifrice ingestion and fluorosis of the permanent incisors. JADA 137:645-52.

ENDPOINT STUDIED:	Dental fluorosis (permanent incisors)
TYPE OF STUDY:	Cohort study PROFILER'S NOTE: Franzman et al. used data from Iowa Fluoride Study (IFS); see also Hong *et al* 2006a and Hong *et al*, 2006b.
POPULATION STUDIED:	US/Iowa: Children (343; 49% males and 51% females) aged birth to 36 months which were originally part of the Iowa Fluoride Study was used for this study. Franzman et al. (2006) used data about fluoride exposure at ages 16, 24 and 36 months and the data obtained from the dental examinations conducted on these children between the ages of 7 and 11 years old. PROFILER'S NOTE: Large proportions of the subjects were first children and had white mothers; mothers and fathers were well-educated, with almost 50% having at least a four-year college degree; and only 11% of the families had a yearly income below $20,000 at baseline making limited applicability to the entire U.S. population.
CONTROL POPULATION:	Control group (n=227) included children from the cohort without fluorosis.
EXPOSURE PERIOD:	Birth to 36 months (and beyond)
EXPOSURE GROUPS:	Children were part of the original Iowa Fluoride Study and those included in this analysis were those whom questionnaires were returned at ages 16, 24 and 36 months and had received a mixed dentition examination. Fluoride intake was evaluated from water, food, beverages, supplements, and dentifrices.
EXPOSURE ASSESSMENT	Fluoride intake of children from water, food, dietary fluoride supplements and fluoride dentifrice was estimated from questionnaires completed by their parents at ages 16, 24 and 36 months. Fluoride intake (mg/kg BW/day) from water was estimated by multiplying each subject's water intake by his or her water source fluoride concentrations and product-specific water fluoride assay results. (See Analytical Methods below.) Parents reported daily ingested quantities of water by itself, milk, ready-to-drink juices and juice drinks, carbonated beverages, beverages mixed from powdered and frozen concentrates, foods made with almost all water, foods made with some water and foods cooked in and absorbing substantial amounts of water. The fluoride intake from beverages other than water and the selected foods was determined by multiplying the daily intake in each category by the average fluoride levels for those specific categories from the series of assays. Fluoride intake from prescribed fluoride supplements was calculated using parental estimates of frequency and dosage, paired with study data documenting the amount of fluoride contained in the supplement. Estimates of the amount of fluoride dentifrice used were based on parents' responses as to which diagrams of toothbrushes best depicted the amount that the child used most often to clean his or her teeth and the estimated amount that the child swallowed (≤25, 50 or ≥75%). The fluoride intakes from beverages, selected foods and dietary supplements were combined to estimate fluoride ingestion from sources other than dentifrice. Medians, along with 25th and 75th percentiles, were calculated to summarize fluoride ingestion (mg/kg BW/day) from dentifrice for the study sample. Cumulative estimates (16 to 36 months) of fluoride ingestion from dentifrice and diet/supplements were calculated using the area-under-the-curve (AUC) trapezoidal method (expressed as mg F/kg BW per day).
ANALYTICAL METHODS:	Fluoride assays of water and most beverages were conducted using a fluoride ion-specific electrode (Model 9609, Orion Research) and an ion analyzer (Model 920, Orion Research) after using a total ionic strength adjustment buffer (TISAB II buffer, Orion Research) to

	provide constant ionic strength, free up the fluoride and adjust the pH. Random samples were read again at the end of the day to verify electrode accuracy, repeat readings on standards to confirm the standard curve and analyze approximately 6 to 20% of samples in duplicate. Mean reproducibility was 97 to 99%. Solids and selected beverages were analyzed with a modified Taves hexamethyldisiloxane microdiffusion method, and the fluoride concentration of the resulting solution then was assessed using the method described above. More than 20% of samples were done in duplicate with mean reproducibility of 98%.
STUDY DESIGN	As part of the Iowa Fluoride Study, children were followed from birth to 36 months with questionnaires at 6 weeks and 3 months of age and then at three-, four- and six-month intervals thereafter to estimate daily fluoride intake (mg/kg BW) from water, beverages, selected foods, fluoride supplements and dentifrice. One mixed-dentition caries and fluorosis examination was conducted on each subject between the ages of 7 and 11 years (mean 9.1 yrs) by one of two trained dentist examiners. This study used IFS data to describe the influence of estimated fluoride dentifrice ingestion at ages 16, 24 and 36 months (both individually and combined) on fluorosis experience in the early-erupting permanent dentition. Total fluoride intake was estimated from parental questionnaires administered at ages 16, 24 and 36 months. The reliability of the questionnaire was assessed for a portion of the participants via follow-up telephone calls within two weeks of completing the questionnaires. Telephone interviewers assessed recall agreements with regard to use of fluoride supplements, toothbrushing frequency and type of water used (tap, bottled or both). A total of 343 children (49% males and 51% females) were examined for fluorosis in permanent teeth using the Fluorosis Risk Index (FRI; see NRC, 2006, page 90). The FRI was adapted to include assessment of four enamel zones (the incisal edge/occlusal table, the incisal third, the middle third and the gingival third) on each tooth, with the zones grouped according to the age at which enamel formation was initiated. Mothers provided information about their age, education, family income and number of children in the household. Informed consent was obtained from the mothers before the investigation; children provided assent before the dental examinations at ages 7 through 11 years.
PARAMETERS MONITORED:	Dental fluorosis on permanent teeth was determined at 7-10 years of age (mean 9.1 years) by one of two trained dentist examiners using the FRI. Before the examination, teeth were dried. Fluorosis was differentiated from demarcated non-fluorosis opacities by the criteria of Russell (1961). The FRI was adapted to include assessment of four enamel zones (the incisal edge/occlusal table, the incisal third, the middle third and the gingival third) on each tooth, with the zones grouped according to the age at which enamel formation was initiated The gingival third zone was excluded from the analyses because it was not consistently erupted. Fluorosis cases were defined as those in which two or more of the eight permanent incisors had definitive fluorosis (according to FRI criteria in which a score of 2 is assigned if 50% or more of a zone has definitive fluorosis versus a score of 3 for severe fluorosis, which also involves staining, pitting and/or other deformity). Non-fluorosis cases were defined as those in which there was no definitive fluorosis in the permanent incisors. Dental examiners conducted duplicate examinations in 39 subjects to assess interexaminer reliability (using percentage agreement and kappa statistics), but the results were not reported. Twenty-three subjects with one incisor with fluorosis were excluded from the analyses.
STATISTICAL METHODS:	Descriptive statistics were obtained for baseline measures and for tooth-brushing behaviors at ages 16, 24 and 36 months. Medians, along with 25th and 75th percentiles, were calculated to summarize fluoride ingestion from dentifrice for the study sample. Because fluoride ingestion measures did not uniformly exhibit normal distribution qualities (the data were skewed), tests of association used the Wilcoxon rank sum test (flurosis cases versus nonfluorosis cases) and the Kruskal-Wallis test for multilevel baseline measures. Multiple logistic regression models at each time point and for 16 to 36 months (AUC) tested associations between fluorosis and fluoride ingested from diet and supplements. A joint test was added to the combined intake for each model. P levels below 0.05 were considered

significant.

RESULTS:

A description of the study sample is shown in Table 1directly from Franzman, 2006. Results of the study in Tables 2 through 4 are shown directly from Franzman, 2006.

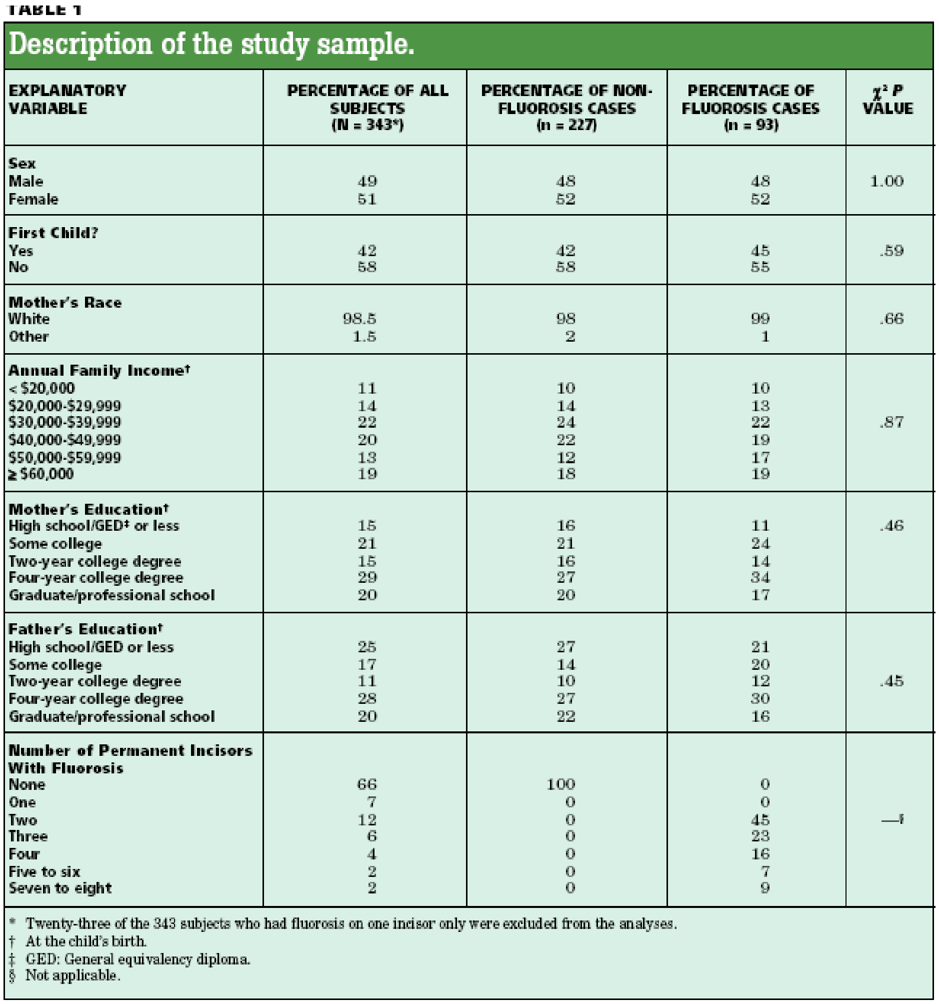


TABLE 1

Description of the study sample.

EXPLANATORY VARIABLE	PERCENTAGE OF ALL SUBJECTS (N = 343*)	PERCENTAGE OF NON-FLUOROSIS CASES (n = 227)	PERCENTAGE OF FLUOROSIS CASES (n = 93)	χ^2 P VALUE
Sex				
Male	49	48	48	1.00
Female	51	52	52	
First Child?				
Yes	42	42	45	.59
No	58	58	55	
Mother's Race				
White	98.5	98	99	.66
Other	1.5	2	1	
Annual Family Income†				
< $20,000	11	10	10	
$20,000-$29,999	14	14	13	
$30,000-$39,999	22	24	22	.87
$40,000-$49,999	20	22	19	
$50,000-$59,999	13	12	17	
≥ $60,000	19	18	19	
Mother's Education†				
High school/GED‡ or less	15	16	11	.46
Some college	21	21	24	
Two-year college degree	15	16	14	
Four-year college degree	29	27	34	
Graduate/professional school	20	20	17	
Father's Education†				
High school/GED or less	25	27	21	
Some college	17	14	20	
Two-year college degree	11	10	12	.45
Four-year college degree	28	27	30	
Graduate/professional school	20	22	16	
Number of Permanent Incisors With Fluorosis				
None	66	100	0	
One	7	0	0	
Two	12	0	45	—§
Three	6	0	23	
Four	4	0	16	
Five to six	2	0	7	
Seven to eight	2	0	9	

* Twenty-three of the 343 subjects who had fluorosis on one incisor only were excluded from the analyses.
† At the child's birth.
‡ GED: General equivalency diploma.
§ Not applicable.

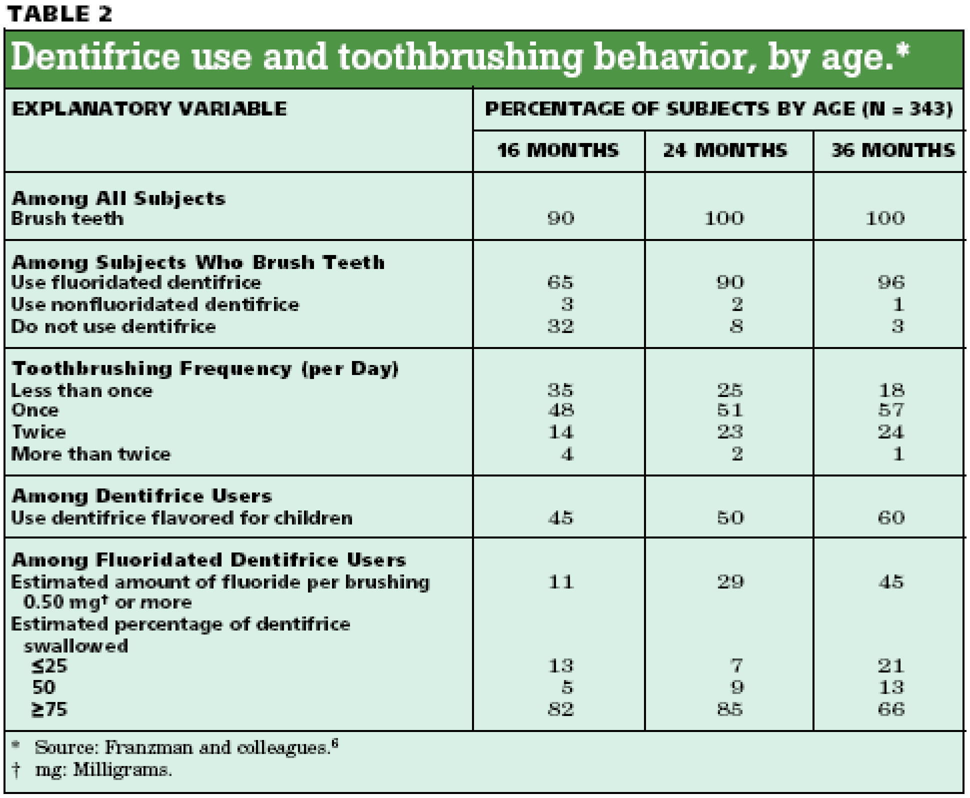


TABLE 2

Dentifrice use and toothbrushing behavior, by age.*

EXPLANATORY VARIABLE	PERCENTAGE OF SUBJECTS BY AGE (N = 343)		
	16 MONTHS	24 MONTHS	36 MONTHS
Among All Subjects			
Brush teeth	90	100	100
Among Subjects Who Brush Teeth			
Use fluoridated dentifrice	65	90	96
Use nonfluoridated dentifrice	3	2	1
Do not use dentifrice	32	8	3
Toothbrushing Frequency (per Day)			
Less than once	35	25	18
Once	48	51	57
Twice	14	23	24
More than twice	4	2	1
Among Dentifrice Users			
Use dentifrice flavored for children	45	50	60
Among Fluoridated Dentifrice Users			
Estimated amount of fluoride per brushing 0.50 mg† or more	11	29	45
Estimated percentage of dentifrice swallowed			
≤25	13	7	21
50	5	9	13
≥75	82	85	66

* Source: Franzman and colleagues.[6]
† mg: Milligrams.

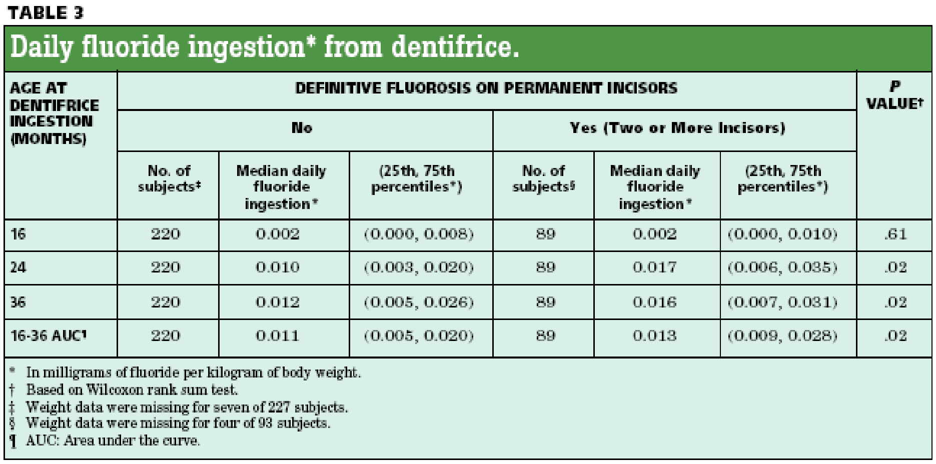


TABLE 3

Daily fluoride ingestion* from dentifrice.

AGE AT DENTIFRICE INGESTION (MONTHS)	DEFINITIVE FLUOROSIS ON PERMANENT INCISORS						P VALUE†
	No			Yes (Two or More Incisors)			
	No. of subjects‡	Median daily fluoride ingestion*	(25th, 75th percentiles*)	No. of subjects§	Median daily fluoride ingestion*	(25th, 75th percentiles*)	
16	220	0.002	(0.000, 0.008)	89	0.002	(0.000, 0.010)	.61
24	220	0.010	(0.003, 0.020)	89	0.017	(0.006, 0.035)	.02
36	220	0.012	(0.005, 0.026)	89	0.016	(0.007, 0.031)	.02
16-36 AUC¶	220	0.011	(0.005, 0.020)	89	0.013	(0.009, 0.028)	.02

* In milligrams of fluoride per kilogram of body weight.
† Based on Wilcoxon rank sum test.
‡ Weight data were missing for seven of 227 subjects.
§ Weight data were missing for four of 93 subjects.
¶ AUC: Area under the curve.

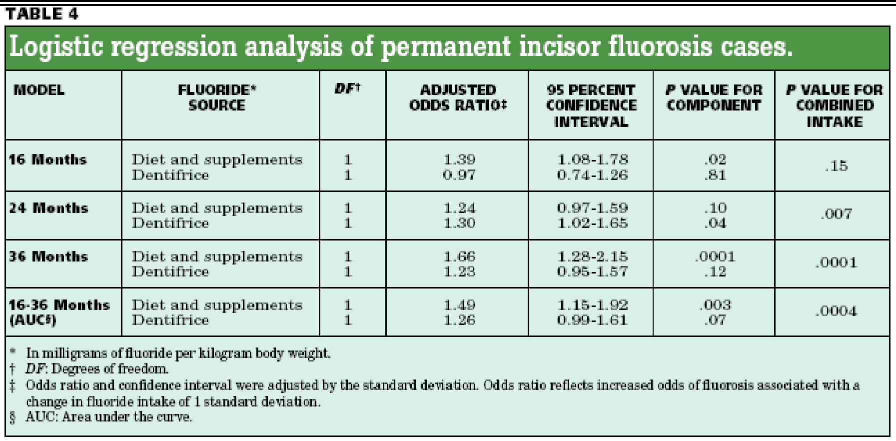


TABLE 4

Logistic regression analysis of permanent incisor fluorosis cases.

MODEL	FLUORIDE* SOURCE	*DF*†	ADJUSTED ODDS RATIO‡	95 PERCENT CONFIDENCE INTERVAL	*P* VALUE FOR COMPONENT	*P* VALUE FOR COMBINED INTAKE
16 Months	Diet and supplements Dentifrice	1 1	1.39 0.97	1.08-1.78 0.74-1.26	.02 .81	.15
24 Months	Diet and supplements Dentifrice	1 1	1.24 1.30	0.97-1.59 1.02-1.65	.10 .04	.007
36 Months	Diet and supplements Dentifrice	1 1	1.66 1.23	1.28-2.15 0.95-1.57	.0001 .12	.0001
16-36 Months (AUC§)	Diet and supplements Dentifrice	1 1	1.49 1.26	1.15-1.92 0.99-1.61	.003 .07	.0004

* In milligrams of fluoride per kilogram body weight.
† *DF*: Degrees of freedom.
‡ Odds ratio and confidence interval were adjusted by the standard deviation. Odds ratio reflects increased odds of fluorosis associated with a change in fluoride intake of 1 standard deviation.
§ AUC: Area under the curve.

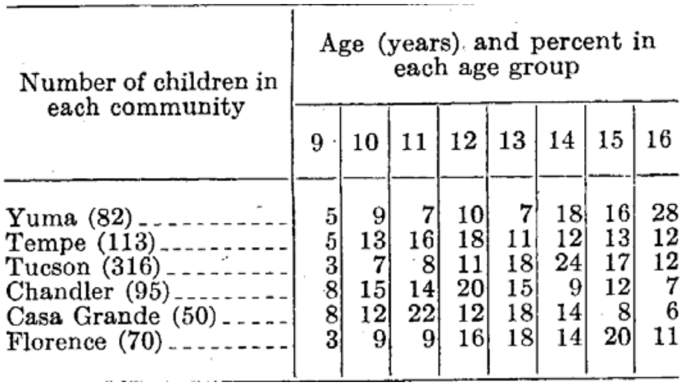
STUDY AUTHORS' CONCLUSIONS:		The study authors concluded that the results of the study affirm the link between use of fluoride dentifrice and the development of mild dental fluorosis; in particular, the data suggest that this relationship is most pronounced at about age 24 months. The findings suggest that health professionals need to emphasize the proper use of small quantities of dentifrice among toddlers, with appropriate parental supervision, to limit the amount of ingested dentifrice.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Hong, L., S.M. Levy, J.J. Warren, B. Broffitt, and J. Cavanaugh. 2006a. Fluoride intake levels in relation to fluorosis development in permanent maxillary central incisors and first molars. Caries Research. 40:494-500. Hong, L., S.M. Levy, B. Broffitt, J.J. Warren, M. J. Kanellis, J.S. Wefel, and D.V. Dawson. 2006b. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. Community Dent Oral Epidemiol 34:299-309. Russell, A.I. 1961. The differential diagnosis of fluoride and non-fluoride enamel opacities. J Public Health Dent 21:143-146.
PROFILER'S REMARKS	***Initials /Date*** VAD/12-30-06	Large proportions of the cohort were first children and had white mothers; mothers and fathers were well-educated, with almost 50% having at least a four-year college degree; and only 11% of the families had a yearly income below $20,000 at baseline. Therefore, results are not representative of the general US population. Parents reported the data and investigators did not directly observe the toothbrushing behaviours of children. Some information was missing as a result of some parents' failure to return questionnaires, which may have affected the results. Severe fluorosis was observed in only 3 of 39 subjects; therefore, it was not possible to assess the association of dentifrice use with this more involved dental fluorosis.
PROFILER's ESTIM. NOAEL		The study design did not identify a no-fluorosis intake dose.
PROFILER'S ESTIM. LOAEL		The study design did not identify a lowest fluorosis intake dose.
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable,(X); Poor (_); Medium (_); Strong (_) Not suitable for dose response modelling as the amount of fluoride intake associated with the three cases of severe fluorosis (which is considered to be adverse) was not given. The study could be used, however as a relative source contribution as to the effect that fluoride from dentifrice ingested at a young age can affect the incidence of fluorosis in permanent dentition.
CRITICAL EFFECTS:		Dental fluorosis (permanent incisors)

Galagan, D.J. and G.G. Lamson. 1953. Climate and endemic dental fluorosis. Public Health Reports. Vol. 68, No. 5: 497-508.

ENDPOINT STUDIED: Dental fluorosis

TYPE OF STUDY: Cross-sectional survey

POPULATION STUDIED: US/Arizona; Fourth through ninth grade (ages 9-16) children from public and parochial schools in 6 Arizona communities made up the study population with 83% being of Spanish descent. To be included in the study, the children were required to have exposure to the water in that community from birth through age 9. The following table copied directly from Galagan and Lamson (1953) provides the number of children in each city and the age during the study. No distinction was made between male and female children.



Number of children in each community	Age (years) and percent in each age group							
	9	10	11	12	13	14	15	16
Yuma (82)	5	9	7	10	7	18	16	28
Tempe (113)	5	13	16	18	11	12	13	12
Tucson (316)	3	7	8	11	18	24	17	12
Chandler (95)	8	15	14	20	15	9	12	7
Casa Grande (50)	8	12	22	12	18	14	8	6
Florence (70)	3	9	9	16	18	14	20	11

CONTROL POPULATION: None

EXPOSURE PERIOD: A requirement for children to be included in the study was exposure to the community drinking water from birth through their 9th year.

EXPOSURE GROUPS: The following table was constructed by combining data in two separate tables in Galagan and Lamson (1953) to indicate the fluoride levels identified in the water, the source of the water supply and the number of samples taken from each community.

Data for children in Arizona communities fluoride study

Community	Source of supply	Treatment done	# of samples	Mean fluoride content
Yuma	Colorado River	Desilting, Al SO_4, flocculation, $CuSO_4$, filtration, chlorination	79	0.4
Tempe	4 wells	chlorination	7	0.5
Tucson	17 wells	chlorination, ammoniation	31	0.7
Chandler	4 wells	None	16	0.8
Casa Grande	5 wells	Do.	20	1.0
Florence	4 wells	Do.	22	1.2

PROFILER'S NOTE: Although not stated in the table, the profiler assumes the mean fluoride in the table should be in "ppm".

Some explanations about disruptions to water supplies and/or changing wells were explained in the study article and are included below.
Yuma: In the summer of 1937, sewage backed up in the Colorado River making the drinking water unsafe. Water for drinking was redirected from a well that was used to fill the city's municipal pool for 3 months. Fluoride levels from the pool well were not

	obtained during the time of its use, however, a sample in May 12, 1951 indicated a fluoride concentration of 0.6 ppm. This indicates that possibly for a 3-month time period, the 16-year old children would have been exposed to 0.6 ppm instead of 0.4 ppm. Tucson: The city of Tucson has two different systems of drinking water; one for the Northside and one for the Southside. Because the Southside has a higher amount of fluoride, the study used children well within the boundries of the Southside system. The two systems have had two sets of controls since 1938, so prior to 1938, there might have been some cross- mixing between the two systems. Since the Northside fluoride is 0.3 ppm, the result would have been exposure to a lesser amount of fluoride for a short time. Chandler: Two of Chandler's four wells had their casings break in 1938 and water from outside entered the wells. Replacement wells were added, one in 1944 and one in 1948. The mean of fluoride concentrations taken with the original wells was 0.75 ppm and with the new wells, 0.85 ppm. Fluoride levels were only checked once during the casing breakage when outside water was entering the wells and it was 0.8 ppm. These values all indicate a fairly stable fluoride concentration in the area. Case Grande: The five wells in this community were put into place in 1922, 1930, 1937, 1946 and 1950. The addition of new wells did not appear to affect any of the fluoride levels as twenty analysis from 1931 to 1951 have ranged from 0.9 to 1.2 ppm. Florence: During the study period, the community used 4 wells; two were originally from 1919. A new well replaced these two in 1939 and another well was added in 1947. A total of 21 fluoride samples were taken with 14 taken prior to July 1939 and 7 taken after July 1939. Both averaged 1.2 ppm of fluoride indicating the well change did not affect the fluoride levels. PROFILER'S NOTE: Although there have been well replacements and changes to some systems, overall, the fluoride levels were not adversely affected, and no confounding evidence was identified.
EXPOSURE ASSESSMENT:	Only fluoride exposure from drinking water was considered in this study. However, Galagan and Lamson (1953) did state that the study children lived in desert cities with a mean annual temperature of 70°F, a mean relative humidity of 37%, 80-85% sunshine and extremely high day-time temperatures which all could have increased the amount of water the study population drank. The authors did note that field irrigation is common in Arizona thus possibly allowing fluoride to be absorbed into the crops and that most of the children in Arizona were of Spanish descent with beans making up a large portion of their diet. Most of the beans, in cooking preparation, are soaked in or boiled in water for long periods of time and could create another source of exposure. While both of these were noted, the authors did not think the soil contamination was substantial and the scope of the paper did not include the dietary exposure possibilities.
ANALYTICAL METHODS:	Fluoride levels for the water were analyzed intermittently from 1935 to 1950 and quarterly through 1951, although the method for analysis used was not provided in the study. No other chemical parameters in the water were provided.
STUDY DESIGN	Children were chosen from the 4th to 9th grade in private and parochial schools within the study communities. Children were only included if they had been residents of their community. A questionnaire confirming the residency was sent home to the children's parents and/or guardians. If residency was confirmed, the children were scheduled for a dental examination. All children were examined by the same examiner. Examinations were performed with the children seated in a dental chair using a mouth mirror and Burton light. Compressed air was available, if needed. Each tooth was given a fluorosis score based on Dean's Index (1942). These classifications were later put into a child-classification and used to compute the community fluorosis index (CFI).
PARAMETERS	Dean's Index (1942) was used to rate fluorosis on the teeth of the study children. The

MONITORED:

community fluorosis index (CFI) was also calculated according to Dean (1942).

PROFILER'S NOTE: Dean's Index (1942) is described in Section 2 of the report.

STATISTICAL METHODS:

No statistical methods were included in the study report.

RESULTS:

Dental fluorosis

Table 4 was copied directly from Galagan and Lamson (1953) and indicates the prevalence and severity of fluorosis in the children within each Arizona community. The results show that as the fluoride concentration rose, the community fluorosis index increased and the number of children without visible fluorosis decreased.

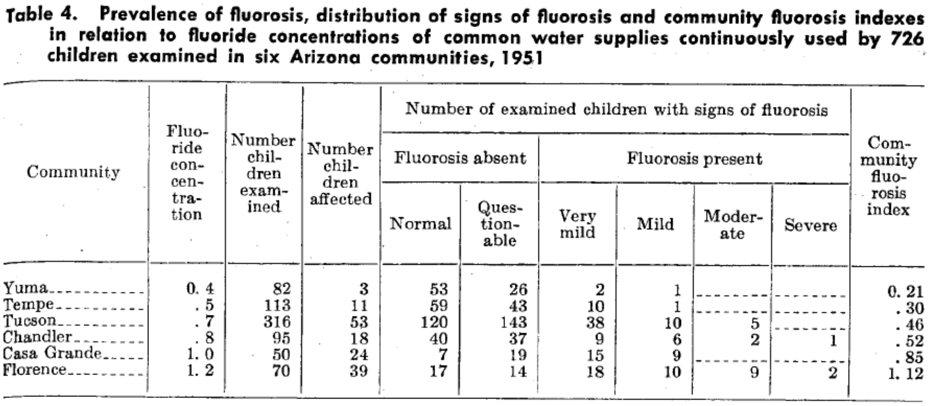


Table 4. Prevalence of fluorosis, distribution of signs of fluorosis and community fluorosis indexes in relation to fluoride concentrations of common water supplies continuously used by 726 children examined in six Arizona communities, 1951

Community	Fluoride concentration	Number children examined	Number children affected	Number of examined children with signs of fluorosis						Community fluorosis index
				Fluorosis absent		Fluorosis present				
				Normal	Questionable	Very mild	Mild	Moderate	Severe	
Yuma	0. 4	82	3	53	26	2	1	--------	--------	0. 21
Tempe	. 5	113	11	59	43	10	1	--------	--------	. 30
Tucson	. 7	316	53	120	143	38	10	5	--------	. 46
Chandler	. 8	95	18	40	37	9	6	2	1	. 52
Casa Grande	1. 0	50	24	7	19	15	9	--------	--------	. 85
Florence	1. 2	70	39	17	14	18	10	9	2	1. 12

PROFILER'S NOTE: The children in Casa Grande (1.0 ppm) did not show the same trend toward increasing severity in fluorosis that the other communities indicated, although the CFI did. This is possibly due to the smaller number of children that were examined in the area as compared to the other communities.

Comparisons of effects in areas with different climatological variables

Table 5 was copied directly from Galagan and Lamson (1953) and indicates the prevalence and severity of fluorosis in the children within each Arizona community as compared to ten Mid-west communities (Dean, 1946) with similar fluoride concentrations but having very different climatological variables. Figure 3 was also copied directly from Galagan and Lamson (1953) and shows the relationship between the fluorosis indices of the different communities. The Mid-west communities used in comparison have a mean average annual temperature of 50°F, whereas, the Arizona communities have one of 70°F. The chart shows that the Arizona communities had a higher percentage of children affected by fluorosis when compared to cities with similar fluoride levels but cooler temperatures. The figure shows that the communities in Arizona have a much steeper slope and the index line accelerates at twice the rate of the Mid-west communities into the borderline zone (CFI value of 0.4- 0.6 ppm). Dean stated that a CFI of below 0.4 ppm has little or no public health concern, 0.4-0.6 ppm is borderline and >0.6 ppm means that excess fluoride should be removed from the water. The figure suggests that the children in Arizona would develop twice as much fluorosis as the Mid-west children, although discrepancies between the two examiners must be considered. The author concludes that the higher temperatures in the Southwest and the increased amount of sunshine present per day (radiant heat) must help contribute to the increased fluorosis present by causing an increase in water intake.

Table 5. Prevalence of fluorosis, percentage distribution of signs of fluorosis and community fluorosis indexes in relation to fluoride concentration of common water supplies of 16 communities in two temperature zones

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Community	Fluoride concentration	Community fluorosis index	Number children examined	Percent children affected	Percentage distribution of signs of fluorosis						Mean annual temperature ° F.[1]
					Absent		Present				
					Normal	Questionable	Very mild	Mild	Moderate	Severe	
Arizona											
Yuma	0.4	0.21	82	4	65	32	2	1	------	------	72.2
Tempe	.5	.30	113	10	52	38	9	1	------	------	68.6
Tuscon	.7	.46	316	17	38	45	12	3	2	------	67.4
Chandler	.8	.52	95	19	42	39	9	6	2	1	67.6
Case Grande	1.0	.85	50	48	14	38	30	18	------	------	71.0
Florence	1.2	1.12	70	56	24	20	26	14	13	3	69.3
Midwest											
Marion, Ohio	.4	.25	263	6	57	37	5	1	------	------	52.1
Elgin, Ill	.5	.22	403	4	61	35	4	1	------	------	49.4
Pueblo, Colo	.6	.17	614	7	72	21	6	(2)	------	------	52.6
Kewanee, Ill	.9	.31	123	12	53	35	10	2	------	------	50.9
Aurora, Ill	1.2	.32	633	15	53	32	14	1	------	------	49.4
East Moline, Ill	1.2	.49	152	32	37	32	30	2	------	------	50.9
Maywood, Ill	1.2	.51	171	33	39	28	29	4	------	------	50.1
Joliet, Ill	1.3	.46	447	25	41	34	22	3	------	------	49.4
Elmhurst, Ill	1.8	.67	170	40	28	32	30	9	1	------	50.1
Galesburg, Ill	1.9	.69	273	48	25	27	40	6	1	------	50.9

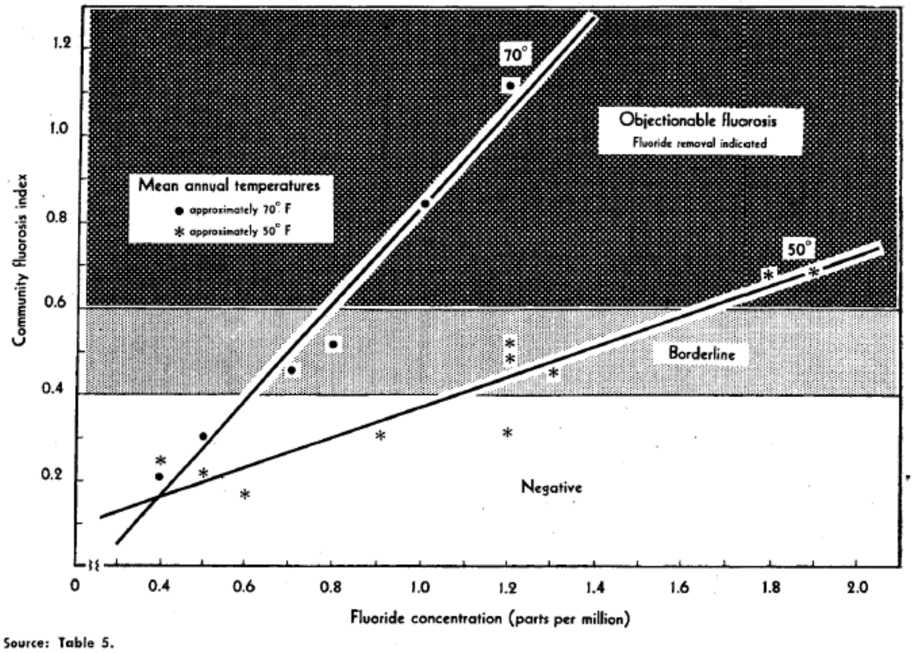
[1] Average: Arizona, 69.3° F.; Middle West, 50.6° F.

[2] Less than 0.5 percent.

NOTE: Age range for Arizona group, 9–16 years; midwestern group, 12–14 years.

SOURCES: Fluorosis data for midwestern communities from Dean, H. T.: Epidemiological studies i United States. American Association for the Advancement of Science: Dental caries and fluorine, Science Lancaster, Pa., 1946; mean annual temperature for 6 Arizona communities from Smith, H. V.: The clim Arizona. University of Arizona, Agricultural Experiment Station, Bulletin No. 197, July 1945; for midw communities; from U. S. Department of Commerce, Weather Bureau: Climatological data. Monthly and a summaries: The mean annual temperature for Aurora, Joliet, and Elgin is represented by the 19-year average temperature for Aurora; that for Kewanee, East Moline, and Galesburg by the 19-year average mean tempe for Galva; and that for Maywood and Elmhurst by the 19-year average mean temperature for Chicago.

Figure 3. Relationship between fluoride concentration of municipal waters and fluorosis index for communities with mean annual temperatures of approximately 50° F. (Midwest) and 70° F. (Arizona).



Source: Table 5.

PROFILER’S NOTE: The trend toward higher fluorosis was observed in the Arizona communities at a lower fluoride concentration; but there were no details provided to indicate whether the fluorosis occurred in primary or permanent teeth. The data from Arizona included children as young as 9 indicating some still would have primary teeth; the data from the Mid-west was for children 12-16 years old indicating mostly permanent dentition. To get a true picture of comparison, only the older Arizona children should have been compared to the older Mid-west children. The study does not indicate whether the children in the Mid-west had the same time of exposure (birth through 9 years) as the Arizona children.

STUDY AUTHORS' CONCLUSIONS:		Galagan and Lamson (1953) summarized that in the Arizona communities studied, fluoride concentrations above 0.8 ppm resulted in objectionable dental fluorosis, 0.6 to 0.8 ppm resulted in occasional diagnosis of fluorosis and concentrations below 0.6 ppm caused no objectionable dental fluorosis. Also, when comparing the CFI's, fluorosis occurred at about twice the intensity in Arizona communities when compared to Mid-west communities with comparable fluoride concentrations but different climatic factors. As a result of the increased temperature and radiant heat gain, Arizona children drink more water than those living in more temperate climates causing increased ingestion of fluoride in relation to the concentration found in the water supply.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Dean, H.T. 1946. Epidemiology studies in the United States. In Dental caries and fluorine, edited by F.R. Moulton. Lancaster, Science Press, p. 5-31.
PROFILER'S REMARKS	***DFG/2-13-07***	The survey clearly shows a difference in the amount of fluorosis identified based on climate changes, although a stronger study would involve the same examiner observing children from each area to prevent examiner differences and comparisons of the same aged children. The profiler agrees that different acceptable fluoride levels might be needed based on the area of the country one inhabits. An examination into the food fluoride content should be conducted in this community to include some of the food preparation habits that the children were exposed to. Also, a true measure of the drinking habits of the children in the area would also help support the finding of increased exposure to ensure the children actually do drink more water than the Mid-west children. The study lacked any statistical analysis.
PROFILER'S ESTIM. NOEL/NOAEL		Although the study is limited by a small number of data points, a NOAEL of 0.7 ppm was established based on no children exhibiting severe fluorosis at this concentration.
PROFILER'S ESTIM. LOEL/ LOAEL		Although the study is limited by a small number of data points, a LOAEL of 0.8 ppm was established based on the number of children with severe fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable ( ), Poor (), Medium (X), Strong ( ) While the study is not ideal due to the small number of data points and the lack of data on true water intake, it does indicate an increase in fluorosis severity as fluoride concentrations increase and could be used in conjunction with other studies to provide weight-of-evidence to set some guidelines in areas with similar climates. One could also use the CFI values from the study to set up guidance for other similar geographic areas.
CRITICAL EFFECT(S):		Dental fluorosis based on climate variables

Gopalakrishnan et al., 1999. Prevalence of dental fluorosis and associated risk factors in Alappuzha district, Kerala. Nat. Med. Jour. India, Vol. 12, No. 3: 99-103.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Community-based, cross-sectional study of fluorosis and fluoride levels in drinking water.
POPULATION STUDIED:	India, 1142 school children (630 girls, 512 boys), ages 10-17 yrs.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	10-17 yrs, from birth to time of oral examination of teeth in January & February, 1998
EXPOSURE GROUPS:	Drinking-water fluoride levels based on data from the water department of Alappuzha. The exposure groups were 0.7, 1.1, 1.2, and 1.4 ppm.
EXPOSURE ASSESSMENT:	Drinking water was the main exposure route evaluated. However, brick-tea intake, sea fish intake, dry-fish consumption, and toothpaste used for dental cleaning were also evaluated.
ANALYTICAL METHODS:	Not stated what analytical method the water department used to analyze for the fluoride levels in the drinking water.
STUDY DESIGN	The prevalence of dental fluorosis was studied in Indian school children, ages 10-17 yr, and the contribution of potential risk factors was evaluated. A dental specialist evaluated each child for the presence and severity of dental fluorosis, using a modified Dean's index of Fluorosis (see below), as well as any other dental conditions. Printed questionnaires were given to the students 1-2 days before the dental examinations (to be returned at the examination) with questions concerning socioeconomic status, occupation and level of education of the parents, the source of drinking water, amount of water consumed, brick-tea consumption, sea-fish intake, and use of fluoride-containing toothpaste by the student. The fluoride content of the water was obtained from the local water department. The prevalence of dental fluorosis was estimated by taking all cases of dental fluorosis as the numerator and the total child population evaluated in the age group of 10-17 years old as the denominator. A Community Fluorosis Index, as described by Dean (1942), was computed.
PARAMETERS MONITORED:	The study authors reported that Dean's was used to evaluate the grade of dental fluorosis; however, as described, the scoring system was modified to include only five categories: normal, questionable, mild, moderate, and severe, and furthermore, the severe level was described as cases where white areas covered more than 50% of the surface areas of the teeth; no mention is made of pitting or brown staining.. A Community Fluorosis Index, as described by Dean (1942), was computed.
STATISTICAL METHODS:	The association of dental fluorosis with select individual risk factors was studied using Chi-square and Chi-square trend tests. Multivariable logistic regression (with step-wise forward selection) was used to evaluate the independent association of select risk factors with the prevalence of dental fluorosis. A p value of <0.01 was used for entry of the variables in the multivariable models. Odds ratios (and their 95% CI) for the association of the predictor variables with the dependent variable were computed. A p value of <0.05 was taken to indicate statistical significance.
RESULTS:	
Dental fluorosis	See Table II for the prevalence of dental fluorosis in the study sample, Table III for the prevalence of dental fluorosis according to the source of drinking water, and Table IV for the variation in prevalence of dental fluorosis in the different regions according to the fluoride content of the drinking water.

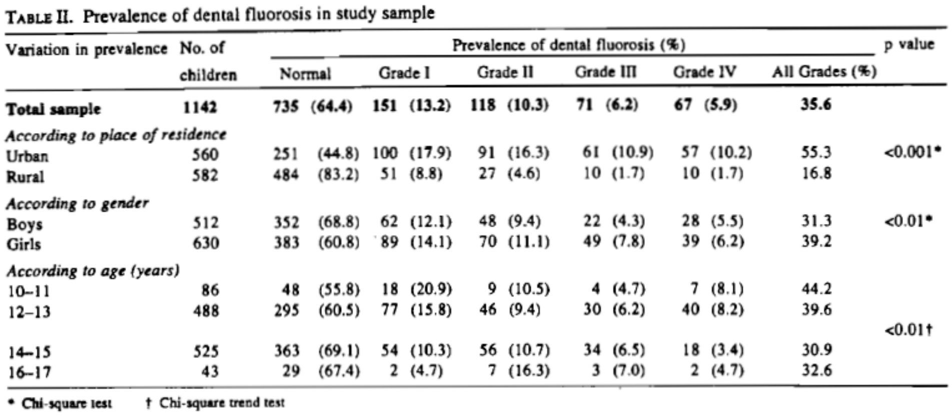


TABLE II. Prevalence of dental fluorosis in study sample

Variation in prevalence	No. of children	Prevalence of dental fluorosis (%)						p value
		Normal	Grade I	Grade II	Grade III	Grade IV	All Grades (%)	
Total sample	**1142**	**735 (64.4)**	**151 (13.2)**	**118 (10.3)**	**71 (6.2)**	**67 (5.9)**	**35.6**	
According to place of residence								
Urban	560	251 (44.8)	100 (17.9)	91 (16.3)	61 (10.9)	57 (10.2)	55.3	<0.001*
Rural	582	484 (83.2)	51 (8.8)	27 (4.6)	10 (1.7)	10 (1.7)	16.8	
According to gender								
Boys	512	352 (68.8)	62 (12.1)	48 (9.4)	22 (4.3)	28 (5.5)	31.3	<0.01*
Girls	630	383 (60.8)	89 (14.1)	70 (11.1)	49 (7.8)	39 (6.2)	39.2	
According to age (years)								
10–11	86	48 (55.8)	18 (20.9)	9 (10.5)	4 (4.7)	7 (8.1)	44.2	
12–13	488	295 (60.5)	77 (15.8)	46 (9.4)	30 (6.2)	40 (8.2)	39.6	<0.01†
14–15	525	363 (69.1)	54 (10.3)	56 (10.7)	34 (6.5)	18 (3.4)	30.9	
16–17	43	29 (67.4)	2 (4.7)	7 (16.3)	3 (7.0)	2 (4.7)	32.6	

* Chi-square test † Chi-square trend test

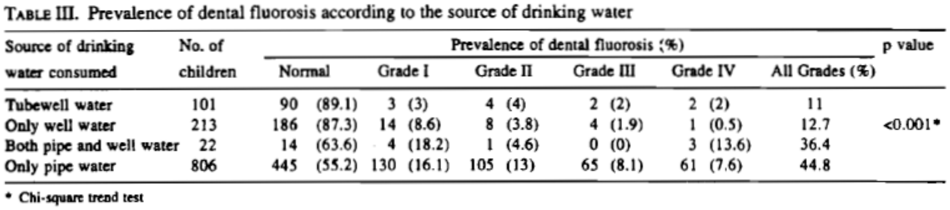


TABLE III. Prevalence of dental fluorosis according to the source of drinking water

Source of drinking water consumed	No. of children	Prevalence of dental fluorosis (%)						p value
		Normal	Grade I	Grade II	Grade III	Grade IV	All Grades (%)	
Tubewell water	101	90 (89.1)	3 (3)	4 (4)	2 (2)	2 (2)	11	
Only well water	213	186 (87.3)	14 (8.6)	8 (3.8)	4 (1.9)	1 (0.5)	12.7	<0.001*
Both pipe and well water	22	14 (63.6)	4 (18.2)	1 (4.6)	0 (0)	3 (13.6)	36.4	
Only pipe water	806	445 (55.2)	130 (16.1)	105 (13)	65 (8.1)	61 (7.6)	44.8	

* Chi-square trend test

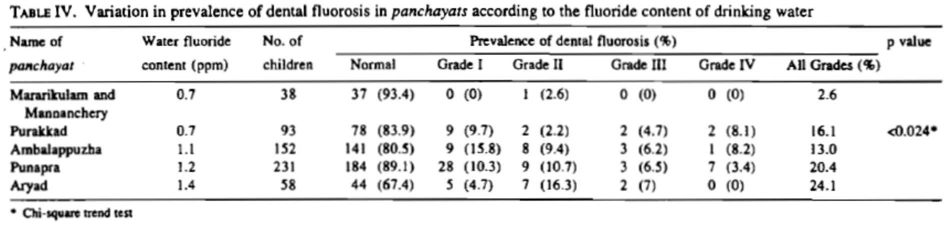


TABLE IV. Variation in prevalence of dental fluorosis in *panchayats* according to the fluoride content of drinking water

Name of *panchayat*	Water fluoride content (ppm)	No. of children	Prevalence of dental fluorosis (%)						p value
			Normal	Grade I	Grade II	Grade III	Grade IV	All Grades (%)	
Mararikulam and Mannanchery	0.7	38	37 (93.4)	0 (0)	1 (2.6)	0 (0)	0 (0)	2.6	
Purakkad	0.7	93	78 (83.9)	9 (9.7)	2 (2.2)	2 (4.7)	2 (8.1)	16.1	<0.024*
Ambalappuzha	1.1	152	141 (80.5)	9 (15.8)	8 (9.4)	3 (6.2)	1 (8.2)	13.0	
Punapra	1.2	231	184 (89.1)	28 (10.3)	9 (10.7)	3 (6.5)	7 (3.4)	20.4	
Aryad	1.4	58	44 (67.4)	5 (4.7)	7 (16.3)	2 (7)	0 (0)	24.1	

* Chi-square trend test

STUDY AUTHORS' CONCLUSIONS:

The authors noted a significant positive association between water fluoride content and prevalence of dental fluorosis. A step-wise increase in the prevalence of dental fluorosis was noted with a corresponding increase in the water fluoride content in different regions. The socioeconomic status of the parents, brick-tea drinking, sea- or dry-fish consumption, and the use of toothpaste were not associated with the prevalence of dental fluorosis.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

None

PROFILER'S REMARKS

Initials/date SBG 3/27/07

This study was in India and there was no control group with low fluoride levels in the drinking water, so it would not be representative of the U.S. population. In addition, the authors assumed that the fluoride content in the water had not changed over the last 15 years (when fluorosis occurs during early childhood during the time of calcification of the teeth), which could be a big assumption.

The fact that severe fluorosis occurred in the study population exposed to drinking water fluoride concentrations of 0.7 to 1.2 ppm, but not at 1.4 ppm suggests that other factors were contributing to total fluoride exposure. The authors state, however, that brick tea consumption, ingestion of fish and the use of toothpaste were not positively associated with fluorosis (quantitative data were not presented in the publication). The inconsistency of the results reduces the value of the data for dose-response modelling, but it does provide evidence that severe fluorosis can occur at low water fluoride levels in hot tropical climates.

PROFILER'S ESTIM. NOEL/NOAEL	Based on the data presented in Table IV, there does not appear to be a NOAEL for severe dental fluorosis (Dean's Index of 4) identified in this study.
PROFILER'S ESTIM. LOEL/ LOAEL	Based on the data presented in Table IV, the LOAEL for severe dental fluorosis (Dean's Index of 4) appears to be 0.7 ppm.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (_), Poor (x), Medium (_), Strong (_) This study seems to be poorly suited for dose-response modelling because of the inconsistency of the results, which may have been due to the fact that the range of fluoride concentrations was small (i.e., 0.7 to 1.4 ppm). Furthermore, for the level of severe fluorosis there was no clear dose response.
CRITICAL EFFECT(S):	Dental fluorosis

Grobler, S.R., Louw, A.J., and Van W. Kotze, T.J. 2001. Dental fluorosis and caries experience in relation to three different drinking water fluoride levels in South Africa. International Journal of Paediatric Dentistry. 11: 372-379.

ENDPOINT STUDIED:	Dental fluorosis; caries
TYPE OF STUDY:	Cohort study
POPULATION STUDIED:	South Africa/ Leeu Gamka: 120 children (45 girls, 75 boys), aged 10-15 years old, and lifelong residents. The average altitude and annual rainfall are 550 m and 150 mm, respectively. South Africa/Kuboes: 115 children (63 girls, 52 boys), aged 10-15 years old, and lifelong residents. The average altitude and annual rainfall are 200 m and 100 mm, respectively. South Africa/Sanddrif: 47 children (31 girls, 16 boys), aged 10-15 years old, and lifelong residents. The average altitude and annual rainfall are 22 m and 50 mm, respectively. The children in all groups had similar ethnic and socio-economic status, nutrition and dietary habits, and virtually no dental care or any fluoride therapy. The subjects were of mixed ethnic origin, originating from Khoi, Caucasian, and Negroid roots, developed into a homogenous ethic group over hundreds of years. The socio-economic status was low, as reflected in residence in subeconomic housing units. The staple diet consisted of bread and potatoes, with occasional intake of other vegetables and meat. No dietary habits were flagged that would significantly contribute to fluoride ingestion, including the use of naturally occurring salt deposits containing high levels of fluoride.
CONTROL POPULATION:	The study group in Sanddrif served as the control population.
EXPOSURE PERIOD:	From birth to age 10-15 yr. The dates when the examinations were conducted were not reported.
EXPOSURE GROUPS:	Leeu Gamka water supply (boreholes) naturally fluoridated at 3.0 ppm (range 2.7-3.3 ppm). Kuboes water supply (boreholes) naturally fluoridated at 0.48 ppm (range 0.45-0.50 ppm). Sanddrif water supply (Orange River) naturally fluoridated at 0.19 ppm (range 0.15-0.23 ppm). The fluoride levels correspond to averages “over the last ten years”, with at least one sample analyzed each year. NOTE: children were 0-5 yr old when the first measurements were taken.
EXPOSURE ASSESSMENT:	The study authors state that communication with personal health care personnel indicated that there were no dietary habits that may have contributed to a significant exposure to fluoride, and it was reported that the children in this region had virtually no dental care and or fluoride therapy, including the use of fluoride dentifrices.
ANALYTICAL METHODS:	The water fluoride level was determined potentiometrically according to the method described by Nicholson and Duff (1981) and was analyzed over a period of approximately 10 years with at least one sample per year.

STUDY DESIGN	The study included 282 children aged 10-15 years with virtually no dental care or any fluoride therapy who lived continuously since birth in three different naturally fluoridated areas of South Africa: Leeu Gamka, 3.0 ppm F (n=120); Kuboes, 0.48 ppm F (n=115); and Sanddrif, 0.19 ppm F (n=47). The children in all groups were of similar ethnic origin and low socio-economic status; nutrition and dietary habits were similar. Dental examinations were made by the second author using portable dental equipment. None of the children refused to be examined. The teeth were examined for caries and fluorosis using DMFT and Dean's indices, respectively, according to WHO guidelines. Caries criteria of the WHO (detectably softened floor, undermined enamel, and/or softened wall) was strictly adhered to in order to distinguish between hypoplastic fluoride lesions and carious cavities; where any doubt existed, caries was not recorded as present. Examinations: Examination details were not reported, including location where examinations occurred (assumed to occur at school), lighting conditions, or equipment used. The examiner was standardized and calibrated for intra- and inter-examiner variability prior to and during examinations; agreement was determined using weighted kappa (k). The intra- and inter-examiner agreement scores for DMFT (k=0.90 and 0.85) and fluorosis index (k=0.78 and 0.78), respectively, were substantial to almost perfect, according to the scale of Landis and Koch, meeting the scientific requirement for validity and reliability. Agreement was also monitored by re-examining 10% of the sample, with the same result as was found in the pre-survey calibration finding.
PARAMETERS MONITORED:	Dental caries and fluorosis were measured using the mean number of decayed, missing, and filled permanent teeth (DMFT) and Dean's indices, respectively, according to WHO guidelines. Fluorosis was scaled as none (0), questionable (1), very mild (2), mild (3), moderate (4), or severe (5). No radiographs were taken during the surveys.
STATISTICAL METHODS:	The Mann-Whitney *U* test was used to analyze the data for differences between males and females. The Chi-square test was used to detect differences in age distribution in the fluoride areas. DMFT scores were analyzed by the Kruskall-Wallis test and the Bonferroni test. Correlation between DMFT scores and fluorosis was analyzed by the Spearman correlation test. Significance was set at p ≤0.05.
RESULTS:	
Caries	Tables 1 and 2 were copied directly from Grobler et al. (2001). Table 1 summarizes the mean age (years), DMFT, percent caries-free, mean fluorosis score, and percent fluorosis-free children in each community. No significant difference was found between males and females for each parameter tested (Mann-Whitney *U* test), so the results for the two series were combined. The mean age in the three areas did not differ significantly, although a difference in age distribution was found (Chi-square test), with younger children in the Leeu Gamka area. The mean DMFT scores for the children in Sanddrif and Kuboes were the same (1.64±0.30 and 1.54±0.24, respectively), but significantly higher (1.98±0.22) for Leeu Gamka (Kruskall-Wallis, Bonferroni test). The percentage of children that were caries-free was 47% in Sanddrif, 50% in Kuboes, and only 29% in Leeu Gamka, the high fluoride area. The proportion of caries-free children in Sanddrif and Kuboes did not differ significantly and was significantly higher than Leeu Gamka. The decayed component dominated the DFMT score in all three areas, with significantly (Kruskall-Wallis test, p<0.01) more children affected in the high fluoride area (Leeu Gamka) compared to the other two areas. Both the filled and missing components for all three areas were almost non-existent and did not differ significantly. A strong positive correlation (Spearman correlation test) was found between caries experience and the fluorosis scores of children in the high fluoride area, but there was no correlation in the other two areas.

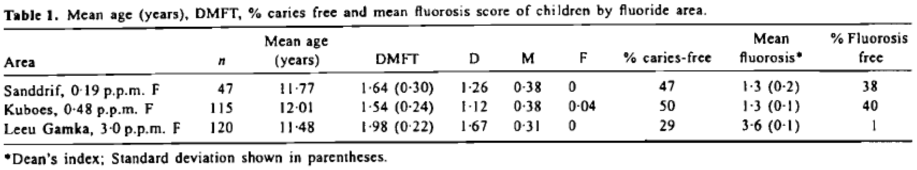


Table 1. Mean age (years), DMFT, % caries free and mean fluorosis score of children by fluoride area.

Area	*n*	Mean age (years)	DMFT	D	M	F	% caries-free	Mean fluorosis*	% Fluorosis free
Sanddrif, 0·19 p.p.m. F	47	11·77	1·64 (0·30)	1·26	0·38	0	47	1·3 (0·2)	38
Kuboes, 0·48 p.p.m. F	115	12·01	1·54 (0·24)	1·12	0·38	0·04	50	1·3 (0·1)	40
Leeu Gamka, 3·0 p.p.m. F	120	11·48	1·98 (0·22)	1·67	0·31	0	29	3·6 (0·1)	1

*Dean's index; Standard deviation shown in parentheses.

PROFILER'S NOTE: The profiler agrees that no difference in caries experience, as measured by mean DMFT score, was found in the two low fluoride areas (Sanddrif and Kuboes), but the DMFT score was comparatively higher in the high fluoride area (Leeu Gamka). This trend was also noted in the percentage of caries-free children; no difference between Sanddrif and Kuboes, but comparatively lower percentage caries-free in Leeu Gamka. A higher DMFT score correlated with a higher mean fluorosis score.

Dental fluorosis

As seen in Table 1 above, mean fluorosis scores were the same in Sanddrif and Kuboes (1.3±0.2 and 1.3±0.1, respectively), but higher in Leeu Gamka (3.6±0.1). The percentage of children fluorosis-free also was similar in the low fluoride areas (38% in Sanddrif and 40% in Kuboes), but much lower in the high fluoride area (1% in Leeu Gamka).

Table 2 summaries dental fluorosis score by fluoride area. The prevalence of fluorosis (scores ≥2) was 47% in Sanddrif, 50% in Kuboes, and 95% in Leeu Gamka. The proportion of children with fluorosis (scores ≥2) did not differ significantly between Sanddrif and Kuboes, but was significantly lower than Leeu Gamka. Approximately half the children in both of the low F areas had no (or questionable) fluorosis (scores ≤1) compared to only 5% in Leeu Gamka. The prevalence of moderate to severe fluorosis (score ≥4) was 4% and 6% in Sanddrif and Kuboes, respectively, but was 61% in Leeu Gamka, the high F area.

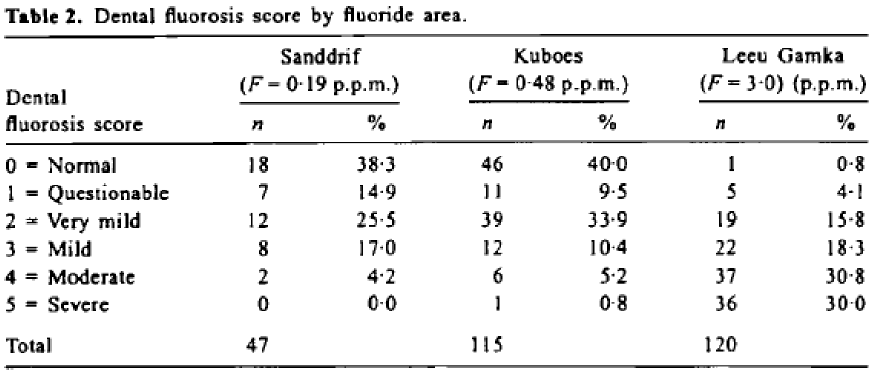


Table 2. Dental fluorosis score by fluoride area.

Dental fluorosis score	Sanddrif (F = 0·19 p.p.m.)		Kuboes (F = 0·48 p.p.m.)		Leeu Gamka (F = 3·0) (p.p.m.)	
	n	%	*n*	%	*n*	%
0 = Normal	18	38·3	46	40·0	1	0·8
1 = Questionable	7	14·9	11	9·5	5	4·1
2 = Very mild	12	25·5	39	33·9	19	15·8
3 = Mild	8	17·0	12	10·4	22	18·3
4 = Moderate	2	4·2	6	5·2	37	30·8
5 = Severe	0	0·0	1	0·8	36	30·0
Total	47		115		120	

PROFILER'S NOTE: The profiler agrees that no difference in fluorosis was found in the two low fluoride areas (Sanddrif and Kuboes), but the fluorosis score was comparatively higher in the high fluoride area (Leeu Gamka). This trend was also noted in the percentage of fluorosis-free children; no difference between Sanddrif and Kuboes, but comparatively lower percentage fluorosis-free in Leeu Gamka.

STUDY AUTHORS' CONCLUSIONS:

The percentage of caries-free children for both lower fluoride areas was higher, with fewer children caries-free in the high fluoride area (Leeu Gamka). Both the fluorosis and DMFT values for Sanddrif and Kuboes did not differ at all. The breakdown in fluorosis scores (Table 2) and DMFT (Table 1) for Sanddrif and Kuboes showed that the difference in the drinking water supplies for these two areas did not make any significant difference whether it was 0.19 or 0.48 ppm fluoride. Most (61%) of the children from the high fluoride area (3.0 ppm F) were classified as having moderate to severe dental fluorosis in comparison with only 4.2% and 6% for the areas with 0.19 ppm F and 0.48 ppm F in the drinking water, respectively. Teeth with moderate and severe fluorosis had dental caries more frequently than teeth with no or very mild to mild fluorosis.

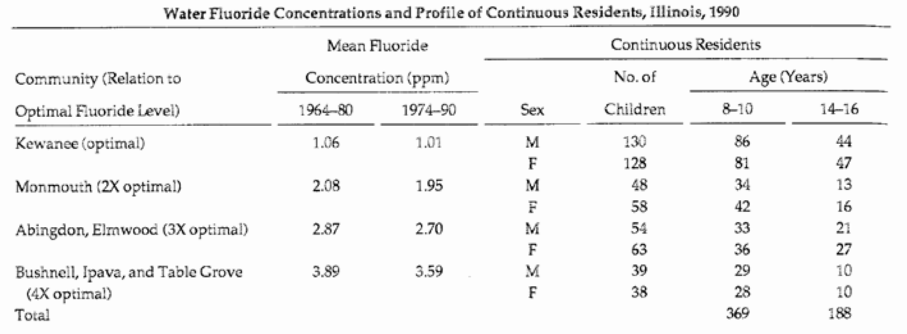
		The results suggest a positive association between high fluoride levels in the drinking water and dental caries. Furthermore, a low caries experience and no difference in DMFT and fluorosis between the two low fluoride areas were found.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Landis, J.R. and Koch, G.G. (1977). The measurement of observer agreement on categorical data. Biometrics 33: 158-174. Nicholson, K. and Duff, E.J. (1981). Fluoride determination in water. Analytical Letters 14A7: 493-517. World Health Organization (1987). Oral Health Surveys: Basic Methods. 3rd ed. WHO, Geneva.
PROFILER'S REMARKS	***Initials/date SJG/ 3/19/07***	Overall, the study was well-conducted and had adequate study design. However, it should be noted that the sample size was not equivalent in all areas, which *might* skew the statistics if not considered; the area with the lowest fluoride level in the water (Sanddrif) had a lower sample size (n=47) compared to the other areas (n=115 and 120). The prevalence of caries was comparatively higher in the high fluoride area (Leeu Gamka) compared to the other two areas (Sanddrif and Kuboes). A lower percentage of caries-free children was noted in Leeu Gamka compared to Sanddrif and Kuboes. The fluorosis score was higher in the high fluoride area (Leeu Gamka) compared with the two low fluoride areas (Sanddrif and Kuboes). A lower percentage of fluorosis-free children was found in Leeu Gamka compared to the other two areas. The prevalence of fluorosis was much higher (95%) in the high fluoride area compared to the other two areas (47% in Sanddrif, 50% in Kuboes); this included a higher prevalence of moderate to severe fluorosis in Leeu Gamka (61%) compared to Sanddrif (4.2%) and Kuboes (6%). No significant differences were found between Sanddrif and Kuboes with respect to caries experience or fluorosis prevalence/severity. A higher DMFT score correlated with a higher mean fluorosis score. Factors, noted by the study authors, that could influence the findings include: 1) Temperature; high average maximum daily temperatures (~25°C) result in elevated water consumption. 2) Age; caries experience increases with age. Leeu Gamka had younger children compared with Sanddrif and Kuboes, negating the possibility that age (as opposed to the high fluoride content in the drinking water) might have contributed to the higher DMFT found in Leeu Gamka. The information presented is useful for evaluating the occurrence of severe fluorosis in populations whose fluoride exposure was not affected by dietary habits or the use of fluoride supplements or dentifrices. Confounding factors are the low socio-economic level of the population, the possible effects of poor dental hygiene, and the arid climate which is likely to increase water consumption and overall fluoride intake. Nevertheless, the data may be useful for comparison with US populations studied in hot arid climates.
PROFILER'S ESTIM. NOEL/ NOAEL		Study design was not suitable for development of a NOAEL for caries experience or threshold dental fluorosis. The NOAEL for severe fluorosis was 0.19 ppm
PROFILER'S ESTIM. LOEL/ LOAEL		Study design was not suitable for development of a LOAEL for caries experience or threshold dental fluorosis. The LOAEL for severe fluorosis was 0.48 ppm (0.8% incidence).
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor ( ), Medium (X), Strong ( ) The study indicated a clear dose-response for the incidence of severe fluorosis (0% at 0.19 ppm, 0.08% at 0.48 ppm and 30% at 3.0 ppm.

CRITICAL EFFECT(S):	Prevalence and severity of dental fluorosis and caries experience

Heifetz, S.B., W.S. Driscoll, H.S. Horowitz, and A. Kingman. 1988. Prevalence of dental caries and dental fluorosis in areas with optimal and above optimal water-fluoride concentrations: a 5 year follow-up survey. J. Amer. Dent. Assoc. 116:490-495.

<table>
<tr><td></td><td></td></tr>
<tr><td>ENDPOINT STUDIED:</td><td>Dental fluorosis</td></tr>
<tr><td></td><td></td></tr>
<tr><td>TYPE OF STUDY:</td><td>Cross-sectional and longitudinal survey performed in 1985; follow-up to a cross-sectional survey conducted in 1980 to test the effect of abrasion and remineralization on existing fluorosis, and to monitor possible changes in fluorosis prevalence.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>POPULATION STUDIED:</td><td>U.S/Illinois.; seven rural communities in Illinois; 432 children 8-10 yrs old and 193 children 13-16 yrs old, who had lived continuously in the same communities. Community water was the primary source of drinking water for all children. Three cohorts: (1) 13-15 year olds in 1980; (2) 8-10 year olds in 1980 who are the 13-15 year olds in 1985; (3) 8-10 year olds in 1985.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>CONTROL POPULATION:</td><td>None</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE PERIOD:</td><td>8-10 yrs and 13-16 yrs. The 13-16 yr old children had been previously examined in a 1980 study (Driscoll et al., 1983). Developing teeth of Cohort 1 were at risk for dental fluorosis from 1965-72; those of Cohort 2 were at risk from 1970-77; while those of Cohort 3 were at risk from 1975-82.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE GROUPS:</td><td>The seven study communities were grouped into four categories based on the concentration of fluoride in their drinking water; optimal, 2x optimal, 3x optimal and 4x optimal. However, the F concentrations at each drinking water “optimal” category were not provided. This information may be included in the 1980 reference survey performed in the same Illinois communities (Driscoll et al 1983).

PROFILER’S NOTE: A later study (Selwitz et al 1995) of this series defines 1 ppm as the optimal water fluoride concentration for the studied geographic area. Selwitz et al (1995) also provides drinking water concentrations for the other areas, as shown below.


Water Fluoride Concentrations and Profile of Continuous Residents, Illinois, 1990
<table>
<tr><td>Community (Relation to Optimal Fluoride Level)</td><td>Mean Fluoride Concentration (ppm)</td><td></td><td>Continuous Residents</td><td></td><td></td><td></td></tr>
<tr><td></td><td>1964–80</td><td>1974–90</td><td>Sex</td><td>No. of Children</td><td>Age (Years)
8–10</td><td>14–16</td></tr>
<tr><td>Kewanee (optimal)</td><td>1.06</td><td>1.01</td><td>M</td><td>130</td><td>86</td><td>44</td></tr>
<tr><td></td><td></td><td></td><td>F</td><td>128</td><td>81</td><td>47</td></tr>
<tr><td>Monmouth (2X optimal)</td><td>2.08</td><td>1.95</td><td>M</td><td>48</td><td>34</td><td>13</td></tr>
<tr><td></td><td></td><td></td><td>F</td><td>58</td><td>42</td><td>16</td></tr>
<tr><td>Abingdon, Elmwood (3X optimal)</td><td>2.87</td><td>2.70</td><td>M</td><td>54</td><td>33</td><td>21</td></tr>
<tr><td></td><td></td><td></td><td>F</td><td>63</td><td>36</td><td>27</td></tr>
<tr><td>Bushnell, Ipava, and Table Grove (4X optimal)</td><td>3.89</td><td>3.59</td><td>M</td><td>39</td><td>29</td><td>10</td></tr>
<tr><td></td><td></td><td></td><td>F</td><td>38</td><td>28</td><td>10</td></tr>
<tr><td>Total</td><td></td><td></td><td></td><td></td><td>369</td><td>188</td></tr>
</table>
Source: Selwitz et al 1995.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE ASSESSMENT:</td><td>Fluoride in drinking water was the only exposure route assessed quantitatively, although the study authors noted that beginning in the early 1970’s there were other possible sources of exposure to fluoride, including commercial infant formula, other processed foods, fluoride dentifrices, and fluoride supplements.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>ANALYTICAL METHODS:</td><td>Methods for measuring the fluoride concentrations in water supplies of study communities were not reported; other water quality parameters were not described.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>STUDY DESIGN</td><td>Dental fluorosis and caries incidence in 432 children 8-10 yrs old and 193 children 13-16 yrs</td></tr>
</table>

old from seven communities in Illinois having different concentrations of fluoride in drinking water (mean values ranging from 1.06-3.89 ppm in 1964-1980 and 1.01-3.59 ppm in 1974-1990) were compared using acceptable methods of diagnosis (TSIF index for fluorosis, and DMFS scores for caries). Methods of statistical analysis were not reported.

PARAMETERS MONITORED:

TSIF index (see Section 2) was used to evaluate fluorosis and DMFS scores (see List of Acronyms) was used to evaluate caries. Only the TSIF index was used in the 1985 survey.

STATISTICAL METHODS:

Not reported. Levels of agreement between examiners individual and combined scores for all tooth surfaces were determined by Kappa values for 1980 (0.48 and 0.65 respectively) and 1985 (0.51 and 0.64 respectively); these Kappa results indicate moderate agreement between the 1980 and 1985 surveys.

RESULTS:

Dental fluorosis

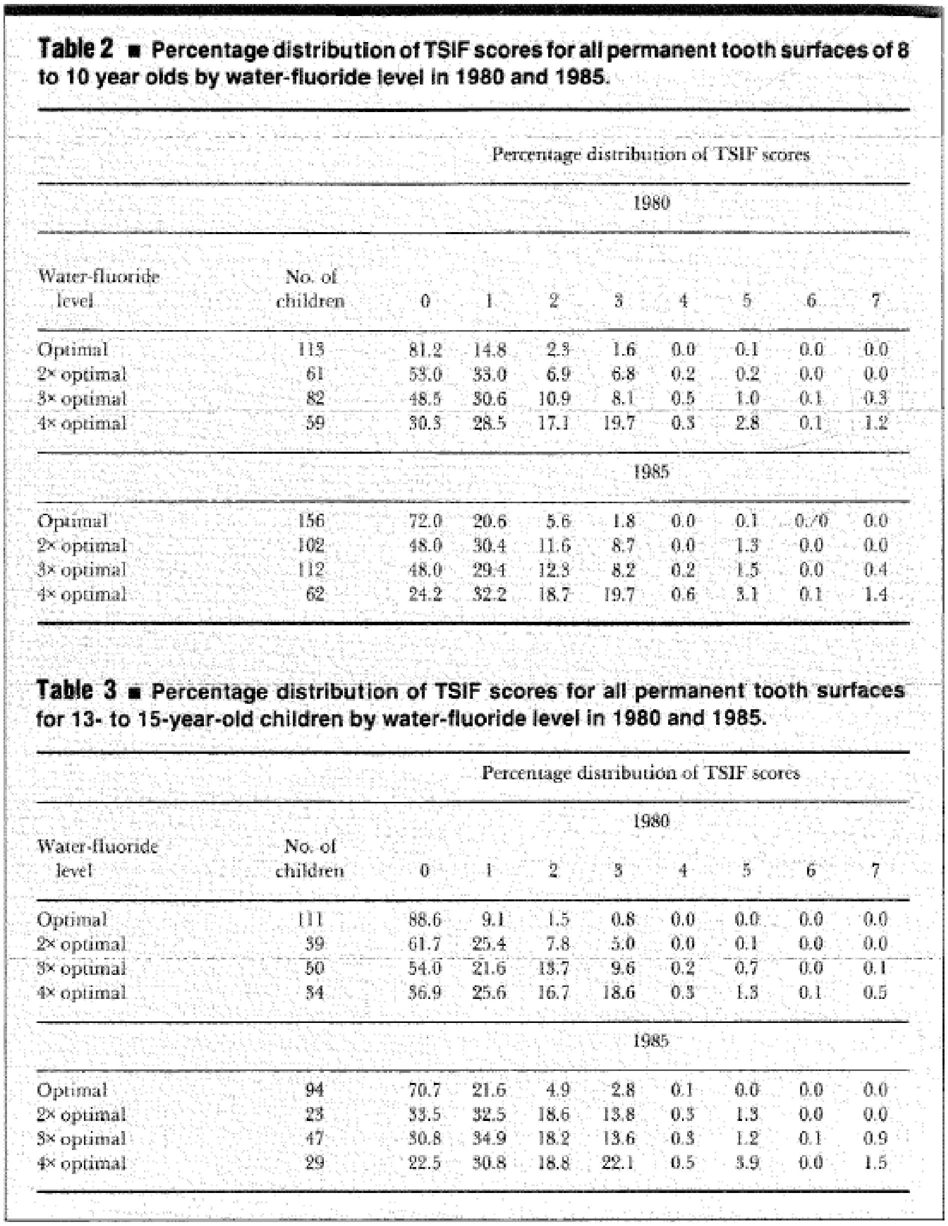


Table 2 ■ **Percentage distribution of TSIF scores for all permanent tooth surfaces of 8 to 10 year olds by water-fluoride level in 1980 and 1985.**

		Percentage distribution of TSIF scores							
		1980							
Water-fluoride level	No. of children	0	1	2	3	4	5	6	7
Optimal	113	81.2	14.8	2.3	1.6	0.0	0.1	0.0	0.0
2× optimal	61	53.0	33.0	6.9	6.8	0.2	0.2	0.0	0.0
3× optimal	82	48.5	30.6	10.9	8.1	0.5	1.0	0.1	0.3
4× optimal	59	30.3	28.5	17.1	19.7	0.3	2.8	0.1	1.2
		1985							
Optimal	156	72.0	20.6	5.6	1.8	0.0	0.1	0./0	0.0
2× optimal	102	48.0	30.4	11.6	8.7	0.0	1.3	0.0	0.0
3× optimal	112	48.0	29.4	12.3	8.2	0.2	1.5	0.0	0.4
4× optimal	62	24.2	32.2	18.7	19.7	0.6	3.1	0.1	1.4

Table 3 ■ **Percentage distribution of TSIF scores for all permanent tooth surfaces for 13- to 15-year-old children by water-fluoride level in 1980 and 1985.**

		Percentage distribution of TSIF scores							
		1980							
Water-fluoride level	No. of children	0	1	2	3	4	5	6	7
Optimal	111	88.6	9.1	1.5	0.8	0.0	0.0	0.0	0.0
2× optimal	39	61.7	25.4	7.8	5.0	0.0	0.1	0.0	0.0
3× optimal	50	54.0	21.6	13.7	9.6	0.2	0.7	0.0	0.1
4× optimal	34	56.9	25.6	16.7	18.6	0.3	1.3	0.1	0.5
		1985							
Optimal	94	70.7	21.6	4.9	2.8	0.1	0.0	0.0	0.0
2× optimal	23	33.5	32.5	18.6	13.8	0.3	1.3	0.0	0.0
3× optimal	47	30.8	34.9	18.2	13.6	0.3	1.2	0.1	0.9
4× optimal	29	22.5	30.8	18.8	22.1	0.5	3.9	0.0	1.5

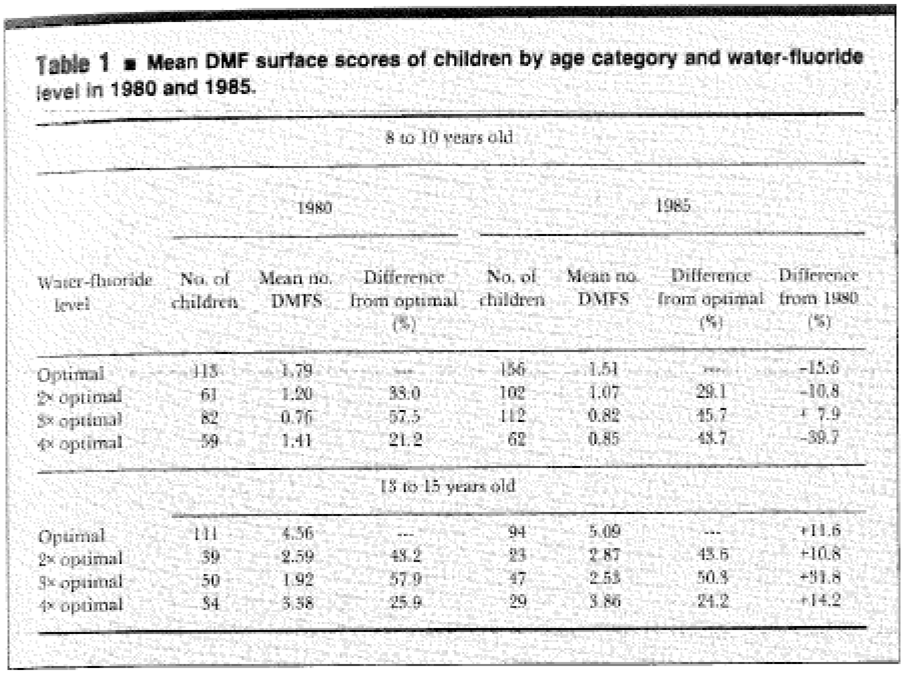
Dental Caries	

Table 1 ■ Mean DMF surface scores of children by age category and water-fluoride level in 1980 and 1985.

	8 to 10 years old						
	1980			1985			
Water-fluoride level	No. of children	Mean no. DMFS	Difference from optimal (%)	No. of children	Mean no. DMFS	Difference from optimal (%)	Difference from 1980 (%)
Optimal	115	1.79	---	156	1.51	---	−15.6
2× optimal	61	1.20	33.0	102	1.07	29.1	−10.8
3× optimal	82	0.76	57.5	112	0.82	45.7	+ 7.9
4× optimal	59	1.41	21.2	62	0.85	43.7	−39.7
	13 to 15 years old						
Optimal	111	4.56	---	94	5.09	---	+11.6
2× optimal	39	2.59	43.2	23	2.87	43.6	+10.8
3× optimal	50	1.92	57.9	47	2.53	50.3	+31.8
4× optimal	54	3.38	25.9	29	3.86	24.2	+14.2

STUDY AUTHORS' CONCLUSIONS:		At 2X optimal fluoride concentration, additional intake from extraneous sources of fluoride could be approaching a critical threshold for producing severe fluorosis. At 2X optimal, 7.6% of labial surfaces of maxillary anterior teeth of 13-15 years olds examined in 1985 exhibited severe fluorosis. The 13-15 yr ols showed little change between 1980 and 1985 in the relative differences in the mean DMFS scores between the optimal and above optimal fluoride areas. For to 8-10 yr olds, the mean DMFS scores in 1980 were substantially higher at 4x optimal than at 3x optimal, but in 1985, there was very little difference between the two groups.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Driscoll, W.S., et al. 1983. Prevalence of dental caries and dental fluorosis in areas with optimal and above optimal water fluoride concentrations. J. Amer. Dent. Assoc. 107(1):42-47. Driscoll, W.S., et al. 1986. Prevalence of dental caries and dental fluorosis in areas with negligible, optimal and above optimal water fluoride concentrations in drinking water. J. Amer. Dent. Assoc. 113(1):29-33.
PROFILER'S REMARKS	***DMO 11/21/06 and 12/15/2006***	The recommended optimal fluoride level for the communities studied was reported in Selwitz (1995) to be 1 ppm. The study authors note that, beginning in the early 1970's, there were other possible sources of exposure to fluoride, including commercial infant formula, and other processed foods, fluoride dentifrices, and fluoride supplements, but these were not quantified. The use of bottled water by the study population was also not addressed. The size of the study groups is sufficiently large for statistical analysis, and a standard method was used by the study authors to evaluate dental fluorosis (TSIF index). The inter-examiner reliability of the scoring system was also verified (Kappa values).
PROFILER'S ESTIM. NOEL/NOAEL		TBD
PROFILER'S ESTIM. LOEL/ LOAEL		TBD
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor (_), Medium (x), Strong (_) Suitability medium to strong for the dental fluorosis endpoint. An adequate number of

	exposure levels were considered and a sufficient number of children were examined.
CRITICAL EFFECT(S):	Dental fluorosis

Heller, K.E., Eklund, S.A., and Burt, B.A. 1997. Dental caries and dental fluorosis at varying water fluoride concentrations. J. Public Health Dent. 57:136-143.

ENDPOINT STUDIED:	Dental caries and dental fluorosis in children aged 5-17 years
TYPE OF STUDY:	Data were obtained from the 1986-1987 National Survey of Oral Health of US Schoolchildren conducted by the National Institute of Dental Research (NIDR).
POPULATION STUDIED:	US: 40,693 children aged 4-22 years were included in the National Survey. The Survey included at least 14 sampling strata, with two strata per geographic region. Only data for children with a single continuous residence (N = 18,755 aged 5-7 for caries analysis; N = 15,532 aged 7-17 for fluorosis analysis) were considered.
CONTROL POPULATION:	No control population was included.
EXPOSURE PERIOD:	Only children with a single continuous residence were included in the current analysis; children who had resided at more than one address at some point in their life were excluded.
EXPOSURE GROUPS:	The fluoride level in the school drinking water was used as a measure of exposure. For the analysis, fluoride levels were presented as <0.3 ppm F, 0.3 to <0.7 ppm F, 0.7-1.2 ppm F, and >1.2 ppm F.
EXPOSURE ASSESSMENT:	The exposure assessment consisted solely of measured fluoride concentrations in the child's school drinking water. A written questionnaire, administered to parent or guardian, included questions regarding the use of fluoride drops, fluoride tablets, professional topical fluoride treatments, and school fluoride rinses; these findings were used for statistical analysis only, not exposure assessment.
ANALYTICAL METHODS:	The method for analyzing fluoride in the drinking water was not described.
STUDY DESIGN	Little information was given in the current publication. Design and conduct of the original survey have been described by US Public Health Service (1989, 1992) and Brunelle and Carlos (1990). Data for the current analysis were obtained from a public use data tape provided by the NIDR. Comparisons between at least 5 field examiners found good agreement on paired t-tests.
PARAMETERS MONITORED:	Oral examinations of children included visual and tactile assessment of dental caries and restorations using the diagnostic criteria of Radike (1972); no radiographs were taken. Children in grade 2 and higher were examined for dental fluorosis. A classification system based on Dean's Fluorosis Index (Dean 1942) was used to evaluate all erupted permanent teeth. Fluorosis prevalence was determined by whether or not the child had at least two teeth with a score of 1 (very mild) or greater. A written questionnaire, administered to parent or guardian, included questions regarding the use of fluoride drops, fluoride tablets, professional topical fluoride treatments, and school fluoride rinses.
STATISTICAL METHODS:	The Statistical Analysis System (SAS) Version 6.10 (16) was used for data management and for descriptive statistical procedures. The SUDAAN (Survey DAta ANalysis) Release 6.40 statistical program (17) was used for statistical tests because of the need to adjust variances for the complex sample design of the NIDR survey. Sample weighting to represent the population of US schoolchildren was used for all analyses.
RESULTS:	
Dental caries	Mean scores for both decayed or filled surfaces (dfs) in children aged 5-10 years and decayed, missing, or filled surfaces (DMFS) of permanent teeth in children aged 5-17 years decreased with increasing fluoride levels (Tables 1 and 2). The mean dfs score for the 0.7-

1.2 ppm F group was statistically different from the <0.3 ppm (p=0.004) and 0.3 to <0.7 ppm (p=0.045) groups. Statistical significance was also found between the >1.2 ppm groups and the <0.3 ppm groups (p=0.031). For the permanent teeth, the mean DMFS score for the 0.7-1.2 ppm group was significantly different from the <0.3 ppm group (p=0.003). No other statistically significant differences were found between DMFS scores.

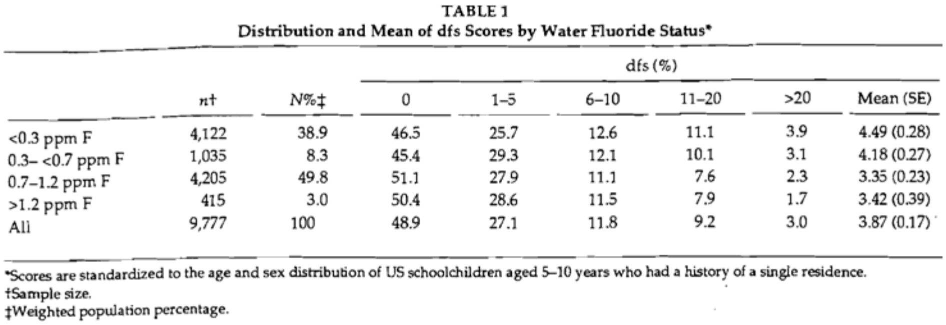


TABLE 1
Distribution and Mean of dfs Scores by Water Fluoride Status*

			dfs (%)					
	n†	*N*%‡	0	1–5	6–10	11–20	>20	Mean (SE)
<0.3 ppm F	4,122	38.9	46.5	25.7	12.6	11.1	3.9	4.49 (0.28)
0.3– <0.7 ppm F	1,035	8.3	45.4	29.3	12.1	10.1	3.1	4.18 (0.27)
0.7–1.2 ppm F	4,205	49.8	51.1	27.9	11.1	7.6	2.3	3.35 (0.23)
>1.2 ppm F	415	3.0	50.4	28.6	11.5	7.9	1.7	3.42 (0.39)
All	9,777	100	48.9	27.1	11.8	9.2	3.0	3.87 (0.17)

*Scores are standardized to the age and sex distribution of US schoolchildren aged 5–10 years who had a history of a single residence.
†Sample size.
‡Weighted population percentage.

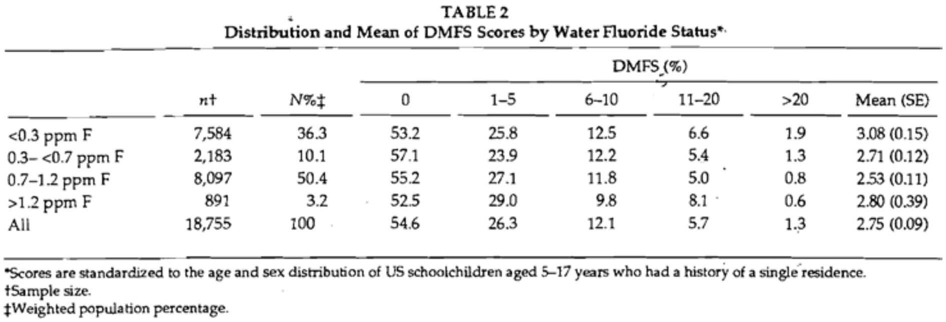


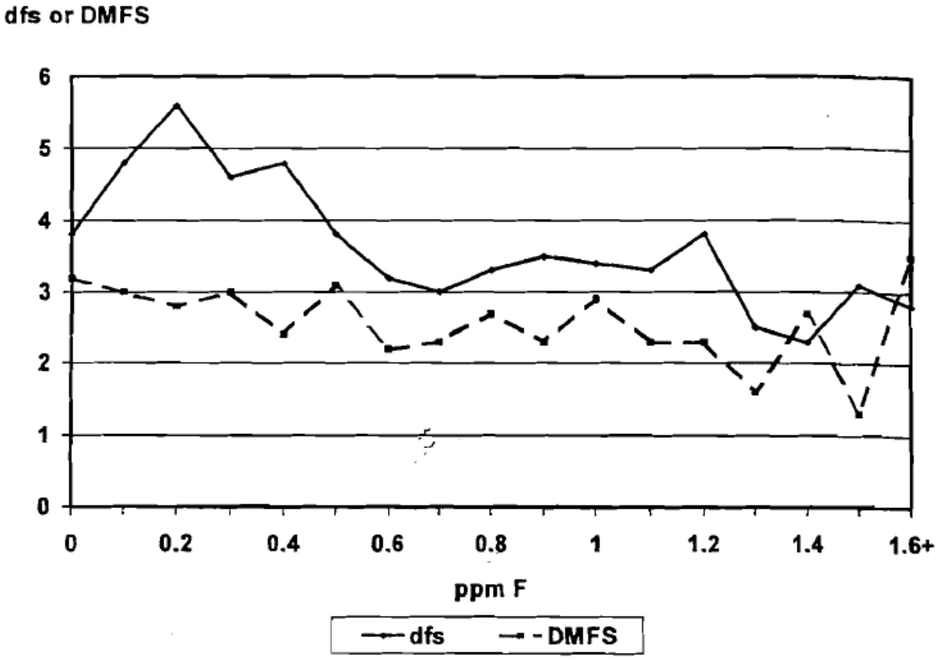
TABLE 2
Distribution and Mean of DMFS Scores by Water Fluoride Status*

			DMFS (%)					
	n†	*N*%‡	0	1–5	6–10	11–20	>20	Mean (SE)
<0.3 ppm F	7,584	36.3	53.2	25.8	12.5	6.6	1.9	3.08 (0.15)
0.3– <0.7 ppm F	2,183	10.1	57.1	23.9	12.2	5.4	1.3	2.71 (0.12)
0.7–1.2 ppm F	8,097	50.4	55.2	27.1	11.8	5.0	0.8	2.53 (0.11)
>1.2 ppm F	891	3.2	52.5	29.0	9.8	8.1	0.6	2.80 (0.39)
All	18,755	100	54.6	26.3	12.1	5.7	1.3	2.75 (0.09)

*Scores are standardized to the age and sex distribution of US schoolchildren aged 5–17 years who had a history of a single residence.
†Sample size.
‡Weighted population percentage.

Additional graphical comparisons and statistical analyses were made between caries levels (dfs or DMFS) and fluoride water levels. As depicted graphically (Fig 1), both dfs in primary dentition and DMFS in permanent dentition decreased between 0 ppm F and 0.6-0.7 ppm F, then plateaued up to 1.2 ppm F; dfs continued to decrease at higher F concentrations.

FIGURE 1
DMFS for Children Aged 5–17 Years, and dfs Scores for Children Aged 5–10 Years, by Water Fluoridation Level for US Schoolchildren with a History of a Single Residence(Scores are age- and sex-standardized to children with one residence aged 5–10 years for dfs and aged 5–17 years for DMFS.)



Multiple regression analyses were made between dental caries levels with demographic and fluoride exposure variables. In primary dentition, a lower dfs score was significantly associated with being female, higher water fluoride levels, and for having ever used fluoride drops. In the permanent dentition, lower DMFS scores were significantly associated with increasing fluoride water levels and the reported use of fluoride tablets. In contrast, increasing age and being female were associated with increasing DMFS scores.

Dental fluorosis

Mean fluorosis severity increased with increasing water fluoride level (Table 5). The mean severity score for the >1.2 ppm F group was significantly greater than all other groups (p=0.045-<0.001) and the mean score for the 0.7-1.2 ppm F group was significantly greater than that of the <0.3 ppm F group (p=<0.001).

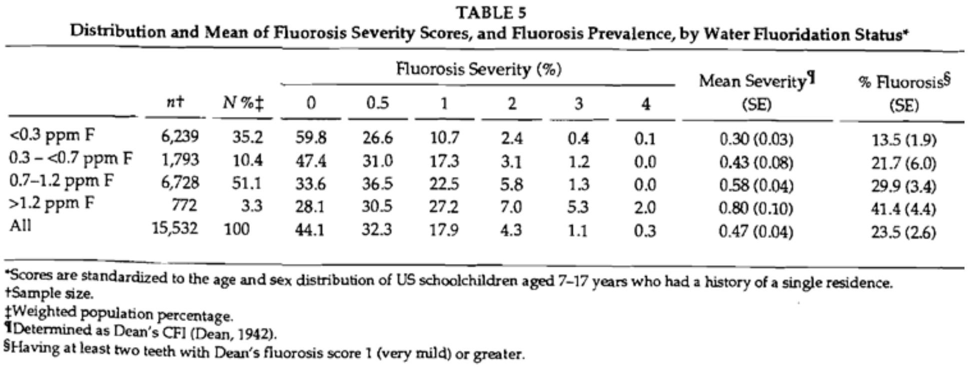
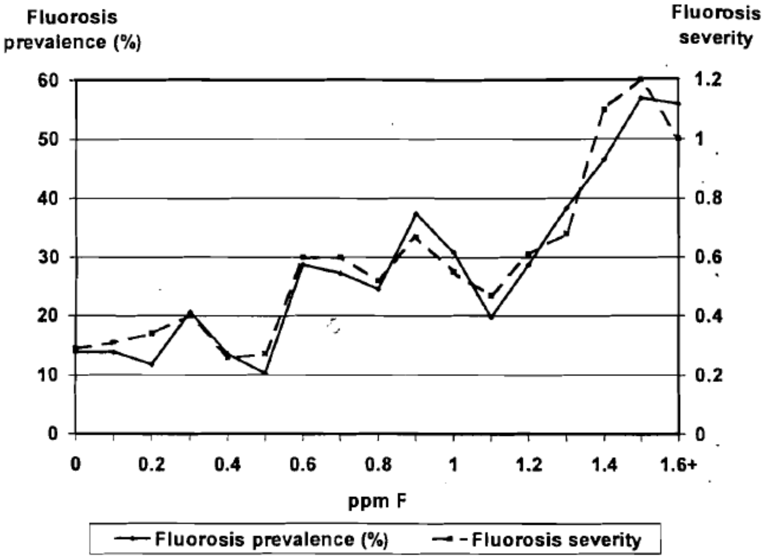
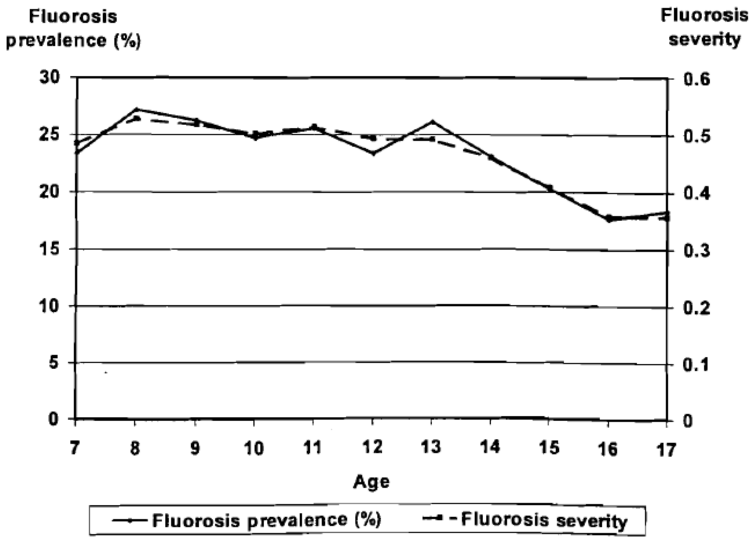


TABLE 5
Distribution and Mean of Fluorosis Severity Scores, and Fluorosis Prevalence, by Water Fluoridation Status*

			Fluorosis Severity (%)						Mean Severity¶	% Fluorosis§
	n†	N %‡	0	0.5	1	2	3	4	(SE)	(SE)
<0.3 ppm F	6,239	35.2	59.8	26.6	10.7	2.4	0.4	0.1	0.30 (0.03)	13.5 (1.9)
0.3 – <0.7 ppm F	1,793	10.4	47.4	31.0	17.3	3.1	1.2	0.0	0.43 (0.08)	21.7 (6.0)
0.7–1.2 ppm F	6,728	51.1	33.6	36.5	22.5	5.8	1.3	0.0	0.58 (0.04)	29.9 (3.4)
>1.2 ppm F	772	3.3	28.1	30.5	27.2	7.0	5.3	2.0	0.80 (0.10)	41.4 (4.4)
All	15,532	100	44.1	32.3	17.9	4.3	1.1	0.3	0.47 (0.04)	23.5 (2.6)

*Scores are standardized to the age and sex distribution of US schoolchildren aged 7–17 years who had a history of a single residence.
†Sample size.
‡Weighted population percentage.
¶Determined as Dean's CFI (Dean, 1942).
§Having at least two teeth with Dean's fluorosis score 1 (very mild) or greater.

Graphical representation showed both fluorosis prevalence (%) and severity increased with increasing water fluoride levels but decreased with increasing age (see study Figs 2 and 3).

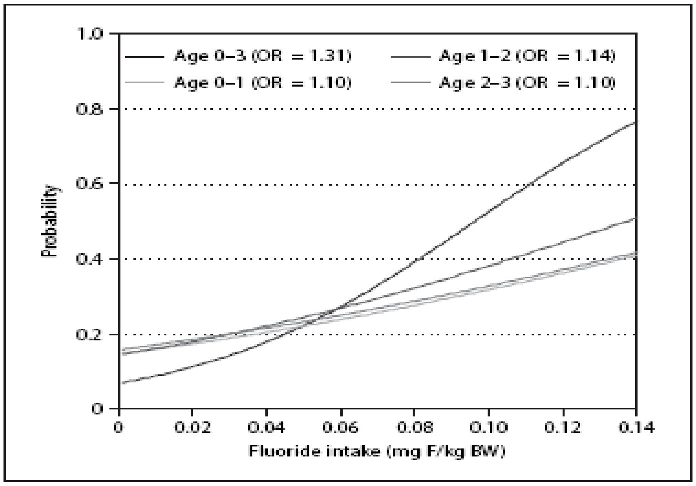
	FIGURE 2 Fluorosis Prevalence and Mean Severity Scores by Water Fluoridation Level for US Schoolchildren Aged 7–17 Years with a History of a Single Residence (Scores are age- and sex-standardized to children aged 5–17 years with a history of a single residence. Fluorosis prevalence was defined as having two or more teeth with very mild fluorosis or greater; mean severity scores were derived in a manner similar to Dean's CFI scores.)  FIGURE 3 Fluorosis Prevalence and Mean Severity Scores for US Schoolchildren Aged 7–17 Years by Age with a History of a Single Residence (Fluorosis prevalence was defined as having two or more teeth with very mild fluorosis or greater; mean severity scores were derived in a manner similar to Dean's CFI score.)  A logistic regression model, controlling for age and fluoride product use, showed children who consumed water at 0.3-<0.7 ppm F, 0.7-1.2 ppm F, or >1.2 ppm F had an odds ratio of 2.07 (95% CI = 0.92, 4.67), 3.32 (2.25, 4.91), or 4.96 (2.87, 8.58), respectively, of developing fluorosis compared to children who consumed water at <0.3 ppm F.
Dose response	Increasing fluoride water concentrations were associated with lower dfs and DMFS scores up to a level of approximately 0.6-0.7 ppm F. Higher fluoride water

	concentrations did not affect DMFS scores while dfs scores showed further decline at >1.2 ppm F. In contrast, increasing fluoride water concentrations were associated with higher prevalence and severity of fluorosis with no apparent plateau of effects. PROFILER'S NOTE: No attempt was made by the authors to estimate intake of fluoride from drinking water consumption; thus, a dose could not be determined.
STUDY AUTHORS' CONCLUSIONS:	A suitable trade-off between caries and fluorosis appears to occur around 0.7 ppm F. Little decline in caries levels were observed between 0.7 and 1.2 ppm F, while considerable dental fluorosis was seen at this water fluoride level.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	US Public Health Service, National Institute of Dental Research. Oral health of United States children. The National Survey of Dental Caries in US Schoolchildren: 1986.1987. National and regional findings. NIH pub no 89-2247. Washington, DC: Government Printing Office, 1989. Brunelle JA, Carlos JP. Recent trends in dental caries in US children and the effects of water fluoridation. J Dent Res 1990; 69 (Spec Iss):723-7. US Public Health Service, National Institute of Dental Research. Oral health of United States children. The National Survey of Dental Caries in US Schoolchildren: 1986-1987. Public use data file documentation and survey methodology. Washington, DC: Government Printing Office, 1992. Radike AW. Criteria for diagnosis of dental caries. In: Proceedings of the conference on the clinical testing of cariostatic agents. Chicago: American Dental Association, 1972:87-8. Dean HT. The investigation of physiological effects by the epidemiological method. In: Moulton FR, ed. Fluorine and dental health. Washington, DC: American Association for the Advancement of Science, 1942, pub no 19:2331.
PROFILER'S REMARKS ***Initials/date: CSW/1/3/07***	This study was an analysis of data collected as part of a larger national survey. The authors assured consistent water fluoride exposure by excluding those children who had resided at more than one address during their lifetime. Only school water fluoride levels were measured; no attempt was made to correlate those levels with home water supplies. It might be assumed that municipal water supplies would be similar between home and school, but this is not true for rural homes which might use well water or cisterns. Despite lack of data on other potential fluoride sources, the study showed clear correlation between increasing school water fluoride levels and decreasing caries with concurrent increasing fluorosis. Severe fluorosis (Dean score of 4) was observed in 2% of the individuals in the >1.2 ppm F group; however, a correlation of fluorosis and a significant increase in caries was not evaluated for individuals in this group. Doses could not be reconstructed because these data were not collected.
PROFILER'S ESTIM. NOEL/NOAEL	Could not be determined.
PROFILER'S ESTIM. LOEL/ LOAEL	Could not be determined.
POTENTIAL SUITABILITY	Not suitable ( ), Poor (X), Medium ( ), Strong ( )

FOR DOSE-RESPONSE MODELING:	A positive correlation was found between increasing water fluoride levels and decreasing caries and increasing fluorosis; however, the data were combined into concentration ranges and therefore may not be suitable for statistical analysis.
CRITICAL EFFECT(S):	Dental caries, fluorosis

Hong, L., S.M. Levy, J.J. Warren, B. Broffitt, and J. Cavanaugh. 2006a. Fluoride intake levels in relation to fluorosis development in permanent maxillary central incisors and first molars. Caries Research. 40:494-500.

ENDPOINT STUDIED:	Dental fluorosis (central incisors and molars)
TYPE OF STUDY:	US/Iowa: Prevalence study of dental fluorosis as part of longitudinal study of daily fluoride intake in male and female children recruited at birth (Iowa Fluoride Study; see also companion report Hong et al 2006b). Study conducted March 1992 to February 1995 included exam of early erupting permanent teeth at mean age 9.3 years.
POPULATION STUDIED:	Children (319 males and 309 females) aged birth to 36 months included in the Iowa Fluoride Study; total fluoride intake estimated from parental questionnaire administered every 3-4 months, and dental fluorosis measured in early erupting permanent teeth at subject age 8-10 yrs. The cohort was 98% Caucasian, from families with a relatively high socioeconomic status (71% having a family income of $30,000 or more and 46% of mothers having completed 4 years of college), 44% were first children, 32% were breast-fed for at least 6 months, 4% had low birth weight (<2,500 g) and 3% had developmental disorders. Children were entered into the study using Institutional Review Board-approved consent procedures.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	Birth to 36 months (and beyond)
EXPOSURE GROUPS:	Estimated daily intake was categorized into three categories: <0.04 mg F/kg BW, 0.04-0.06 mg F/kg BW and >0.06 mg F/kg BW based on questionnaire analysis.
EXPOSURE ASSESSMENT	Fluoride intake from water, beverages, selected foods, dietary supplements and dentrifice was estimated from questionnaires (unvalidated) completed by parents every 3-4 months from subject birth to age three years. Fluoride intake (mg/kg BW per day) for cumulative time periods (AUC) was estimated for 1st year (0-12 months), 2nd year (12-24 months), 3rd year (24-36 months) and composite all 3 years (0-36 months).
ANALYTICAL METHODS:	Study methodologies described previously in Levy et al (2001, 2003)
STUDY DESIGN	The purpose of the study was to report the fluorosis prevalence by levels of estimated daily fluoride intake. As part of the Iowa Fluoride Study, children were followed from birth to 36 months with questionnaires every 3-4 months to estimate daily fluoride intake (mg/kg BW) from water, beverages, selected foods, fluoride supplements and dentrifice. At 8-10 years (mean 9.3 yrs), 628 children (319 males and 309 females) were examined for fluorosis on permanent incisors and first molars using the Fluorosis Risk Index (FRI; see NRC, 2006, page 90). Fluorosis was differentiated from enamel demineralization ("white spot") based on color, texture, demarcation and relationship to gingival margin. The FRI was adapted to include assessment of all visible enamel surfaces, with four zones scored separately on each buccal surface (the incisal edge/occlusal table, the incisal/occlusal third, the middle third and the cervical third).
PARAMETERS MONITORED:	Dental fluorosis on early-erupting permanent teeth (8 incisors and 4 first molars) was determined at 8-10 years of age (mean 9.3 years, range 7.7-12.0) using the FRI. Fluorosis was differentiated from non-fluorosis opacities by the criteria of Russell (1961). Fluorosis was further differentiated from enamel demineralization ("white spot") based on color, texture, demarcation and relationship to gingival margin. The FRI was adapted to include assessment of all visible enamel surfaces, with four zones scored separately on each buccal surface (the incisal edge/occlusal table, the incisal/occlusal third, the middle third and the cervical third). Scoring criteria differentiated no fluorosis, questionable fluorosis (less than

	50% of zone with white striations), definitive fluorosis (greater than 50% of zone with white striations) and severe fluorosis (zone displays pitting/staining/deformity). Cervical zones were excluded from the analyses due to lack of consistent full eruptions. Incisor fluorosis was defined as having FRI definitive/severe fluorosis (FRI score 2 or 3) on both maxillary central incisors. First molar fluorosis was defined as having definitive/severe fluorosis on at least two first molars.
STATISTICAL METHODS:	Correlations among fluoride intakes for the first three years were assessed using Spearman rank correlation analyses. Logistic regression was used to assess the relationships between estimated fluoride intakes and fluorosis. Fluorosis prevalence rates were calculated by fluoride intake category and relationships were assessed using Cochran-Armitage tests for linear trends using scores equal to the median fluoride intake for each group. Using fluoride intake of <0.04 mg F/kg BW as a reference group, the relative risks for fluorosis were calculated for 0.04-0.06 mg F/kg BW intake and >0.06 mg F/kg BW intake. Similar analyses were used to compare subjects who consistently stayed in the same fluoride intake category for the first two years and those who were consistent for all three years of intake monitoring.
RESULTS:	Most dental fluorosis observed attained a FRI score of 2 (mild to moderate); ≤1.5% exhibited a FRI of 3 (severe fluorosis). Results of the study are shown in Figures 1 and 2 and Tables 1, 2 and 3 directly from Hong (2006) (OR = odds ratio):  **Fig. 1.** Probability of permanent maxillary central incisor fluorosis case by level of fluoride intake (from logistic regression). ORs for increments of 0.01 mg F/kg BW. p values for fluoride intakes were all statistically significant ($p < 0.05$).

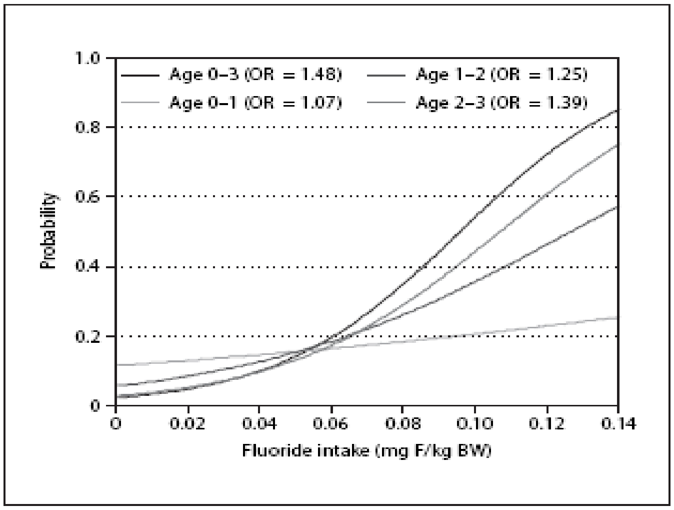


Fig. 2. Probability of permanent first molar fluorosis case by level of fluoride intake (from logistic regression). ORs for increments of 0.01 mg F/kg BW. p values for fluoride intakes were all statistically significant ($p < 0.05$).

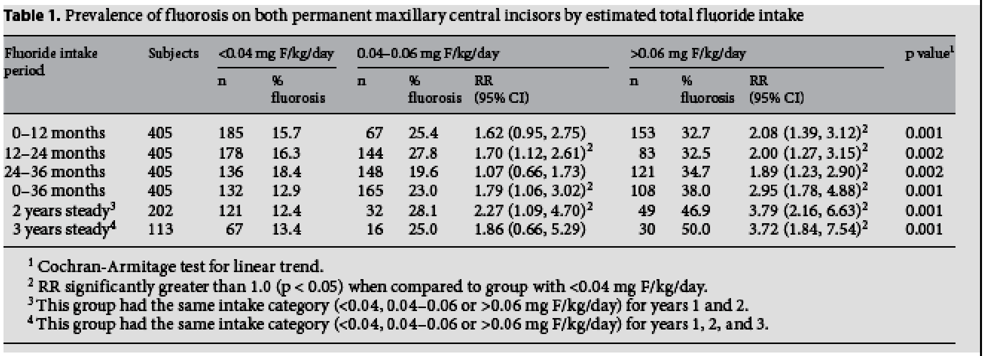


Table 1. Prevalence of fluorosis on both permanent maxillary central incisors by estimated total fluoride intake

Fluoride intake period	Subjects	<0.04 mg F/kg/day		0.04–0.06 mg F/kg/day			>0.06 mg F/kg/day			p value[1]
		n	% fluorosis	n	% fluorosis	RR (95% CI)	n	% fluorosis	RR (95% CI)	
0–12 months	405	185	15.7	67	25.4	1.62 (0.95, 2.75)	153	32.7	2.08 (1.39, 3.12)[2]	0.001
12–24 months	405	178	16.3	144	27.8	1.70 (1.12, 2.61)[2]	83	32.5	2.00 (1.27, 3.15)[2]	0.002
24–36 months	405	136	18.4	148	19.6	1.07 (0.66, 1.73)	121	34.7	1.89 (1.23, 2.90)[2]	0.002
0–36 months	405	132	12.9	165	23.0	1.79 (1.06, 3.02)[2]	108	38.0	2.95 (1.78, 4.88)[2]	0.001
2 years steady[3]	202	121	12.4	32	28.1	2.27 (1.09, 4.70)[2]	49	46.9	3.79 (2.16, 6.63)[2]	0.001
3 years steady[4]	113	67	13.4	16	25.0	1.86 (0.66, 5.29)	30	50.0	3.72 (1.84, 7.54)[2]	0.001

[1] Cochran-Armitage test for linear trend.
[2] RR significantly greater than 1.0 ($p < 0.05$) when compared to group with <0.04 mg F/kg/day.
[3] This group had the same intake category (<0.04, 0.04–0.06 or >0.06 mg F/kg/day) for years 1 and 2.
[4] This group had the same intake category (<0.04, 0.04–0.06 or >0.06 mg F/kg/day) for years 1, 2, and 3.

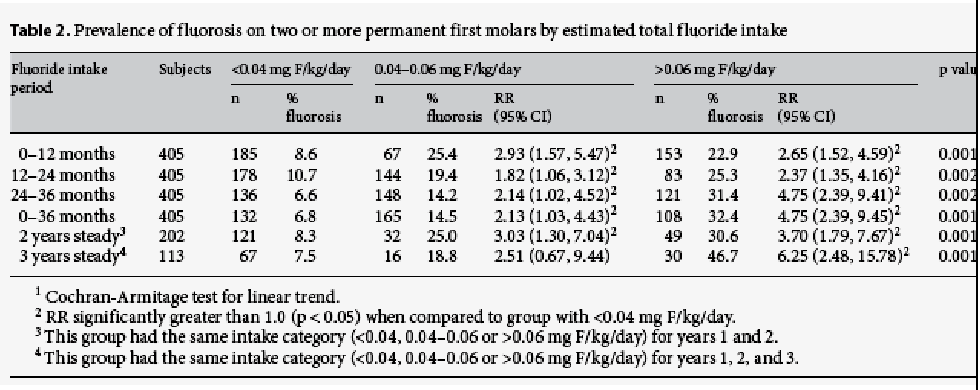


Table 2. Prevalence of fluorosis on two or more permanent first molars by estimated total fluoride intake

Fluoride intake period	Subjects	<0.04 mg F/kg/day		0.04–0.06 mg F/kg/day			>0.06 mg F/kg/day			p valu
		n	% fluorosis	n	% fluorosis	RR (95% CI)	n	% fluorosis	RR (95% CI)	
0–12 months	405	185	8.6	67	25.4	2.93 (1.57, 5.47)[2]	153	22.9	2.65 (1.52, 4.59)[2]	0.001
12–24 months	405	178	10.7	144	19.4	1.82 (1.06, 3.12)[2]	83	25.3	2.37 (1.35, 4.16)[2]	0.002
24–36 months	405	136	6.6	148	14.2	2.14 (1.02, 4.52)[2]	121	31.4	4.75 (2.39, 9.41)[2]	0.002
0–36 months	405	132	6.8	165	14.5	2.13 (1.03, 4.43)[2]	108	32.4	4.75 (2.39, 9.45)[2]	0.001
2 years steady[3]	202	121	8.3	32	25.0	3.03 (1.30, 7.04)[2]	49	30.6	3.70 (1.79, 7.67)[2]	0.001
3 years steady[4]	113	67	7.5	16	18.8	2.51 (0.67, 9.44)	30	46.7	6.25 (2.48, 15.78)[2]	0.001

[1] Cochran-Armitage test for linear trend.
[2] RR significantly greater than 1.0 ($p < 0.05$) when compared to group with <0.04 mg F/kg/day.
[3] This group had the same intake category (<0.04, 0.04–0.06 or >0.06 mg F/kg/day) for years 1 and 2.
[4] This group had the same intake category (<0.04, 0.04–0.06 or >0.06 mg F/kg/day) for years 1, 2, and 3.

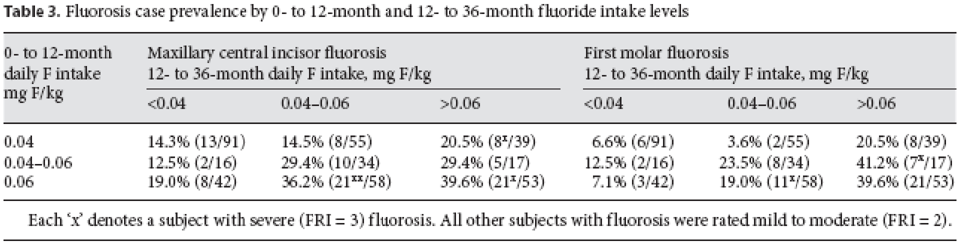


Table 3. Fluorosis case prevalence by 0- to 12-month and 12- to 36-month fluoride intake levels

0- to 12-month daily F intake mg F/kg	Maxillary central incisor fluorosis 12- to 36-month daily F intake, mg F/kg			First molar fluorosis 12- to 36-month daily F intake, mg F/kg		
	<0.04	0.04–0.06	>0.06	<0.04	0.04–0.06	>0.06
0.04	14.3% (13/91)	14.5% (8/55)	20.5% (8^{x}/39)	6.6% (6/91)	3.6% (2/55)	20.5% (8/39)
0.04–0.06	12.5% (2/16)	29.4% (10/34)	29.4% (5/17)	12.5% (2/16)	23.5% (8/34)	41.2% (7^{x}/17)
0.06	19.0% (8/42)	36.2% (21^{xx}/58)	39.6% (21^{x}/53)	7.1% (3/42)	19.0% (11^{x}/58)	39.6% (21/53)

Each ‘x’ denotes a subject with severe (FRI = 3) fluorosis. All other subjects with fluorosis were rated mild to moderate (FRI = 2).

STUDY AUTHORS’ CONCLUSIONS:		The fluorosis prevalence rates increased with increasing fluoride intake levels, although the rates varied substantially across different time periods. Subjects with daily fluoride intake of <0.04 mg F/kg BW had less than 20% probability of developing fluorosis and almost all was of mild severity (FRI score 2). Daily intake of 0.04-0.06 mg F/kg BW had a significant elevated risk for fluorosis while daily intake of >0.06 mg F/kg BW was associated with high risk of fluorosis on early-erupting teeth. However, the data showed different susceptibility for fluorosis by tooth type with maxillary central incisors having greater fluorosis prevalence than first molars. Hong et al (2006) consider that fluorosis development relates to not only stages of enamel formation, but also to duration of fluoride intake level.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Hong, L., S.M. Levy, B. Broffitt, J.J. Warren, M. J. Kanellis, J.S. Wefel, and D.V. Dawson. 2006b. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. Community Dent Oral Epidemiol 34: 299-309. Russell, A.I. 1961. The differential diagnosis of fluoride and non-fluoride enamel opacities. J Public Health Dent 21:143-146.
PROFILER’S REMARKS	***Initials/Date*** VAD/12-26-06	Since the cohort was 98% Caucasian and 71% were from families of high socioeconomic status, results are not representative of the general US population. Individual fluoride intake estimates varied with approximately 50% of subjects staying within the same category (<0.04, 0.04-0.06 or >0.06 mg F/kg/day) for two years and 28% in the same category for three years. No data on the fluoride intake levels were supplied for those children with severe fluorosis (FRI score of 3). In addition, there was a discrepancy in the study report as to how many children had severe fluorosis. The first sentence of the Results section states that 8 individuals (1.3%) had severe fluorosis (FRI score of 3), whereas the Discussion section refers to 6 subjects (approximately 1.5%) with severe fluorosis (FRI score of 3). Fluoride intake was estimated for the first three years of life, whereas fluorosis evaluations were done at 8-10 years. The contribution of fluoride intake for the five years that intake estimates were not performed (between 3 years of age and date of dental fluorosis exam) was not addressed. This raises issues related to the window of vulnerability.
PROFILER’s ESTIM. NOAEL		The study design did not identify a no-fluorosis intake dose. The probability of fluorosis on either the maxillary central incisors or permanent first molars at each dose category was calculated. All but 6 or 8 of the 628 children (see Profiler’s Remarks) had mild to moderate fluorosis (FRI score of 2). No data on the fluoride intake dose categories for the children with severe fluorosis (FRI score of 3) were provided.
PROFILER’S ESTIM. LOAEL		The variations in fluoride intake over the three years of study estimates complicated the establishment of a LOAEL. Only 113 of the 628 children in the study were in the same dose category for three years. The influence of this fluctuation, especially increases in fluoride intake, was not assessed.
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable,(_); Poor (_); Medium (X); Strong (_)
CRITICAL EFFECTS:		Dental fluorosis (central incisors and molars)

Hong, L., S.M. Levy, B. Broffitt, J.J. Warren, M.J. Kanellis, J.S. Wefel and D.V. Dawson. 2006b. Timing of fluoride intake in relation to development of fluorosis on maxillary central incisors. Community Dent Oral Epidemiol 34:299-309.

ENDPOINT STUDIED:	Dental fluorosis (maxillary central incisors)
TYPE OF STUDY:	US/Iowa: Prevalence study of dental fluorosis as part of longitudinal study of daily fluoride intake in male and female children recruited at birth (Iowa Fluoride Study; see also companion report Hong et al 2006a).
POPULATION STUDIED:	Children (297 males and 282 females), age 8-10 yrs (mean age 9.2 years), included in the Iowa Fluoride Study. The cohort was predominately Caucasian, generally healthy, and from families of relatively high socioeconomic status (see Hong, 2006a, for specifics). Children were entered into the study using Institutional Review Board-approved consent procedures.
CONTROL POPULATION:	Control group (n=181) included children from the cohort without fluorosis on either of the maxillary central incisors.
EXPOSURE PERIOD:	Birth to 48 months (and beyond). Study conducted March 1992 to February 1995, included examination of early erupting permanent teeth.
EXPOSURE GROUPS:	Mean daily fluoride intake over 48 months was 0.053 mg/kg/day (range 0.045-0.062 mg/kg/day) in children exhibiting fluorosis and 0.043 mg/kg/day (range 0.038-0.049 mg/kg/day) in children without fluorosis.
EXPOSURE ASSESSMENT	Fluoride intake from water, beverages, selected foods, dietary supplements and dentifrices was estimated from questionnaires (unvalidated) completed by parents every 3-4 months from subject birth to age four years.
ANALYTICAL METHODS:	Study methodologies described previously in Levy et al (2001, 2003).
STUDY DESIGN	The purpose of the study was to establish the relationship of fluoride intake during the first 48 months of life with fluorosis on early-erupting permanent teeth. As part of the Iowa Fluoride Study, children were followed from birth to 48 months with questionnaires filled out by parents every 3-4 months to estimate daily fluoride intake (mg/kg BW) from water, beverages, selected foods, fluoride supplements and dentifrices. Fluoride intake (mg/kg BW) was estimated using means (standard deviation), range and percentiles for individual time periods (four months) and for cumulative time periods (0-12, 12-24, 24-36, 36-48, 0-20, 0-36 and 0-48 months) by the area under the curve (AUC) trapezoidal method. The estimated daily average fluoride intake was categorized into tertiles (low, middle and high fluoride intakes) based on the frequency distribution of average fluoride intake for each of the first 4 years separately. At 8-10 years (mean 9.2 yrs), 579 children (297 males and 282 females) were examined for fluorosis on both maxillary central incisors using the Fluorosis Risk Index (FRI; see NRC, 2006, page 90). Fluorosis was differentiated from enamel demineralization ("white spot") based on color, texture, demarcation and relationship to gingival margin. The FRI was adapted to include assessment of all visible enamel surfaces, with four zones scored separately on each buccal surface (the incisal edge/occlusal table, the incisal/occlusal third, the middle third and the cervical third).
PARAMETERS MONITORED:	Fluorosis was determined using the Fluorosis Risk Index (FRI; see NRC, 2006, page 90). Fluorosis was differentiated from non-fluorosis opacities by the criteria of Russell (1961). Fluorosis was further differentiated from enamel demineralization ("white spot") based on color, texture, demarcation and relationship to gingival margin. The FRI was adapted to include assessment of all visible enamel surfaces, with four zones scored separately on each buccal

	surface (the incisal edge/occlusal table, the incisal/occlusal third, the middle third and the cervical third). Scoring criteria differentiated no fluorosis, questionable fluorosis (less than 50% of zone with white striations), definitive fluorosis (greater than 50% of zone with white striations) and severe fluorosis (zone displays pitting/staining/deformity). As many cervical zones were incompletely erupted and not able to be scored, three zones (incisal/occlusal edge, incisal/occlusal third and middle third) were used in the main analyses. A fluorosis case for regression analyses was defined as having FRI definitive or severe fluorosis on at least one zone of both maxillary central incisors; controls had fluorosis on neither of these incisors. Subjects with only one maxillary central incisor with fluorosis were excluded. Subjects with only FRI questionable fluorosis were grouped as questionable fluorosis, unless they were excluded because the required three zones could not be scored due to reasons such as incomplete eruption. Subjects with questionable fluorosis were not included in the analyses.
STATISTICAL METHODS:	Fluoride intake (mg/kg BW/day) was estimated using means (standard deviation), range and percentiles for individual time periods and for cumulative time periods by the area under the curve (AUC) trapezoidal method. The differences in fluoride intake in mg/kg BW between cases and control were assessed using two-sample t-tests first at the surface zone level and then for combined zones (incisal/occlusal edge, incisal/occlusal third and middle third). The correlations among fluoride intakes for the first 4 years were assessed using Spearman rank correlation analyses. The estimated daily average fluoride intake was categorized into tertiles (low, middle and high fluoride intakes) based on the frequency distribution of average fluoride intake for each of the first 4 years separately. With fluorosis defined as having FRI definitive or severe fluorosis on at least one zone (incisal/occlusal edge, incisal/occlusal third and middle third) of both maxillary central incisors, the relationships between fluoride intake of individual years and fluorosis were assessed using logistic regression analyses. The odds ratio (OR) and corresponding P-values were calculated. Akaike Information Criteria (AIC), a measure of lack-of-fit, was used to assess the fit of the model. Based on the -2 log likelihood estimate, AIC adds a "penalty" for each parameter in the model which offsets the decreased lack-of-fit associated with models using more parameters. Thus, the AIC can be used to compare singe-parameter models (lower AIC is preferable) as well as to compare models with differing numbers of parameters. Generalized R^2 values were used to examine the predictive power of logistic regression models. Fluoride intakes, based on the tertiles during each of the first 4 years of life, as individual predictors of fluorosis on maxillary central incisors and whether these variables remained significant after controlling for other years was tested. The two-way interactions among individual years were assessed; the significance was set at $\alpha = 0.05$. Receiver operating characteristic (ROC) curves were used to assess the relationships between fluoride intake (mg/kg BW) and fluorosis during the different years. A ROC curve is a plot of sensitivity versus (1-specificity) for each possible threshold for the predictor variable. The sensitivity and specificity values were computed for each subject's yearly fluoride intake and saved as output to construct the ROC curves.
RESULTS:	Results of the study are shown in Tables 1 through 5 and Figure 1 directly from Hong (2006b):

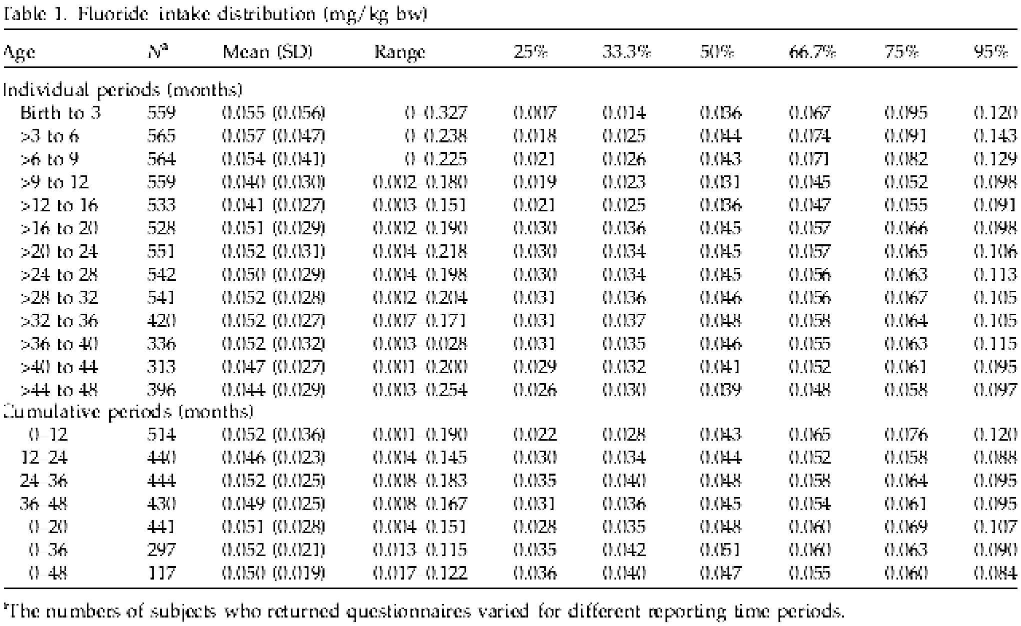


Table 1. Fluoride intake distribution (mg/kg bw)

Age	N[a]	Mean (SD)	Range	25%	33.3%	50%	66.7%	75%	95%
Individual periods (months)									
Birth to 3	559	0.055 (0.056)	0–0.327	0.007	0.014	0.036	0.067	0.095	0.120
>3 to 6	565	0.057 (0.047)	0–0.238	0.018	0.025	0.044	0.074	0.091	0.143
>6 to 9	564	0.054 (0.041)	0–0.225	0.021	0.026	0.043	0.071	0.082	0.129
>9 to 12	559	0.040 (0.030)	0.002–0.180	0.019	0.023	0.031	0.045	0.052	0.098
>12 to 16	533	0.041 (0.027)	0.003–0.151	0.021	0.025	0.036	0.047	0.055	0.091
>16 to 20	528	0.051 (0.029)	0.002–0.190	0.030	0.036	0.045	0.057	0.066	0.098
>20 to 24	551	0.052 (0.031)	0.004–0.218	0.030	0.034	0.045	0.057	0.065	0.106
>24 to 28	542	0.050 (0.029)	0.004–0.198	0.030	0.034	0.045	0.056	0.063	0.113
>28 to 32	541	0.052 (0.028)	0.002–0.204	0.031	0.036	0.046	0.056	0.067	0.105
>32 to 36	420	0.052 (0.027)	0.007–0.171	0.031	0.037	0.048	0.058	0.064	0.105
>36 to 40	336	0.052 (0.032)	0.003–0.028	0.031	0.035	0.046	0.055	0.063	0.115
>40 to 44	313	0.047 (0.027)	0.001–0.200	0.029	0.032	0.041	0.052	0.061	0.095
>44 to 48	396	0.044 (0.029)	0.003–0.254	0.026	0.030	0.039	0.048	0.058	0.097
Cumulative periods (months)									
0–12	514	0.052 (0.036)	0.001–0.190	0.022	0.028	0.043	0.065	0.076	0.120
12–24	440	0.046 (0.023)	0.004–0.145	0.030	0.034	0.044	0.052	0.058	0.088
24–36	444	0.052 (0.025)	0.008–0.183	0.035	0.040	0.048	0.058	0.064	0.095
36–48	430	0.049 (0.025)	0.008–0.167	0.031	0.036	0.045	0.054	0.061	0.095
0–20	441	0.051 (0.028)	0.004–0.151	0.028	0.035	0.048	0.060	0.069	0.107
0–36	297	0.052 (0.021)	0.013–0.115	0.035	0.042	0.051	0.060	0.063	0.090
0–48	117	0.050 (0.019)	0.017–0.122	0.036	0.040	0.047	0.055	0.060	0.084

[a] The numbers of subjects who returned questionnaires varied for different reporting time periods.

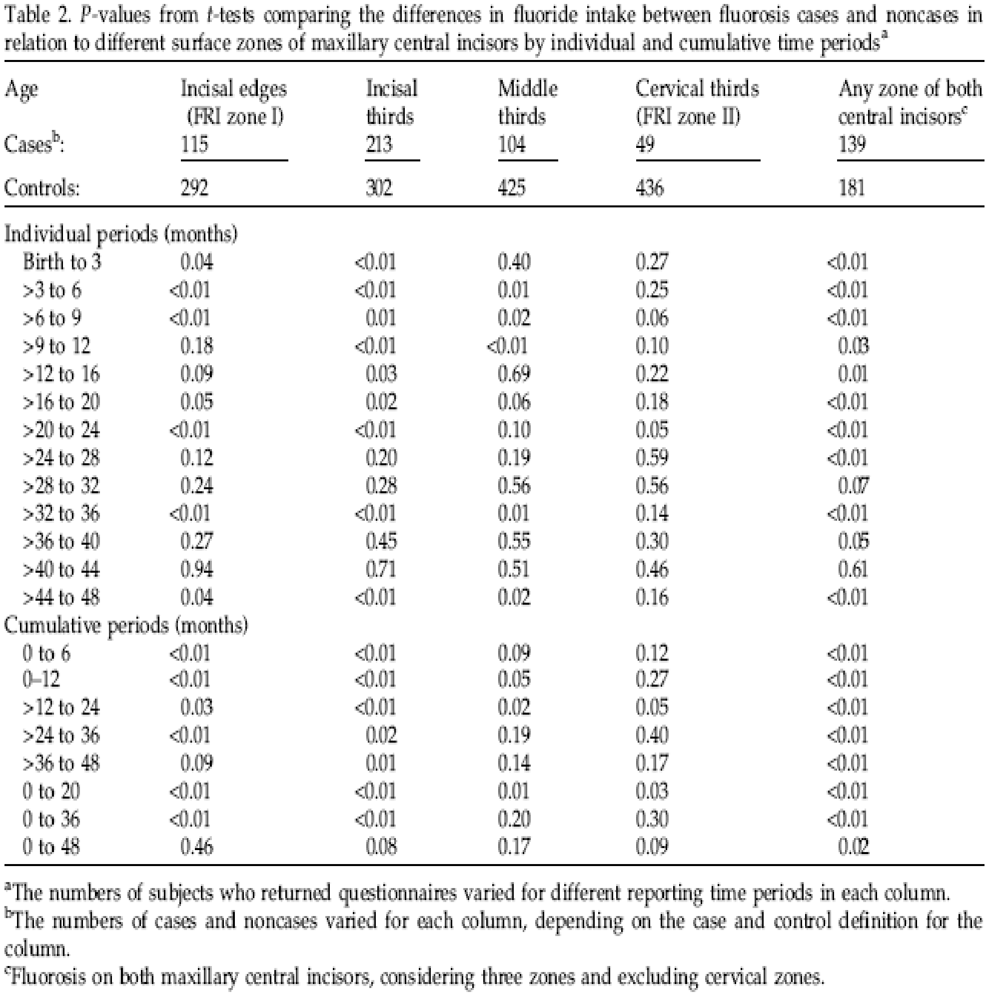


Table 2. *P*-values from *t*-tests comparing the differences in fluoride intake between fluorosis cases and noncases in relation to different surface zones of maxillary central incisors by individual and cumulative time periods[a]

Age	Incisal edges (FRI zone I)	Incisal thirds	Middle thirds	Cervical thirds (FRI zone II)	Any zone of both central incisors[c]
Cases[b]:	115	213	104	49	139
Controls:	292	302	425	436	181
Individual periods (months)					
Birth to 3	0.04	<0.01	0.40	0.27	<0.01
>3 to 6	<0.01	<0.01	0.01	0.25	<0.01
>6 to 9	<0.01	0.01	0.02	0.06	<0.01
>9 to 12	0.18	<0.01	<0.01	0.10	0.03
>12 to 16	0.09	0.03	0.69	0.22	0.01
>16 to 20	0.05	0.02	0.06	0.18	<0.01
>20 to 24	<0.01	<0.01	0.10	0.05	<0.01
>24 to 28	0.12	0.20	0.19	0.59	<0.01
>28 to 32	0.24	0.28	0.56	0.56	0.07
>32 to 36	<0.01	<0.01	0.01	0.14	<0.01
>36 to 40	0.27	0.45	0.55	0.30	0.05
>40 to 44	0.94	0.71	0.51	0.46	0.61
>44 to 48	0.04	<0.01	0.02	0.16	<0.01
Cumulative periods (months)					
0 to 6	<0.01	<0.01	0.09	0.12	<0.01
0–12	<0.01	<0.01	0.05	0.27	<0.01
>12 to 24	0.03	<0.01	0.02	0.05	<0.01
>24 to 36	<0.01	0.02	0.19	0.40	<0.01
>36 to 48	0.09	0.01	0.14	0.17	<0.01
0 to 20	<0.01	<0.01	0.01	0.03	<0.01
0 to 36	<0.01	<0.01	0.20	0.30	<0.01
0 to 48	0.46	0.08	0.17	0.09	0.02

[a] The numbers of subjects who returned questionnaires varied for different reporting time periods in each column.
[b] The numbers of cases and noncases varied for each column, depending on the case and control definition for the column.
[c] Fluorosis on both maxillary central incisors, considering three zones and excluding cervical zones.

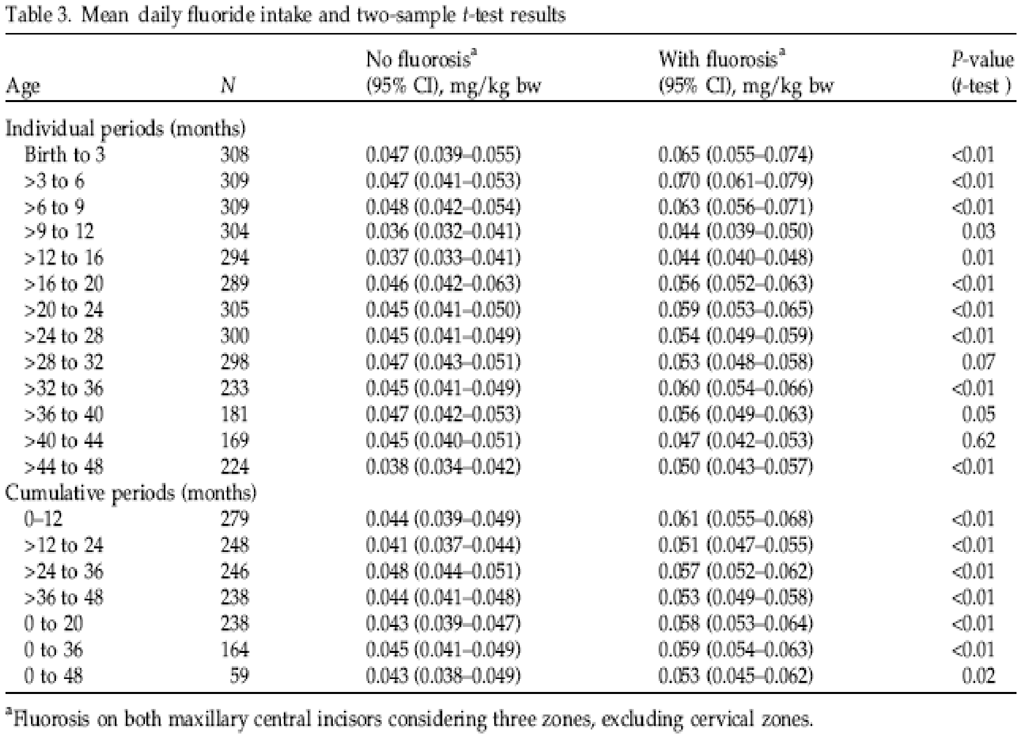


Table 3. Mean daily fluoride intake and two-sample *t*-test results

Age	*N*	No fluorosis[a] (95% CI), mg/kg bw	With fluorosis[a] (95% CI), mg/kg bw	*P*-value (*t*-test)
Individual periods (months)				
Birth to 3	308	0.047 (0.039–0.055)	0.065 (0.055–0.074)	<0.01
>3 to 6	309	0.047 (0.041–0.053)	0.070 (0.061–0.079)	<0.01
>6 to 9	309	0.048 (0.042–0.054)	0.063 (0.056–0.071)	<0.01
>9 to 12	304	0.036 (0.032–0.041)	0.044 (0.039–0.050)	0.03
>12 to 16	294	0.037 (0.033–0.041)	0.044 (0.040–0.048)	0.01
>16 to 20	289	0.046 (0.042–0.063)	0.056 (0.052–0.063)	<0.01
>20 to 24	305	0.045 (0.041–0.050)	0.059 (0.053–0.065)	<0.01
>24 to 28	300	0.045 (0.041–0.049)	0.054 (0.049–0.059)	<0.01
>28 to 32	298	0.047 (0.043–0.051)	0.053 (0.048–0.058)	0.07
>32 to 36	233	0.045 (0.041–0.049)	0.060 (0.054–0.066)	<0.01
>36 to 40	181	0.047 (0.042–0.053)	0.056 (0.049–0.063)	0.05
>40 to 44	169	0.045 (0.040–0.051)	0.047 (0.042–0.053)	0.62
>44 to 48	224	0.038 (0.034–0.042)	0.050 (0.043–0.057)	<0.01
Cumulative periods (months)				
0–12	279	0.044 (0.039–0.049)	0.061 (0.055–0.068)	<0.01
>12 to 24	248	0.041 (0.037–0.044)	0.051 (0.047–0.055)	<0.01
>24 to 36	246	0.048 (0.044–0.051)	0.057 (0.052–0.062)	<0.01
>36 to 48	238	0.044 (0.041–0.048)	0.053 (0.049–0.058)	<0.01
0 to 20	238	0.043 (0.039–0.047)	0.058 (0.053–0.064)	<0.01
0 to 36	164	0.045 (0.041–0.049)	0.059 (0.054–0.063)	<0.01
0 to 48	59	0.043 (0.038–0.049)	0.053 (0.045–0.062)	0.02

[a] Fluorosis on both maxillary central incisors considering three zones, excluding cervical zones.

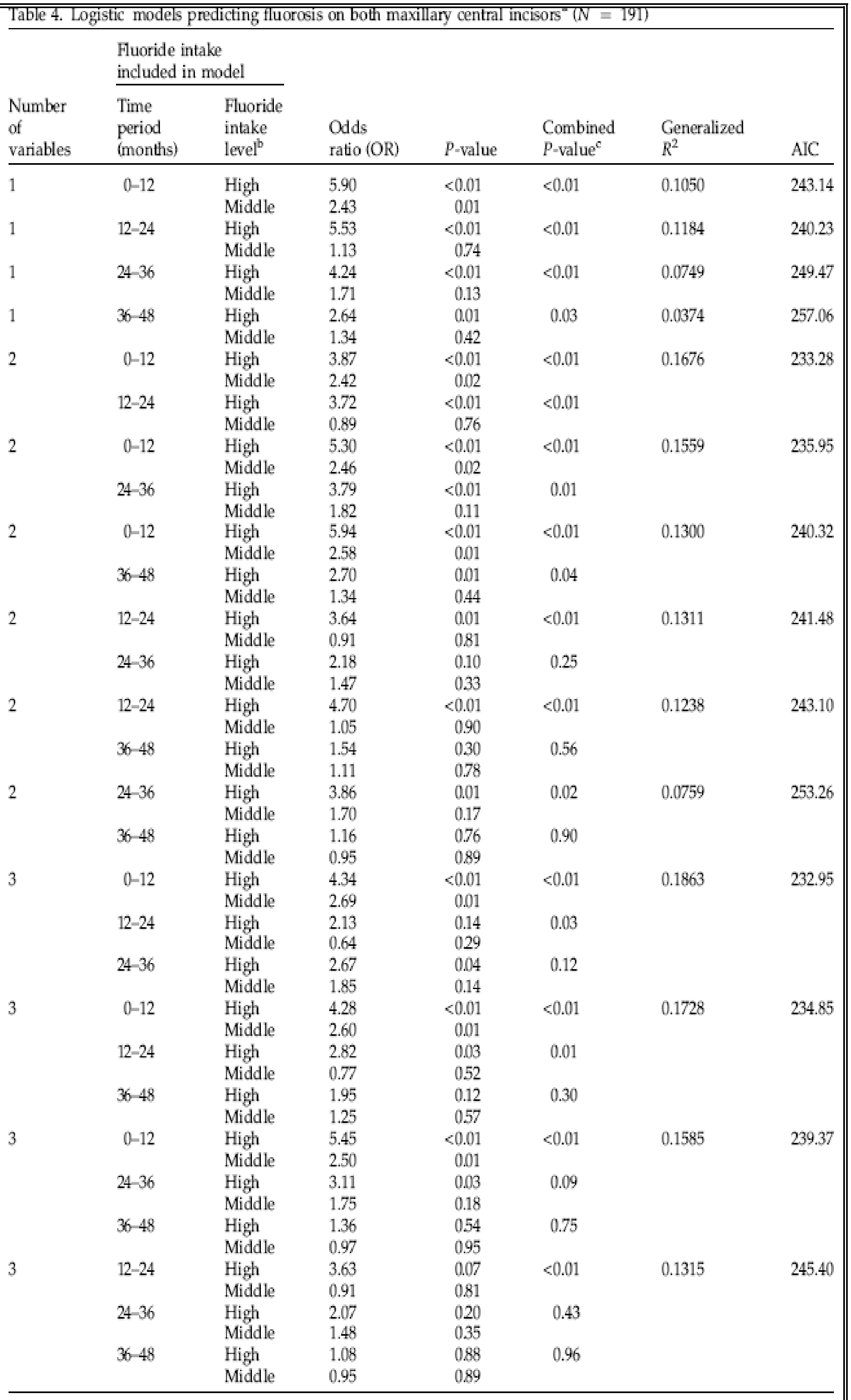


Table 4. Logistic models predicting fluorosis on both maxillary central incisors[a] ($N = 191$)

	Fluoride intake included in model						
Number of variables	Time period (months)	Fluoride intake level[b]	Odds ratio (OR)	*P*-value	Combined *P*-value[c]	Generalized R^2	AIC
1	0–12	High	5.90	<0.01	<0.01	0.1050	243.14
		Middle	2.43	0.01			
1	12–24	High	5.53	<0.01	<0.01	0.1184	240.23
		Middle	1.13	0.74			
1	24–36	High	4.24	<0.01	<0.01	0.0749	249.47
		Middle	1.71	0.13			
1	36–48	High	2.64	0.01	0.03	0.0374	257.06
		Middle	1.34	0.42			
2	0–12	High	3.87	<0.01	<0.01	0.1676	233.28
		Middle	2.42	0.02			
	12–24	High	3.72	<0.01	<0.01		
		Middle	0.89	0.76			
2	0–12	High	5.30	<0.01	<0.01	0.1559	235.95
		Middle	2.46	0.02			
	24–36	High	3.79	<0.01	0.01		
		Middle	1.82	0.11			
2	0–12	High	5.94	<0.01	<0.01	0.1300	240.32
		Middle	2.58	0.01			
	36–48	High	2.70	0.01	0.04		
		Middle	1.34	0.44			
2	12–24	High	3.64	0.01	<0.01	0.1311	241.48
		Middle	0.91	0.81			
	24–36	High	2.18	0.10	0.25		
		Middle	1.47	0.33			
2	12–24	High	4.70	<0.01	<0.01	0.1238	243.10
		Middle	1.05	0.90			
	36–48	High	1.54	0.30	0.56		
		Middle	1.11	0.78			
2	24–36	High	3.86	0.01	0.02	0.0759	253.26
		Middle	1.70	0.17			
	36–48	High	1.16	0.76	0.90		
		Middle	0.95	0.89			
3	0–12	High	4.34	<0.01	<0.01	0.1863	232.95
		Middle	2.69	0.01			
	12–24	High	2.13	0.14	0.03		
		Middle	0.64	0.29			
	24–36	High	2.67	0.04	0.12		
		Middle	1.85	0.14			
3	0–12	High	4.28	<0.01	<0.01	0.1728	234.85
		Middle	2.60	0.01			
	12–24	High	2.82	0.03	0.01		
		Middle	0.77	0.52			
	36–48	High	1.95	0.12	0.30		
		Middle	1.25	0.57			
3	0–12	High	5.45	<0.01	<0.01	0.1585	239.37
		Middle	2.50	0.01			
	24–36	High	3.11	0.03	0.09		
		Middle	1.75	0.18			
	36–48	High	1.36	0.54	0.75		
		Middle	0.97	0.95			
3	12–24	High	3.63	0.07	<0.01	0.1315	245.40
		Middle	0.91	0.81			
	24–36	High	2.07	0.20	0.43		
		Middle	1.48	0.35			
	36–48	High	1.08	0.88	0.96		
		Middle	0.95	0.89			

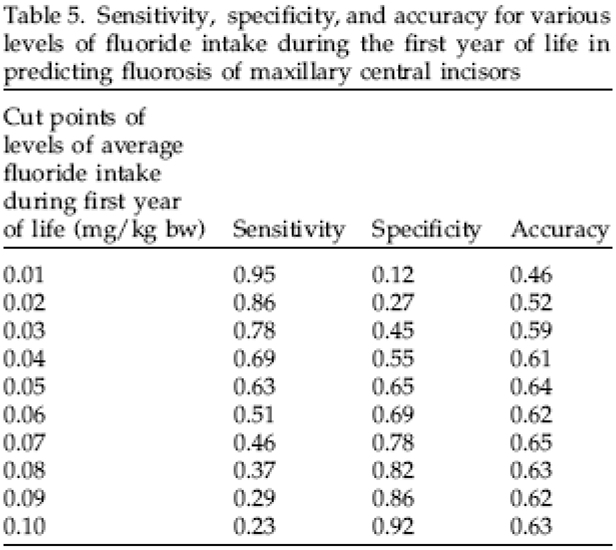


Table 5. Sensitivity, specificity, and accuracy for various levels of fluoride intake during the first year of life in predicting fluorosis of maxillary central incisors

Cut points of levels of average fluoride intake during first year of life (mg/kg bw)	Sensitivity	Specificity	Accuracy
0.01	0.95	0.12	0.46
0.02	0.86	0.27	0.52
0.03	0.78	0.45	0.59
0.04	0.69	0.55	0.61
0.05	0.63	0.65	0.64
0.06	0.51	0.69	0.62
0.07	0.46	0.78	0.65
0.08	0.37	0.82	0.63
0.09	0.29	0.86	0.62
0.10	0.23	0.92	0.63

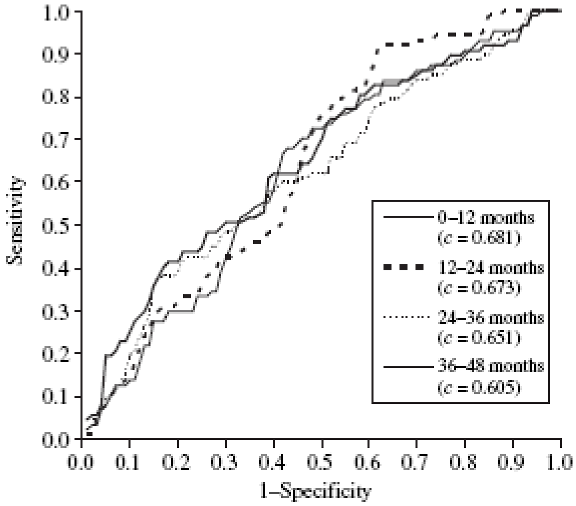


Fig. 1. Comparison of receiver operating characteristic (ROC) curves for fluoride intake during the first 4 years of life.

STUDY AUTHORS' CONCLUSIONS:	Of 579 children, 139 (24%) had fluorosis on both maxillary central incisors. Mean fluoride intake per unit BW ranged from 0.040 to 0.057 mg/kg BW, with higher intake during earlier time periods and relative stability after 16 months. In bivariate analyses, fluoride intakes during each of the first 4 years were individually significantly related to fluorosis on maxillary central incisors, with the first year most important (P<0.01), followed by the second (P<0.01), third (P<0.01) and fourth year (P=0.03). Multivariable logistic regression analyses showed that, after controlling for the first year, the later years individually were still statistically significant. When all four time periods were in the model, the first (P<0.01) and second years (P=0.04) were still significant, but the third (P=0.32) and fourth (P=0.82) were not. The study authors concluded that the first two years were most important to fluorosis development in permanent maxillary central incisors; however, the study also suggested the importance of other individual years.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Hong, L., S.M. Levy, J.J. Warren, B. Broffitt, and J. Cavanaugh. 2006a. Fluoride intake levels in relation to fluorosis development in permanent maxillary central incisors and first molars. Caries Research. 40:494-500. Russell, A.I. 1961. The differential diagnosis of fluoride and non-fluoride enamel opacities. J Public Health Dent 21:143-146.

PROFILER'S REMARKS	***Initials/Date*** VAD/12-29-06	As described in Hong, 2006a, the cohort was 98% Caucasian and 71% were from families of high socioeconomic status; therefore, results are not representative of the general US population. Incomplete questionnaire data resulted in only 191 subjects available for logistic regression analyses after four years of life. Fluoride intake data were obtained through self-administrated questionnaires by parents without direct verification. The fluoride intake estimates were based on assessment at 3-4 points during each year and did not account for period variations in intake. Some potentially important source of fluoride, such as fluoride rinses and gels, were not included in the intake estimates. The study report did not adequately describe the FRI scoring system, i.e., numerical scores for mild, moderate and severe fluorosis. All but 4 of 139 cases were considered mild fluorosis; therefore, the fluoride intake estimates are only predictive of this gradation, and are not predictive for severe fluorosis. Incisors were chosen because they were considered to be aesthetically important teeth; however, other permanent teeth may be more susceptible to fluorosis.
PROFILER's ESTIM. NOAEL		In children not exhibiting fluorosis of the maxillary central incisors, mean daily fluoride intake over 48 months was 0.043 mg/kg/day (range 0.038-0.049 mg/kg/day).
PROFILER'S ESTIM. LOAEL		In children exhibiting fluorosis of the maxillary central incisors, mean daily fluoride intake over 48 months was 0.053 mg/kg/day (range 0.045-0.062 mg/kg/day).
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable,(_); Poor (_); Medium (X); Strong (_)
CRITICAL EFFECTS:		Dental fluorosis (maxillary central incisors)

Horowitz, H.S., 1989. Fluoride and enamel defects. Adv. Dent Res. 3(2):143-146.

ENDPOINT STUDIED:		Dental fluorosis
TYPE OF STUDY:		Literature review.
POPULATION STUDIED:		Human and lab animal
CONTROL POPULATION:		NA
EXPOSURE PERIOD:		NA
EXPOSURE GROUPS:		NA
EXPOSURE ASSESSMENT:		NA
ANALYTICAL METHODS:		NA
PARAMETERS MONITORED:		NA
STATISTICAL METHODS:		NA
RESULTS:		NA
STUDY AUTHORS' CONCLUSIONS:		Based on currently available information (pre-1989), the author concluded that the concentration of fluoride in drinking water was the major determinant of the prevalence and severity of dental fluorosis in a community. The author further notes that some recent reports suggest that the maturation stages of enamel development are as important as or even more important than the secretory stages as the time when fluorosis can be produced.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		NA
PROFILER'S REMARKS	***Initials/date: DMO 1/12/07***	May be a source of information on early fluorosis studies.
PROFILER'S ESTIM. NOEL/NOAEL		NA
PROFILER'S ESTIM. LOEL/ LOAEL		NA
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( )
CRITICAL EFFECT(S):		Dental fluorosis

Ishii, T. and Suckling, G. 1991. The Severity of Dental Fluorosis in Children Exposed to Water with a High Fluoride Content for Various Periods of Time. J Dent Res. 70(6): 952-956.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Retrospective
POPULATION STUDIED:	Japan/Ikeno District: 86 children, aged 11 months to seven years old at the removal of the high fluoride water (February 1973), that were inhabitants of the Ikeno district of Japan. The children included in the study were examined at school between 1973 and 1984. Between 1973 and 1981, all permanent residents attending school were examined annually. The number of subjects varied from year to year. A final examination of 16 children still at school was completed in 1984. In 1973, 1977, 1978, 1980, and 1984, three photographs were taken of the teeth of each child examined; 41 children had two or more serial photographs available for inspection.
CONTROL POPULATION:	No control population was examined in this study.
EXPOSURE PERIOD:	Inhabitants of the Ikeno district of Japan were exposed to high levels of fluoride in the water supply for 12 years, from December 1960 until February 1973. The results included in this study spanned 11 years, from 1973 to 1984.
EXPOSURE GROUPS:	The water supply had high levels of fluoride (7.8 ppm) from December 1960 until February 1973, when it was replaced with low fluoride water (<0.2 ppm. High fluoride exposure was prolonged (from birth for 7-12 years) for 26 children, restricted to a shorter time during early tooth development for 38 children and late tooth development for 22 children.
EXPOSURE ASSESSMENT:	Other potential sources of fluoride exposure were not included.
ANALYTICAL METHODS:	Data for measuring the fluoride concentrations were not included in the study report. Water quality parameters were not reported.
STUDY DESIGN	The current study included 86 children in the vulnerable age range (11 months to seven years old at the removal of the high fluoride water in February 1973), that were inhabitants of the Ikeno district of Japan. Between 1973 and 1981, all permanent residents attending school were examined annually. The number of subjects varied from year to year. A final examination of 16 children still at school was completed in 1984. In 1973, 1977, 1978, 1980, and 1984, three photographs were taken of the teeth of each child examined. A single examiner carried out all examinations as follows: Examinations: The teeth were not dried, but were cleaned with gauze if required. Individual teeth were checked for dental fluorosis using Dean's criteria. The fluorosis grade of three teeth—the most severely affected of the first permanent molars (molars), upper central incisors (incisors), and first premolars (premolars)—was assessed for each child at his/her last examination before leaving primary school. These gradings were used to determine tooth-type susceptibility to the high fluoride water. Serial sets of photographs, in combination with the fluorosis score, facilitated assessment of post-eruptive enamel loss and changes with time for the molars and incisors.
PARAMETERS MONITORED:	Fluorosis was assessed in all fully erupted permanent teeth following Dean's criteria. Fluorosis was scaled as normal (N), very mild (Vm), mild (Mi), moderate (Mo) or severe (S).
STATISTICAL METHODS:	No statistical methods or levels of significance were reported in this study.

RESULTS:

Fluorosis

Figures 1 and 2 were copied directly from Ishii and Suckling (1991) and summarize the severity of fluorosis according to Dean's criteria in three tooth types [molar (A), incisor (B), and premolar (C)]. Figure 1 relates fluorosis to high fluoride water use from birth and ending at different ages, while Figure 2 relates fluorosis to high fluoride water use beginning at different ages and ending at eruption or 7 years of age.

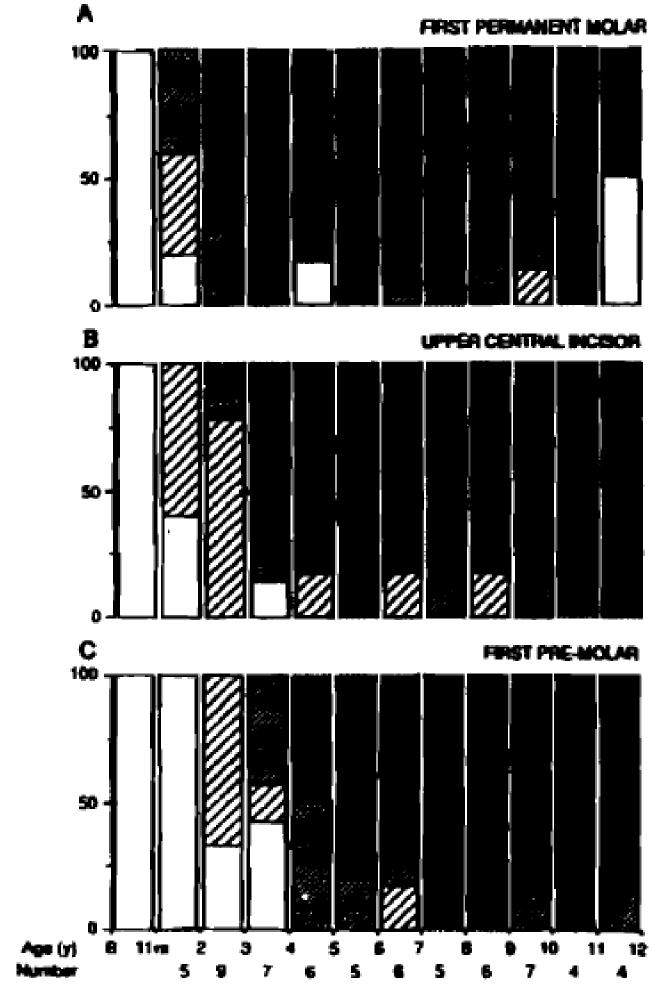


Fig. 1 — Severity of fluorosis in three tooth types assessed according to Dean's criteria and related to use of drinking water containing 7.8-ppm F from birth (B) but ending at different ages. Number of children in each age group is given. ☐ = N or Q, ▨ = Vm, ▩ = Mi, and ■ = Mo or S.

When high fluoride intake lasted throughout development, mild, moderate, or severe defects predominated in all three tooth types (Figure 1) with a few exceptions. With limited exposure, fluorosis resulted when exposure starting at birth continued for longer than 11 months for the molars, 1 year for the incisors, and 2 years for the premolars (Figure 1), or when the high fluoride intake began before the age of 3 years for the molars and 4 years for the incisors and premolars (Figure 2). Moderate or severe defects predominated among the molars, incisors, and premolars when the high fluoride intake, starting at birth, continued for more than 2, 3, and 5 years, respectively (Figure 1). Such severe defects were less evident in the molars and incisors when exposure started later in tooth development (Figure 2).

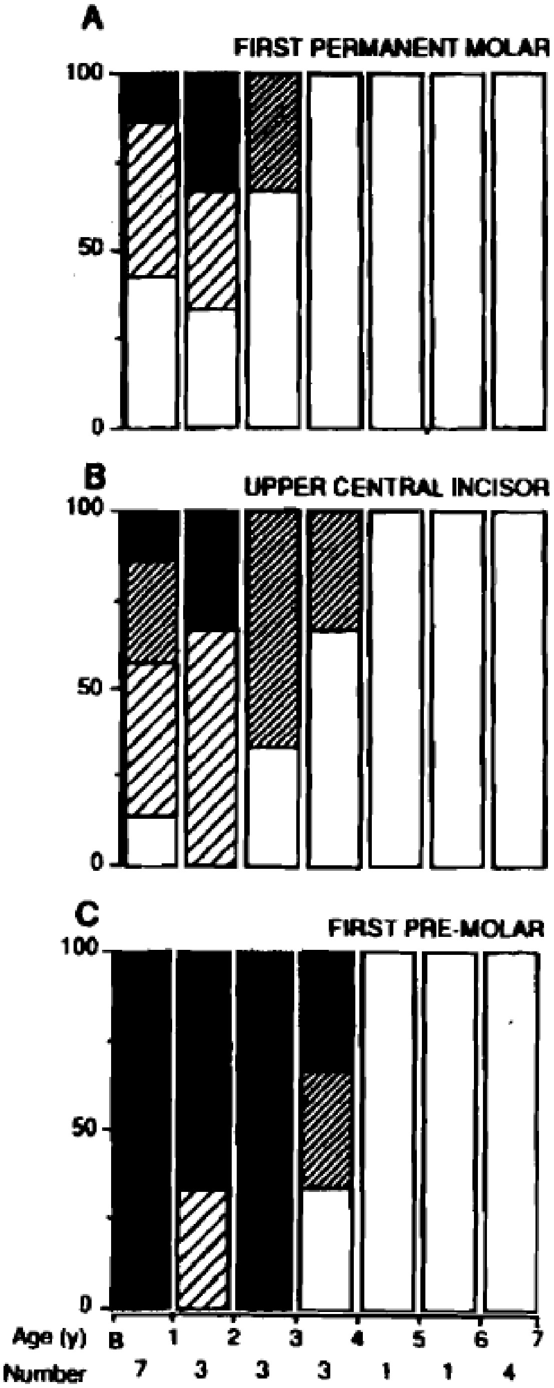
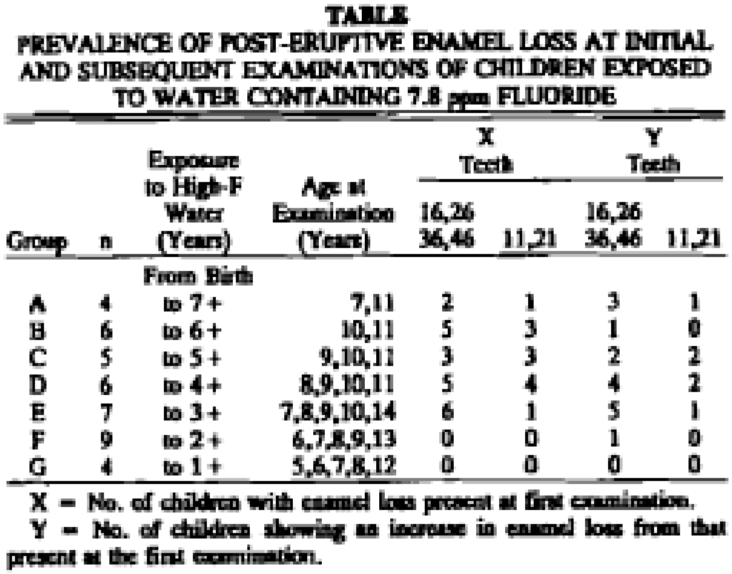


Fig. 2 — Severity of fluorosis in three tooth types assessed according to Dean's criteria and related to use of drinking water containing 7.8-ppm F starting at different ages and ending at eruption or age seven y. Number of children in each group is given. ☐ = N or Q, ▨ = Vm, ▦ = Mi, and ■ = Mo or S.

The following table was copied directly from Ishii and Suckling (1991) and summarizes the prevalence of post-eruptive enamel loss according to the number of children in each age group, the period of high fluoride exposure, and the approximate age at each examination. Enamel loss (pits) was observed in the molars or incisors of some members of all groups, except Group G, whose exposure to high fluoride ceased before 2 years of age.



TABLE

PREVALENCE OF POST-ERUPTIVE ENAMEL LOSS AT INITIAL AND SUBSEQUENT EXAMINATIONS OF CHILDREN EXPOSED TO WATER CONTAINING 7.8 ppm FLUORIDE

				X Teeth		Y Teeth	
Group	n	Exposure to High-F Water (Years)	Age at Examination (Years)	16,26 36,46	11,21	16,26 36,46	11,21
		From Birth					
A	4	to 7+	7,11	2	1	3	1
B	6	to 6+	10,11	5	3	1	0
C	5	to 5+	9,10,11	3	3	2	2
D	6	to 4+	8,9,10,11	5	4	4	2
E	7	to 3+	7,8,9,10,14	6	1	5	1
F	9	to 2+	6,7,8,9,13	0	0	1	0
G	4	to 1+	5,6,7,8,12	0	0	0	0

X = No. of children with enamel loss present at first examination.

Y = No. of children showing an increase in enamel loss from that present at the first examination.

The duration of fluoride exposure determined the initial degree of fluorosis, but did not seem to influence subsequent changes. Pits were restricted to teeth assessed at the first examination as moderate or severe. No obvious pattern was evident in the subsequent changes. Teeth graded severe showed variation in the timing and position of any change. The child exposed throughout tooth development had more severe fluorosis compared to those exposed only early or late.

PROFILERS NOTE: The profiler agrees that, according to the figures as presented in Ishii and Suckling (1991), the pattern for development of fluorosis varies among tooth type and generally is more severe when high fluoride exposure started at birth and continued for more than 2-4 years and when high fluoride exposure started before 3-4 years of age. However, the statistical significance of such a statement is questionable. Significant conclusions can not be made.

STUDY AUTHORS' CONCLUSIONS:

The information presented here suggests that continuous exposure ending below the age of 11 months or starting above the age of seven years will not result in alteration to the macroscopic appearance of the permanent teeth (third molars excluded). The upper age limit, from 4.8 to 7 years, is quite variable. The factors influencing the initial shape of the pits and the subsequent changes require further investigation. Due to the small sample size, the conclusions for "at-risk" periods of susceptibility to fluorosis should be used with caution.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

None.

PROFILER'S REMARKS

Initials/date: SJG/ 1/17/07 DMO 03/02/07

Overall, the paper was difficult to follow and the results were not presented in a sufficiently clear manner to draw conclusions. The study was not designed for development of a dose response to fluoride; the emphasis was on monitoring the severity of dental fluorosis in children exposed to high levels of fluoride in the water for various periods of time in order to predict critical periods of vulnerability to fluorosis development. The authors conclude that children were "at-risk" for fluorosis development if exposure to high fluoride in the water (7.8 ppm) started after 11 months and ended before 7 years of age.

However, there were not enough quantified data to perform any statistical analyses to support the conclusions set forth in the study. Due to the small sample size (n=1-9 for each age group with limited exposure), the accuracy of any predicted "at-risk" period

		should be used with caution, as the study authors note. Further, data from photographs should have been quantified in a manner to include all subjects (41 children had two or more serial photographs available for inspection), rather than providing only a select few in the study report. Other issues to consider in drawing conclusions about the “at-risk” periods of susceptibility to fluorosis include: Eruption of teeth is governed by circumstances operating years earlier, with different tooth types developing at different ages. An accurate retrospective history of fluoride ingestion from all sources (e.g., infant formula, fluoride supplements, and fluoridated toothpaste) is difficult to obtain; fluoride/kg body weight is likely to vary.
PROFILER’S ESTIM. NOEL/NOAEL		Study design was not suitable for development of a NOAEL for fluorosis.
PROFILER’S ESTIM. LOEL/ LOAEL		Study design was not suitable for development of a LOAEL for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( ) The study design was not conducive to provide data for a dose-response. The study only indicated the prevalence and severity of fluorosis in children exposed to high levels of fluoride in the water supply over various periods of time. The study did not address any issues of caries, plaque, or gingivitis. The study is of value, however, in identifying sensitive age groups.
CRITICAL EFFECT(S):		Prevalence and severity of fluorosis

Jackson, R.D., S.A. Kelly, B.P. Katz, J.R. Hull, and G.K. Stookey. 1995. Dental fluorosis and caries prevalence in communities with different levels of fluoride in the water. J. Public Health Dentistry 55:79-84.

ENDPOINT STUDIED: Dental fluorosis; dental caries

TYPE OF STUDY: Prevalence survey

POPULATION STUDIED: U.S./Indiana/Connersville, Brownsburg, Lowell: Children age 7-14 yr (born between 1978 and 1985). The demographic characteristics of the three communities were similar, and all three were in the same climatic zone. All the participants had to meet the following inclusion criteria: be willing to read and sign a letter of consent, and obtain parental consent; have no factors in their medical history that would contraindicate a dental examination; meet the criteria for defining lifetime residency; be available during the examination period; be of proper age at the time of examination; and provide a residency information indicating that they had used the city water supply or a source with a comparable fluoride level (±0.1 ppm) since birth. Lifetime residency was defined as being born to parents residing in the community and not being absent from the community for more than two weeks in any one year.

CONTROL POPULATION: None

EXPOSURE PERIOD: 7-14 yr, from 1978-1985 until the time of examination in February of 1992.

EXPOSURE GROUPS: Fluoride drinking water levels in the three communities were 0.2 ppm (negligible, or NF), 1.0 ppm (optimal or OPF), and 4.0 ppm (4X OPF). The number of children in each group are listed in Table 1 copied directly from Jackson et al. (1995):

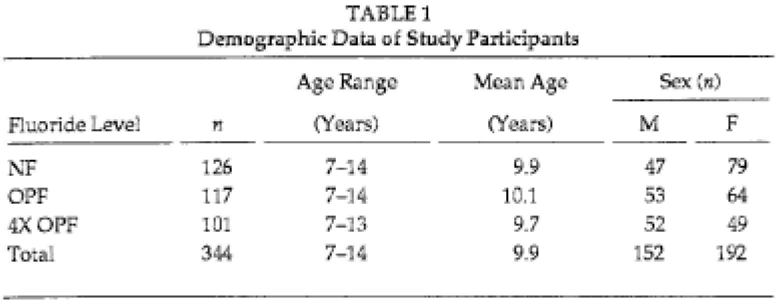


TABLE 1
Demographic Data of Study Participants

Fluoride Level	n	Age Range (Years)	Mean Age (Years)	Sex (n) M	F
NF	126	7–14	9.9	47	79
OPF	117	7–14	10.1	53	64
4X OPF	101	7–13	9.7	52	49
Total	344	7–14	9.9	152	192

EXPOSURE ASSESSMENT: Drinking water for all three communities was obtained from deep wells. Each community exhibited a documented water fluoride concentration history for the preceding 50 years. The optimum fluoride concentration for the geographic region was 1.0 ppm based on the data presented by Galagan and Vermillion (1957). History of the use of fluoride pediatric supplements and commercial products containing fluoride was evaluated in the study populations by the use of questionnaires.

ANALYTICAL METHODS: Methods used for measuring the fluoride concentrations in the drinking water were not reported. Other water quality parameters (such as calcium levels) were not reported.

STUDY DESIGN Dental fluorosis and caries incidence in children age 7-14 yr (born between 1978 and 1985) from three communities in Indiana having different levels of fluoride in drinking water (0.2 ppm; 1.0 ppm; and 4.0 ppm) were compared using acceptable methods of diagnosis (TSIF index and Dean's index for fluorosis, and DMF teeth and DMF surface scores for caries) and statistical analysis (two way ANOVA).

PARAMETERS MONITORED:

Fluorosis was evaluated using the TSIF index and Dean's index (see Section 2 for descriptions). Only permanent teeth were examined. To distinguish between fluorosis and non-fluoride opacities, the criteria developed by Russell (1961) were used. Caries was assessed in terms of DMF teeth and DMF surface scores (Council on Dental Research and Council on Dental Therapeutics, 1972; see List of Acronyms in report for definitions).

STATISTICAL METHODS:

Scores of Dean's index (minimum of the two highest readings for each child) were compared across communities and age groups using a two way ANOVA. Statistical analysis of maximum TSIF scores was performed using the ranks of values, and comparisons between communities and age groups were evaluated using two way ANOVA on the ranked values.

RESULTS:

Dental fluorosis

As shown in Tables 2 and 3 (copied directly from Jackson et al., 1995), the incidence of fluorosis increased with increasing fluoride concentration in drinking water.

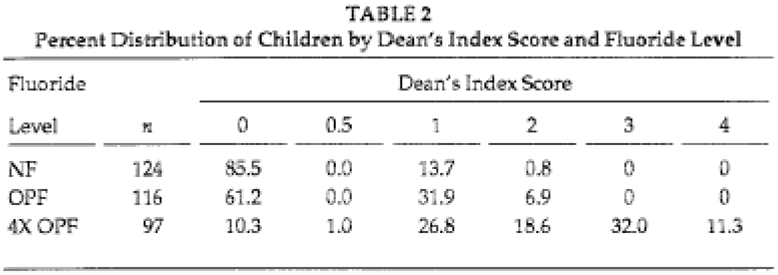


TABLE 2
Percent Distribution of Children by Dean's Index Score and Fluoride Level

Fluoride		Dean's Index Score					
Level	n	0	0.5	1	2	3	4
NF	124	85.5	0.0	13.7	0.8	0	0
OPF	116	61.2	0.0	31.9	6.9	0	0
4X OPF	97	10.3	1.0	26.8	18.6	32.0	11.3

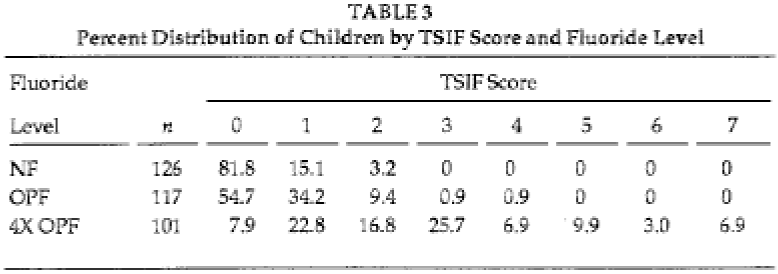


TABLE 3
Percent Distribution of Children by TSIF Score and Fluoride Level

Fluoride		TSIF Score							
Level	n	0	1	2	3	4	5	6	7
NF	126	81.8	15.1	3.2	0	0	0	0	0
OPF	117	54.7	34.2	9.4	0.9	0.9	0	0	0
4X OPF	101	7.9	22.8	16.8	25.7	6.9	9.9	3.0	6.9

Distribution of TSIF scores by permanent tooth surface (Table 5) showed the same pattern with higher levels of fluorosis in the 4x OPF community.

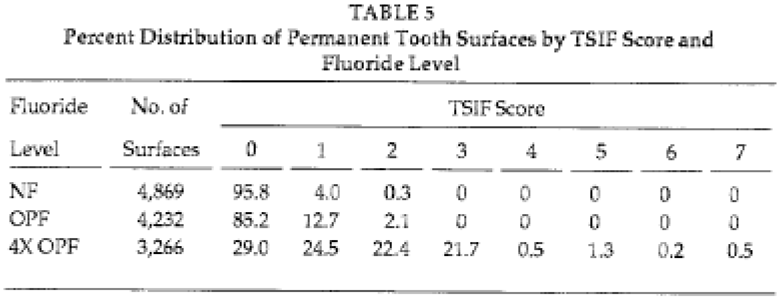


TABLE 5
Percent Distribution of Permanent Tooth Surfaces by TSIF Score and Fluoride Level

Fluoride	No. of	TSIF Score							
Level	Surfaces	0	1	2	3	4	5	6	7
NF	4,869	95.8	4.0	0.3	0	0	0	0	0
OPF	4,232	85.2	12.7	2.1	0	0	0	0	0
4X OPF	3,266	29.0	24.5	22.4	21.7	0.5	1.3	0.2	0.5

Evaluation of percent distribution of children by TSIF score, fluoride level and age (Table 4) indicates that there were no substantial age-related differences within the communities, but clear difference in TSIF score between and among the three communities.

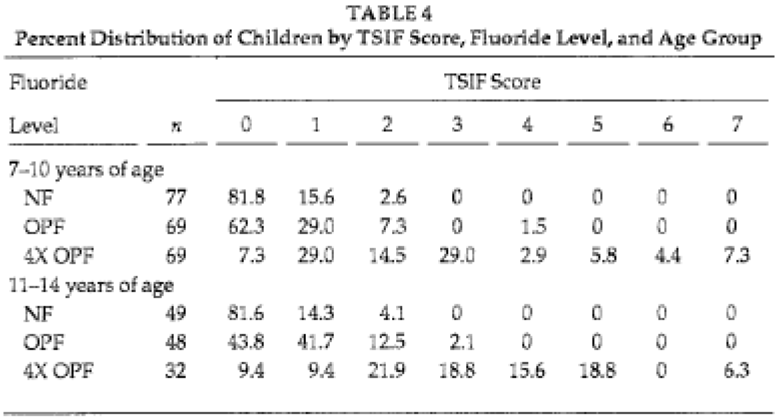


TABLE 4
Percent Distribution of Children by TSIF Score, Fluoride Level, and Age Group

Fluoride Level	n	TSIF Score 0	1	2	3	4	5	6	7
7–10 years of age									
NF	77	81.8	15.6	2.6	0	0	0	0	0
OPF	69	62.3	29.0	7.3	0	1.5	0	0	0
4X OPF	69	7.3	29.0	14.5	29.0	2.9	5.8	4.4	7.3
11–14 years of age									
NF	49	81.6	14.3	4.1	0	0	0	0	0
OPF	48	43.8	41.7	12.5	2.1	0	0	0	0
4X OPF	32	9.4	9.4	21.9	18.8	15.6	18.8	0	6.3

The Community Fluorosis Index (Dean, 1942; see Section 2 for description) was determined to be 0.15 for the NF community, 0.46 for the OPF community and 2.06 for the 4x OPF community. Dean indicates that a score of 0.4 or less warrants no public health concern, while a score of 0.6 begins to constitute a public health problem warranting further consideration.

Other effects

The mean DMFT score of the OPF group was not significantly different from that of the other two exposure groups, but the mean DMFT score of the 4X OPF group was significantly lower than that of the NF group (Table 6, from Jackson et al., 1995). The mean DMFS scores for both the OPF and 4x OPF groups were significantly lower than that of the NF group.

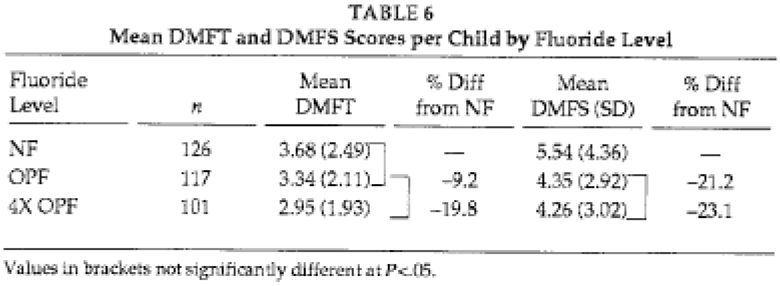


TABLE 6
Mean DMFT and DMFS Scores per Child by Fluoride Level

Fluoride Level	n	Mean DMFT	% Diff from NF	Mean DMFS (SD)	% Diff from NF
NF	126	3.68 (2.49)	—	5.54 (4.36)	—
OPF	117	3.34 (2.11)	−9.2	4.35 (2.92)	−21.2
4X OPF	101	2.95 (1.93)	−19.8	4.26 (3.02)	−23.1

Values in brackets not significantly different at $P<.05$.

Analysis of the DMFT and DMFS scores by age (Table 7 from Jackson et al., 1995) indicates that only the older children showed significant decreases in these scores at the higher fluoride levels.

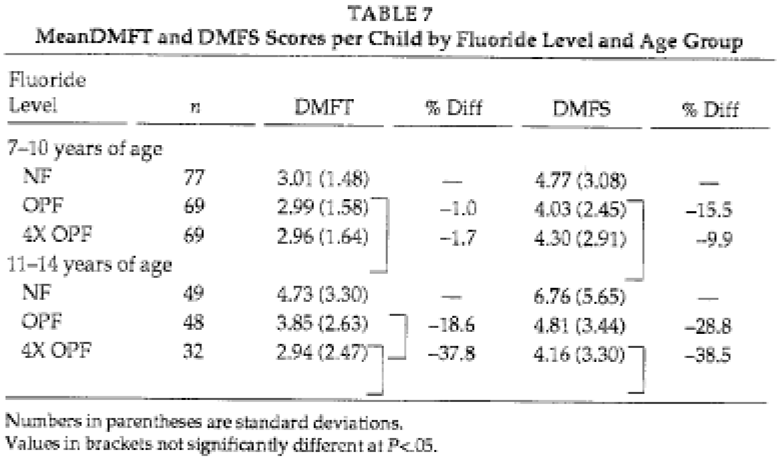


TABLE 7
MeanDMFT and DMFS Scores per Child by Fluoride Level and Age Group

Fluoride Level	n	DMFT	% Diff	DMFS	% Diff
7–10 years of age					
NF	77	3.01 (1.48)	—	4.77 (3.08)	—
OPF	69	2.99 (1.58)	–1.0	4.03 (2.45)	–15.5
4X OPF	69	2.96 (1.64)	–1.7	4.30 (2.91)	–9.9
11–14 years of age					
NF	49	4.73 (3.30)	—	6.76 (5.65)	—
OPF	48	3.85 (2.63)	–18.6	4.81 (3.44)	–28.8
4X OPF	32	2.94 (2.47)	–37.8	4.16 (3.30)	–38.5

Numbers in parentheses are standard deviations.
Values in brackets not significantly different at $P<.05$.

The reported history of fluoride supplement use resulted in an increase in the incidence of fluorosis (see Table 8 from Jackson et al., 1995), particularly in the NF group, and a decrease in DMFS scores (in the NF and 4x OPF groups but not in the OPF group, see Table 9 from Jackson et al., 1995). Based on information provided in the text, the data in Table 8 pertain to fluoride supplement use during infancy.

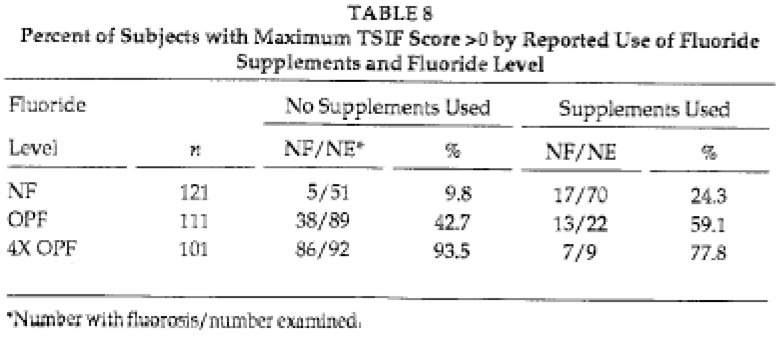


TABLE 8
Percent of Subjects with Maximum TSIF Score >0 by Reported Use of Fluoride Supplements and Fluoride Level

Fluoride		No Supplements Used		Supplements Used	
Level	n	NF/NE*	%	NF/NE	%
NF	121	5/51	9.8	17/70	24.3
OPF	111	38/89	42.7	13/22	59.1
4X OPF	101	86/92	93.5	7/9	77.8

*Number with fluorosis/number examined.

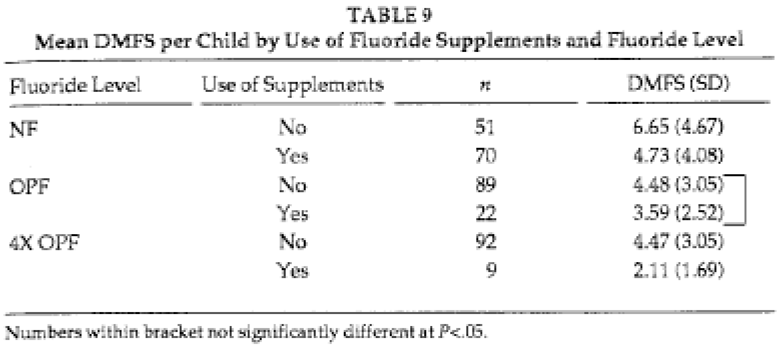


TABLE 9
Mean DMFS per Child by Use of Fluoride Supplements and Fluoride Level

Fluoride Level	Use of Supplements	n	DMFS (SD)
NF	No	51	6.65 (4.67)
	Yes	70	4.73 (4.08)
OPF	No	89	4.48 (3.05)
	Yes	22	3.59 (2.52)
4X OPF	No	92	4.47 (3.05)
	Yes	9	2.11 (1.69)

Numbers within bracket not significantly different at $P<.05$.

STUDY AUTHORS' CONCLUSIONS:

"The ingestion of water containing 1 ppm or less fluoride during the time of tooth development may result in dental fluorosis, albeit in its milder forms". The milder forms observed included a maximum Dean's score of 2 associated with white opacities, but no pitting or staining. Pitting and staining (Dean's score of 3 and 4) were observed only in the 4x OPF community. The study author observed improper use of fluoride supplements in communities with optimal and above optimal fluoride levels in drinking water.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT

Council on Dental Research and Council on Dental Therapeutics. 1972. Proceeding of the Conference on the Clinical Testing of Cariostatic Agents. Amer. Dental Assoc., Chicago.

FOUND IN NRC (2006)		Galagan, D.J. and J.R. Vermillion. 1957. Determining optimum fluoride concentrations. Public Health Rept. 72:491-493. Russell, A.L. 1961. The differential diagnosis of fluoride and nonfluoride opacities. J. Public Health Dent. 21:143-146.
PROFILER'S REMARKS	***DMO/ 11/20/06 12/15/06***	The study authors noted that the 4x OPF group contained 23 children who did not meet the strict criteria set for this group, some had resided in the study area for only the first 6 years of their life and some had not resided in the study area during their first year of life; however, the study authors state that the fluorosis and caries scores for these children were not significantly different from children in the 4xOPF group who were full time residents. Nevertheless, the study author indicated that these children thereafter consumed household well water with negligible amounts of fluoride as defined by the authors' protocol. The use of fluoride supplements during infancy may have confounded the prevalence of dental fluorosis in all three study communities. The study authors did not report on the frequency of use of bottled drinking water in the study populations. Severe fluorosis occurred in about 11% of the children in the 4x OPF group based on Dean's index (score of 4) and in about 20% based on TSIF scores (scores of 5-7). No children in the NF and OPF groups exhibited severe dental fluorosis.
PROFILER'S ESTIM. NOEL/NOAEL		TBD – The NOAEL for severe fluorosis appears to be 1 ppm.
PROFILER'S ESTIM. LOEL/ LOAEL		TBD – The LOAEL appears to be between 1 and 4 ppm.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor (X), Medium (_), Strong (_) The study includes three fluoride exposure levels. Fluoride supplements were consumed by some of the study participants during infancy (57.9% in the NF group; 19.8% in the OPF group, and 8.9% in the 4x OPF group. This is a potential confounder. Further consideration should be given to potential statistical evaluation of CFI scores to estimate the fluoride level where the CFI would be at an acceptable level. According to Dean (1946, as cited by Jackson et al., 1995), a CFI of 0.6 would be the highest acceptable score without a public health concern.
CRITICAL EFFECT(S):		Dental fluorosis

Khan, A., Moola, M.H., and Cleaton-Jones, P. 2005. Global trends in dental fluorosis from 1980 to 2000: a systematic review. SADJ 60:418-421.

ENDPOINT STUDIED:	Dental fluorosis in children aged 0-19 years
TYPE OF STUDY:	Data were obtained from primary articles published in peer-reviewed journals from January 1, 1980 to December 31, 2000.
POPULATION STUDIED:	Global: only articles with children aged 0-19 years were included in the analysis.
CONTROL POPULATION:	No control population was included.
EXPOSURE PERIOD:	Only studies with individuals with a life-long residence or those who had lived in the study area for the first seven years of life were included in the current analysis.
EXPOSURE GROUPS:	Water fluoride levels were divided into three categories: <0.3 ppm F, >0.3 to <0.7 ppm F, and >0.7-1.4 ppm F.
EXPOSURE ASSESSMENT:	The exposure assessment consisted solely of reported fluoride concentrations in the water. It is assumed that community drinking water was measured in each study, but this was not stated.
ANALYTICAL METHODS:	The methods for analyzing fluoride in the water of each study included were not described.
STUDY DESIGN	Articles were identified in an on-line literature search using PubMed and supplemented by a hand search using references obtained from articles found in the initial search. For inclusion each study met the following criteria: - Individuals 0-19 years; both general population and school children were acceptable, but hospital or clinic samples were not; - Be lifelong residents or had lived in the study area for the first seven years of life; - In an area with water fluoride concentration up to 1.4 ppm; - Have a specified sample size; - Published between the beginning of 1980 to the end of 2000; - Report fluorosis irrespective of the index used.
PARAMETERS MONITORED:	From studies meeting the above criteria, the prevalence of fluorosis was pooled and the trends over time were determined in the three water F concentration categories. Various indices examined included the Dean Index, the Tooth Surface Index of Fluorosis (TSIF), Thylstrup-Fejerskov Index (TFI), Fluorosis Risk Index (FRI) and the Developmental Dental Defects of Enamel Index (DDE) index.
STATISTICAL METHODS:	The t-test was used to compare the means of fluorosis prevalence for the fluoridated and non-fluoridated communities. In statistical analysis, fluorosis indices were used as continuous variables and the three fluoride concentration groups as categorical variables. Fluorosis indices were compared with a one-way ANOVA. For categorical variables a Chi-square test was done with Cramer's V (to find significant differences in the distribution of scores of the different indices). A Bonferroni test was used to determine differences between the means of the proportions of the prevalence.
RESULTS:	

Fluorosis

The mean percent of fluorosis prevalence increased with increasing fluoride concentration (Table II). The prevalence was significantly greater in the >0.3 to <0.7 ppm (p=0.041) and >0.7-<1.4 ppm (p=0.020) groups compared with the 0-<0.3 ppm group.

Graphical representation of fluorosis prevalence vs year of publication showed slight upward trends over time at all three fluoride concentration levels.

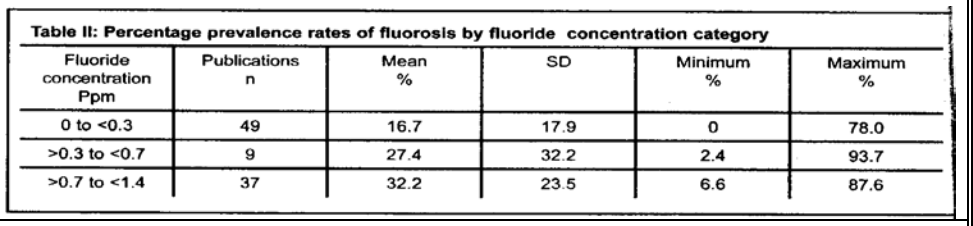


Table II: Percentage prevalence rates of fluorosis by fluoride concentration category

Fluoride concentration Ppm	Publications n	Mean %	SD	Minimum %	Maximum %
0 to <0.3	49	16.7	17.9	0	78.0
>0.3 to <0.7	9	27.4	32.2	2.4	93.7
>0.7 to <1.4	37	32.2	23.5	6.6	87.6

Literature evaluation

A total of 55 publications met the inclusion criteria for this review. Five fluorosis indices were used in the various publications such that too few studies per index were available to assess severity changes over time. Thus, the review concentrated only on fluorosis prevalence since little difference existed in the criteria between indices for the decision of fluorosis vs no fluorosis.

Dose response

Increasing fluoride water concentrations were associated with higher prevalence of fluorosis.

PROFILER’S NOTE: No attempt was made by the authors to estimate fluoride intake from drinking water consumption; thus, a fluoride dose could not be determined.

STUDY AUTHORS’ CONCLUSIONS:

This review confirms observation of an increase in fluorosis prevalence among fluoridated and non-fluoridated communities, although the trend is not statistically significant. Wide variation in fluorosis prevalence implies exposure via non-water sources such as fluoridated salt, beverages, food, toothpaste, dental rinses, etc. Total exposures “must” be taken into account for control of fluorosis. Residence at high altitude may also be a factor in developing dental fluorosis.

Limitations of the review include differences in study quality as well as in the diagnostic criteria employed among and between studies.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

none

PROFILER’S REMARKS ***Initials/date CSW 1/4/2007***

This study was a review and analysis of data in published literature. The authors used specific inclusion criteria to choose studies. However, the quality of the individual publications was not considered.

Doses could not be reconstructed from this review.

PROFILER’S ESTIM. NOEL/NOAEL

Could not be determined.

PROFILER’S ESTIM. LOEL/ LOAEL

Could not be determined.

POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:

Not suitable ( ), Poor (X), Medium ( ), Strong ( )

A positive correlation was found between increasing water fluoride levels and increasing fluorosis prevalence; however, a dose was not estimated. The severity of fluorosis was also

	not assessed.
CRITICAL EFFECT(S):	Dental fluorosis

Klimek, J., H. Prinz, E. Hellwig and G. Ahrens. 1985. Effect of a preventative program based on professional toothcleaning and fluoride application on caries and gingivitis. Community Dent Oral Epidemiol. 13: 295-298.

ENDPOINT STUDIED:	Dental caries, plaque accumulation and gingivitis (no fluorosis observed)
TYPE OF STUDY:	Case-control study
POPULATION STUDIED:	104 (50 boys and 54 girls) schoolchildren, ages 12-14 years old, that were part of the resident population from Marburg, Germany. Most were from families in the higher socioeconomic status.
CONTROL POPULATION:	117 (52 boys and 65 girls) schoolchildren, ages 12-14 years old, that were part of the resident population from Marburg, Germany. Most also were from higher socioeconomic families.
EXPOSURE PERIOD:	The study occurred over a period of 2 years with the first examination taking place in 1981 when participants were between 12-13 years old.
EXPOSURE GROUPS:	The two exposure groups were defined by the level of professional tooth-cleaning and prophylactic dental fluoride treatment received. The test group received a prescribed regime of prophylactic dental care and the control group received none. Children were also exposed to the drinking water from the town of Marburg, Germany which had a negligible (< 0.2 ppm F-) amount of fluoride, but the amount of water consumption was not quantified.
EXPOSURE ASSESSMENT:	All children were examined for dental plaque, gingivitis and caries present over a 2 year period with the test group receiving prophylactic care during that time (See details below). Radiographs were taken before the start of the study and approximately 2 ½ months after the test group received their last prophylactic treatment.
ANALYTICAL METHODS:	Data on how fluoride concentrations in the water were measured were not included in the study report. The fluoride concentration in the varnish applied to the test group was also not included.
STUDY DESIGN	In the study, 104 (50 boys and 54 girls) schoolchildren, ages 12-14 years old, made up the study population and 117 (52 boys and 65 girls) schoolchildren, also ages 12-14 years old, made up the control population. All children were part of the resident population of Marburg, Germany. The two groups underwent different protocols. The study population underwent dental examinations but also received prophylactic treatment; the control population only received dental examinations. Both procedures were as follows: Examinations: Prior to the start of the program and about 2 ½ months after the last prophylactic session for the test group, both the control and test groups were examined clinically and radiographically. Examinations consisted of an assessment of plaque, gingivitis and caries performed by a single examiner. Assessments were performed using an artificial light source, dental mirrors and dental probes. Radiographs taken were two posterior bitewings and were evaluated by two dentists that were blinded to which group the children belonged. Prophylactic treatment: The test group children visited the same oral hygienist 4 times in the first 6 weeks and then visited the same oral hygienist 5 times/year to receive professional oral prophylactic treatment and instructions. Each session included staining for dental plaque, demonstration of tooth-brushing and flossing and professional tooth-cleaning. The abrasive paste used in the cleaning contained no fluoride. Also, a fluoride varnish (Duraphat) was applied twice a year. At the end of each visit, the children were provided with large quantities of toothpaste (each containing NaF), toothbrushes and dental floss. The control children received no prophylactic treatment.
PARAMETERS MONITORED:	Prior to the start of the program and about 2 ½ months after the last prophylactic session for the test group, both the control and test groups were examined clinically and radiographically. Evidence of dental plaque (Pl I) used the criteria and indices of Silness and Löe (1964) with

clinical and radiographic caries recorded according to the indices of Koch (1967). The DFS index (number of new carious and filled surfaces) was used to describe the caries incidence. Gingivitis (GI) was evaluated as proposed by Ramfjord (1959) and Löe and Silness (1963).

During the prophylactic treatment, each session included staining for dental plaque, demonstration of tooth-brushing and flossing and professional tooth-cleaning as described by Axelsson and Lindhe (1974).

STATISTICAL METHODS:

Statistical significance between the test and control groups for plaque, gingivitis and DFS were analyzed with the Mann-Whitney U-test. The Wilcoxon test was also used for determining the significance of differences in each group between the initial and final examination.

RESULTS:

Caries data

Tables 1 and 2 are copied directly from Klimek et al. (1985) and demonstrate the pre- and post-experimental incidence of caries in the test and control group. Table 1 indicates no statistical significant difference between the control and test group in the incidence of caries prior to the start of the prophylactic treatment. Table 2 shows a statistically significant (p value not given) increase in the incidence of caries in the control group after 2 years compared to the test group on all surfaces of the tooth (occlusal, proximal and buccal-lingual). Data shows the control group children developed nearly twice as many carious and filled tooth surfaces when compared to the test group.

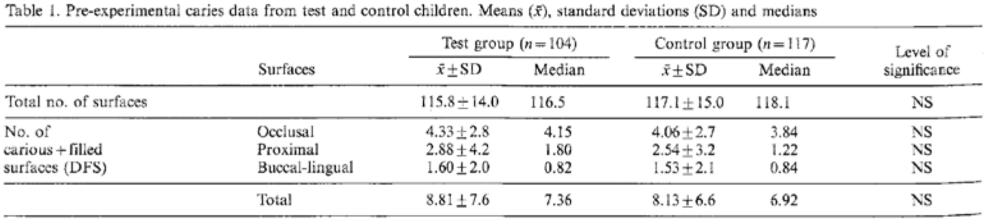


Table 1. Pre-experimental caries data from test and control children. Means ($\bar{x}$), standard deviations (SD) and medians

		Test group ($n=104$)		Control group ($n=117$)		Level of significance
	Surfaces	$\bar{x} \pm SD$	Median	$\bar{x} \pm SD$	Median	
Total no. of surfaces		115.8±14.0	116.5	117.1±15.0	118.1	NS
No. of carious + filled surfaces (DFS)	Occlusal	4.33±2.8	4.15	4.06±2.7	3.84	NS
	Proximal	2.88±4.2	1.80	2.54±3.2	1.22	NS
	Buccal-lingual	1.60±2.0	0.82	1.53±2.1	0.84	NS
	Total	8.81±7.6	7.36	8.13±6.6	6.92	NS

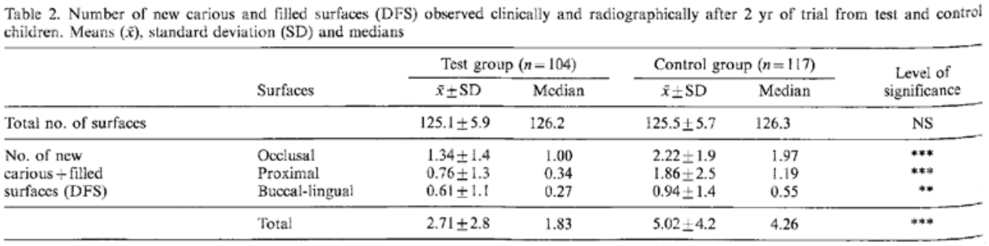


Table 2. Number of new carious and filled surfaces (DFS) observed clinically and radiographically after 2 yr of trial from test and control children. Means ($\bar{x}$), standard deviation (SD) and medians

		Test group ($n=104$)		Control group ($n=117$)		Level of significance
	Surfaces	$\bar{x} \pm SD$	Median	$\bar{x} \pm SD$	Median	
Total no. of surfaces		125.1±5.9	126.2	125.5±5.7	126.3	NS
No. of new carious + filled surfaces (DFS)	Occlusal	1.34±1.4	1.00	2.22±1.9	1.97	***
	Proximal	0.76±1.3	0.34	1.86±2.5	1.19	***
	Buccal-lingual	0.61±1.1	0.27	0.94±1.4	0.55	**
	Total	2.71±2.8	1.83	5.02±4.2	4.26	***

PROFILER'S NOTE: The profiler agrees that the prophylactic treatment decreased the incidence of caries when compared to the non-treated control group. The level of significance (value of p) should have been included in the table.

Plaque and gingivitis

Table 3 was copied directly from Klimek et al. (1985) and shows the incidence of dental plaque (Pl I) and gingivitis (GI) present. No significant differences were observed between the two sets of children in the base-line examination but both values were decreased at the follow-up examination in the test group children. In the control group, the plaque incidence was the same but gingivitis increased after the 2 years.

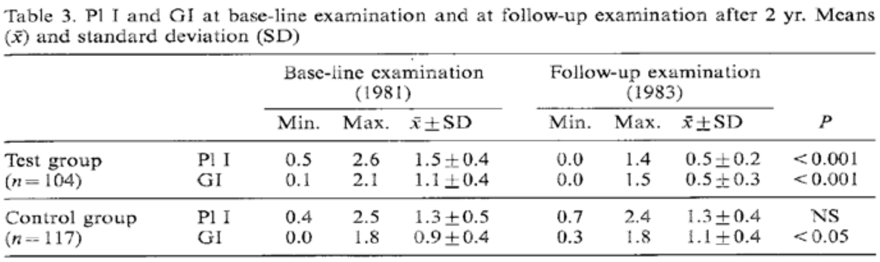


Table 3. Pl I and GI at base-line examination and at follow-up examination after 2 yr. Means ($\bar{x}$) and standard deviation (SD)

		Base-line examination (1981)			Follow-up examination (1983)			
		Min.	Max.	$\bar{x} \pm SD$	Min.	Max.	$\bar{x} \pm SD$	P
Test group ($n=104$)	Pl I	0.5	2.6	1.5±0.4	0.0	1.4	0.5±0.2	<0.001
	GI	0.1	2.1	1.1±0.4	0.0	1.5	0.5±0.3	<0.001
Control group ($n=117$)	Pl I	0.4	2.5	1.3±0.5	0.7	2.4	1.3±0.4	NS
	GI	0.0	1.8	0.9±0.4	0.3	1.8	1.1±0.4	<0.05

		PROFILER'S NOTE: The profiler agrees that the test group had decreased plaque and gingivitis.
STUDY AUTHORS' CONCLUSIONS:		Klimek et al. (1985) concluded that a preventative program based on five prophylactic sessions per year and the additional application of fluoride varnish twice a year was remarkably effective in reducing gingival inflammation and the development of new carious lesions in schoolchildren. The study showed a caries reduction of 46% and a reduction of Pl I and GI mean index values of about 60%.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Axelsson, P. and J. Lindhe. 1974. The effect of a preventative programme on dental plaque, gingivitis and caries in schoolchildren. Results after one and two years. J. Clin. Periodontal, 1: 126-38. Koch, G. 1967. Effect of sodium fluoride in dentrifice and mouthwash on incidence of dental caries in school-children. Thesis. Odontol. Revy; Supple. 12. Löe, H. and J. Silness. 1963. Periodontal disease in pregnancy. Acta Odontol Scand, 2:533-51. Ramfjord, SP. 1959. Indices for prevalence and incidence of periodontal disease. J. Periodontal, 30:51-9. Silness, J and H. Löe. 1964. Periodontal disease in pregnancy, II. Correlation between oral hygiene and periodontal condition. Acta Odontol Scand, 22:121-35.
PROFILER'S REMARKS	***DFG/11-06 and 12/15/06***	The study was well-conducted and had adequate study design. However, the study was not designed for development of a dose response to fluoride as the emphasis was on a total prophylactic program (brushing, dental care, flossing) as well as direct application of a fluoride varnish twice a year. Based on the study design, the observed decrease in incidence of dental caries, plaque and gingivitis cannot be attributed to any one cause.
PROFILER'S ESTIM. NOEL/NOAEL		Study design was not suitable for development of a NOAEL or LOAEL for fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL		Study design was not suitable for development of a NOAEL or LOAEL for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( ) While the study was well-conducted, the study design was not conducive to provide data for a dose-response. The study only indicated that a strong prophylactic program, including the use of fluoride treatments twice a year, does help decrease the incidence of caries, plaque and gingivitis. The study did not address any issues of dental or skeletal fluorosis.
CRITICAL EFFECT(S):		Incidence of dental caries, plaque and gingivitis

Kaur et al. 1987. Changing trends of dental caries and enamel mottling after change of fluoride content in drinking water in endemic fluoride belt. J. Indian Soc. Pedo. Prev. Dent. pp.37-44.

ENDPOINT STUDIED:	Dental caries and dental fluorosis
TYPE OF STUDY:	Cross-sectional study of dental fluorosis and dental caries and fluoride levels in drinking water
POPULATION STUDIED:	India/Punjab: 988 children (sex not specified, ages 6 – 16 yrs old) from three villages. No other information concerning the study population was provided.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	From birth to 6-16 yrs old.
EXPOSURE GROUPS:	3 groups: Group 1 (town of Naruna), previously 2 ppm fluoride in drinking water, changed 9 yrs later to 0.19 ppm fluoride; Group 2 (town of Deon) previously 1.8 ppm fluoride, changed 11 yrs later to 0.19 ppm fluoride; Group 3 (town of Bibiwala) previously 0.9 ppm fluoride, changed 8 yrs later to 0.19 ppm fluoride
EXPOSURE ASSESSMENT:	Drinking water was the only exposure route evaluated.
ANALYTICAL METHODS:	Orion Fluoride Selectrode was used to analyze for the fluoride in drinking water
STUDY DESIGN	Dental caries and fluorosis were investigated in Indian children, ages 6-16 years old, in three villages: two where the initial fluoride levels were 2.0 and 1.8 ppm, and a third where the fluoride level was 0.9 ppm, but a change in the water supply brought all three areas to 0.19 ppm fluoride. Each child was evaluated for dental caries using Moller's Index (Moore, 1966) and the degree of dental fluorosis using Dean's Index of Fluorosis (see Section 2). The prevalence of severity of the dental caries and dental fluorosis was assessed, broken down by the age of the children, and this was correlated with the years that the water supply fluoride levels changed in each area.
PARAMETERS MONITORED:	Dental caries were measured using Moller's Index (Moore, 1966) and dental fluorosis using Dean's Index of Fluorosis (see Section 2)
STATISTICAL METHODS:	Not stated
RESULTS:	
Caries	See Table 5 for the prevalence and severity of dental caries in Village 1 - Naruna (previously 2 ppm fluoride, present 0.19 ppm fluoride), Table 6 for Village 2 - Deon (previously 1.8 ppm fluoride, present 0.19 ppm fluoride), Table 7 for Village 3 - Bibiwala (previously 0.9 ppm fluoride, present 0.19 ppm fluoride) (all tables copied directly from Kaur et al., 1987).

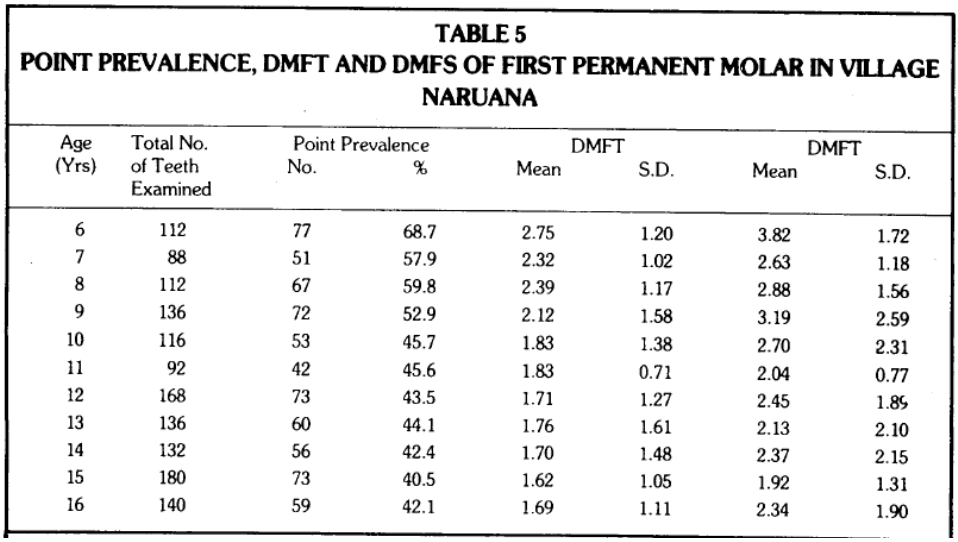


TABLE 5
POINT PREVALENCE, DMFT AND DMFS OF FIRST PERMANENT MOLAR IN VILLAGE NARUANA

Age (Yrs)	Total No. of Teeth Examined	Point Prevalence No.	%	DMFT Mean	S.D.	DMFT Mean	S.D.
6	112	77	68.7	2.75	1.20	3.82	1.72
7	88	51	57.9	2.32	1.02	2.63	1.18
8	112	67	59.8	2.39	1.17	2.88	1.56
9	136	72	52.9	2.12	1.58	3.19	2.59
10	116	53	45.7	1.83	1.38	2.70	2.31
11	92	42	45.6	1.83	0.71	2.04	0.77
12	168	73	43.5	1.71	1.27	2.45	1.89
13	136	60	44.1	1.76	1.61	2.13	2.10
14	132	56	42.4	1.70	1.48	2.37	2.15
15	180	73	40.5	1.62	1.05	1.92	1.31
16	140	59	42.1	1.69	1.11	2.34	1.90

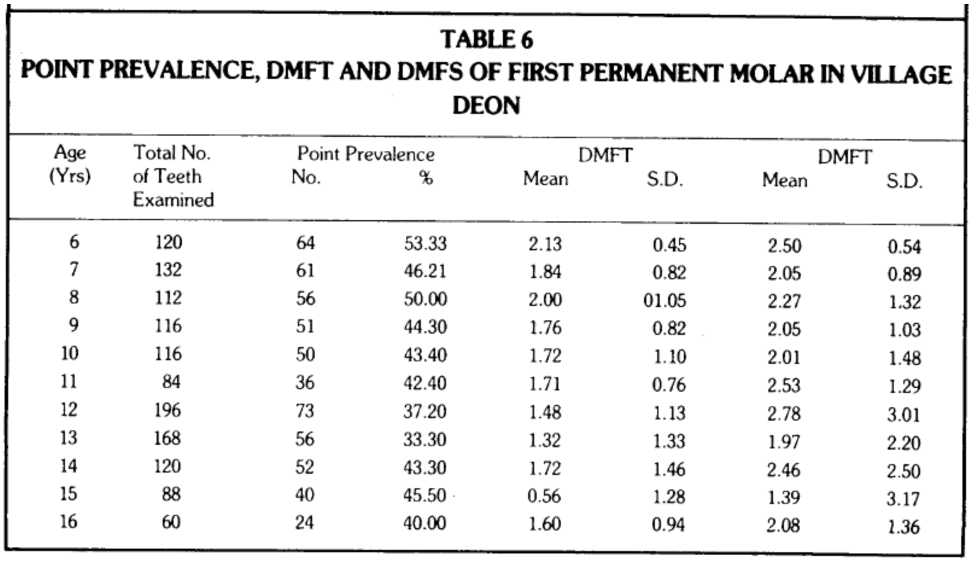


TABLE 6
POINT PREVALENCE, DMFT AND DMFS OF FIRST PERMANENT MOLAR IN VILLAGE DEON

Age (Yrs)	Total No. of Teeth Examined	Point Prevalence No.	%	DMFT Mean	S.D.	DMFT Mean	S.D.
6	120	64	53.33	2.13	0.45	2.50	0.54
7	132	61	46.21	1.84	0.82	2.05	0.89
8	112	56	50.00	2.00	01.05	2.27	1.32
9	116	51	44.30	1.76	0.82	2.05	1.03
10	116	50	43.40	1.72	1.10	2.01	1.48
11	84	36	42.40	1.71	0.76	2.53	1.29
12	196	73	37.20	1.48	1.13	2.78	3.01
13	168	56	33.30	1.32	1.33	1.97	2.20
14	120	52	43.30	1.72	1.46	2.46	2.50
15	88	40	45.50	0.56	1.28	1.39	3.17
16	60	24	40.00	1.60	0.94	2.08	1.36

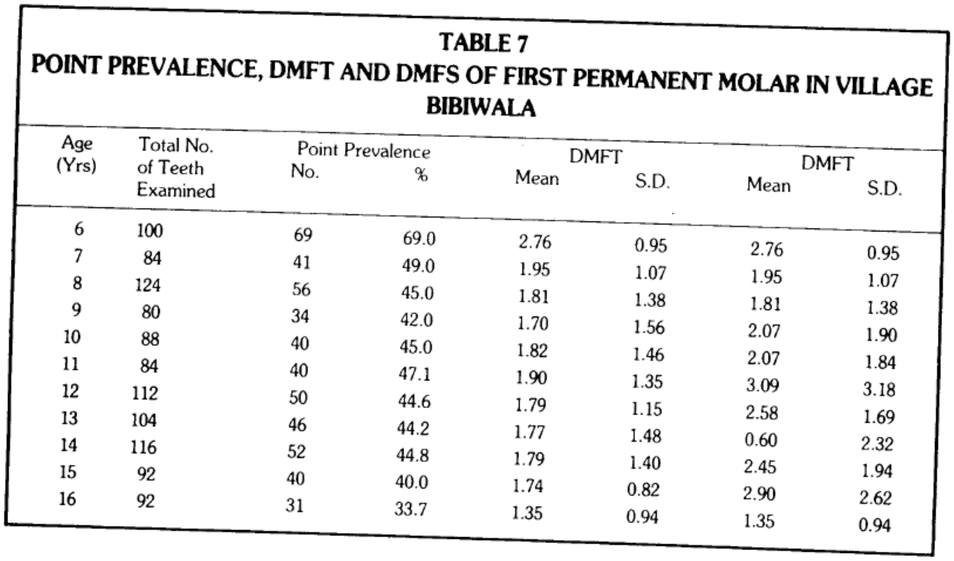


TABLE 7
POINT PREVALENCE, DMFT AND DMFS OF FIRST PERMANENT MOLAR IN VILLAGE BIBIWALA

Age (Yrs)	Total No. of Teeth Examined	Point Prevalence No.	%	DMFT Mean	S.D.	DMFT Mean	S.D.
6	100	69	69.0	2.76	0.95	2.76	0.95
7	84	41	49.0	1.95	1.07	1.95	1.07
8	124	56	45.0	1.81	1.38	1.81	1.38
9	80	34	42.0	1.70	1.56	2.07	1.90
10	88	40	45.0	1.82	1.46	2.07	1.84
11	84	40	47.1	1.90	1.35	3.09	3.18
12	112	50	44.6	1.79	1.15	2.58	1.69
13	104	46	44.2	1.77	1.48	0.60	2.32
14	116	52	44.8	1.79	1.40	2.45	1.94
15	92	40	40.0	1.74	0.82	2.90	2.62
16	92	31	33.7	1.35	0.94	1.35	0.94

PROFILER'S NOTE: It appears that the last two columns in Tables 5-7 refer to DMFS and not DMFT.

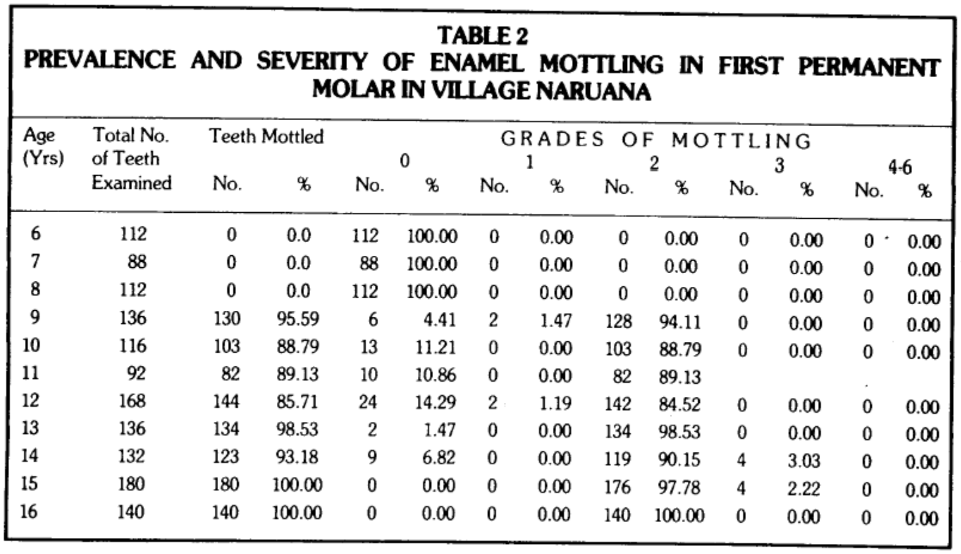
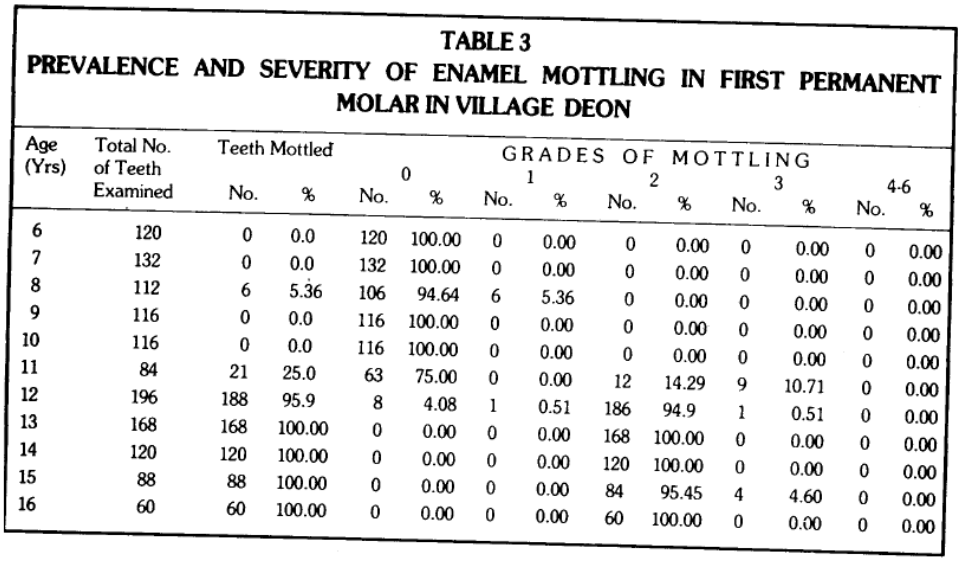
Dental fluorosis	See Table 2 for the prevalence and severity of dental fluorosis in Village 1 – Naruna, Table 3 for Village 2 – Deon; and Table 4 for Village 3 – Bibiwala:  

TABLE 2
PREVALENCE AND SEVERITY OF ENAMEL MOTTLING IN FIRST PERMANENT MOLAR IN VILLAGE NARUANA

Age (Yrs)	Total No. of Teeth Examined	Teeth Mottled		GRADES OF MOTTLING 0		1		2		3		4-6	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
6	112	0	0.0	112	100.00	0	0.00	0	0.00	0	0.00	0	0.00
7	88	0	0.0	88	100.00	0	0.00	0	0.00	0	0.00	0	0.00
8	112	0	0.0	112	100.00	0	0.00	0	0.00	0	0.00	0	0.00
9	136	130	95.59	6	4.41	2	1.47	128	94.11	0	0.00	0	0.00
10	116	103	88.79	13	11.21	0	0.00	103	88.79	0	0.00	0	0.00
11	92	82	89.13	10	10.86	0	0.00	82	89.13				
12	168	144	85.71	24	14.29	2	1.19	142	84.52	0	0.00	0	0.00
13	136	134	98.53	2	1.47	0	0.00	134	98.53	0	0.00	0	0.00
14	132	123	93.18	9	6.82	0	0.00	119	90.15	4	3.03	0	0.00
15	180	180	100.00	0	0.00	0	0.00	176	97.78	4	2.22	0	0.00
16	140	140	100.00	0	0.00	0	0.00	140	100.00	0	0.00	0	0.00

TABLE 3
PREVALENCE AND SEVERITY OF ENAMEL MOTTLING IN FIRST PERMANENT MOLAR IN VILLAGE DEON

Age (Yrs)	Total No. of Teeth Examined	Teeth Mottled		GRADES OF MOTTLING 0		1		2		3		4-6	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
6	120	0	0.0	120	100.00	0	0.00	0	0.00	0	0.00	0	0.00
7	132	0	0.0	132	100.00	0	0.00	0	0.00	0	0.00	0	0.00
8	112	6	5.36	106	94.64	6	5.36	0	0.00	0	0.00	0	0.00
9	116	0	0.0	116	100.00	0	0.00	0	0.00	0	0.00	0	0.00
10	116	0	0.0	116	100.00	0	0.00	0	0.00	0	0.00	0	0.00
11	84	21	25.0	63	75.00	0	0.00	12	14.29	9	10.71	0	0.00
12	196	188	95.9	8	4.08	1	0.51	186	94.9	1	0.51	0	0.00
13	168	168	100.00	0	0.00	0	0.00	168	100.00	0	0.00	0	0.00
14	120	120	100.00	0	0.00	0	0.00	120	100.00	0	0.00	0	0.00
15	88	88	100.00	0	0.00	0	0.00	84	95.45	4	4.60	0	0.00
16	60	60	100.00	0	0.00	0	0.00	60	100.00	0	0.00	0	0.00

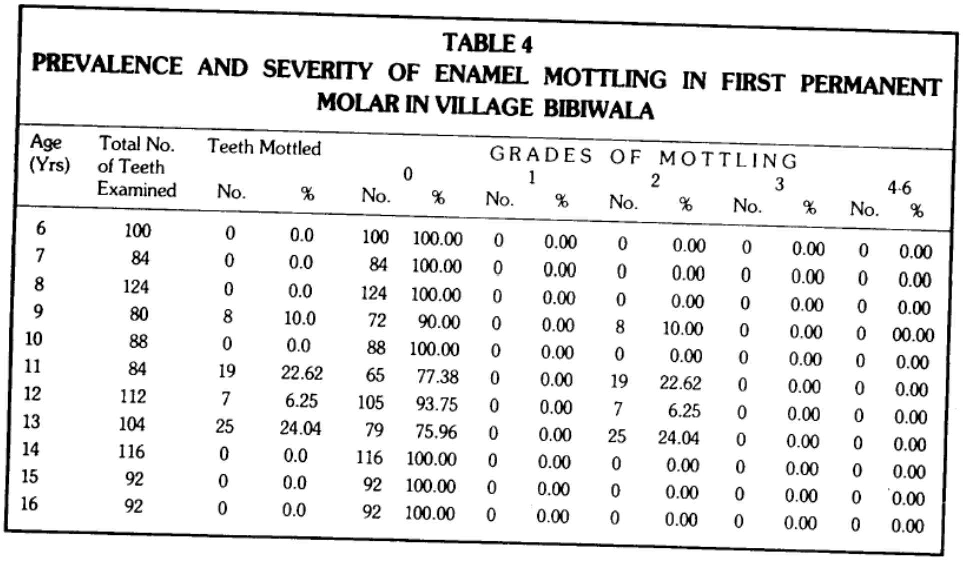


TABLE 4
PREVALENCE AND SEVERITY OF ENAMEL MOTTLING IN FIRST PERMANENT MOLAR IN VILLAGE BIBIWALA

Age (Yrs)	Total No. of Teeth Examined	Teeth Mottled		GRADES OF MOTTLING 0		1		2		3		4-6	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
6	100	0	0.0	100	100.00	0	0.00	0	0.00	0	0.00	0	0.00
7	84	0	0.0	84	100.00	0	0.00	0	0.00	0	0.00	0	0.00
8	124	0	0.0	124	100.00	0	0.00	0	0.00	0	0.00	0	0.00
9	80	8	10.0	72	90.00	0	0.00	8	10.00	0	0.00	0	0.00
10	88	0	0.0	88	100.00	0	0.00	0	0.00	0	0.00	0	00.00
11	84	19	22.62	65	77.38	0	0.00	19	22.62	0	0.00	0	0.00
12	112	7	6.25	105	93.75	0	0.00	7	6.25	0	0.00	0	0.00
13	104	25	24.04	79	75.96	0	0.00	25	24.04	0	0.00	0	0.00
14	116	0	0.0	116	100.00	0	0.00	0	0.00	0	0.00	0	0.00
15	92	0	0.0	92	100.00	0	0.00	0	0.00	0	0.00	0	0.00
16	92	0	0.0	92	100.00	0	0.00	0	0.00	0	0.00	0	0.00

STUDY AUTHORS' CONCLUSIONS:	Regarding dental fluorosis, in Village 1 (where the fluoride level was lowered from 2 ppm to 0.19 ppm), grade 3 dental mottling was observed in only 3% of 14 year old children and 2.2% of 15 year old children. In Village 2 (where the fluoride level was lowered from 1.8 ppm to 0.19 ppm), a similar picture was seen, however grade 1 mottling was seen in more children than in village 1. A low prevalence of grade 3 mottling was seen only at 11, 12, and 15 years of age. In village 3 (where the fluoride level was lowered from 0.9 ppm to 0.19 ppm), a low prevalence of mottling was observed in 9, 11, and 13 year old children. Grade 3 mottling was not seen in any child. Regarding dental caries, in Village 1, the percentage of first molars with caries in 9 year old children was 52.91, in children younger than 9 years old the percentage of carious molars ranged from 57.9 to 68.7, in children older than 9 years old, the percentage was 40.5-45.7. In Village 2, a similar picture was observed, with the 6-10 year old children showing a higher prevalence than the 12-16 year olds (with the water supply being changed at 11 years). In Village 3, a trend of sudden increase in decayed, missing, and filled (DMF) teeth and prevalence of carious molars after the year of the change of the water supply was also observed.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Moore, I.J. 1966. Clinical criteria for the diagnosis of the incipient caries lesion. Advanc. Fluori. Res. 4: 57-72.
PROFILER'S REMARKS ***Initials/date SBG 3/28/2007***	This study is limited in its usefulness because no statistical analyses were carried out. Although confounding factors which may have contributed to total fluoride intake were not addressed, the study does suggest that for the study population a NOAEL for severe fluorosis corresponds to about 2 ppm fluoride in drinking water.
PROFILER'S ESTIM. NOEL/NOAEL	Based on the results in Tables 2, 3, and 4, a NOAEL of 2 ppm for severe dental fluorosis (Grades 4-6) can be identified, because none of the children in Village 1 (even the older children who were drinking water at 2 ppm fluoride when their teeth erupted) showed this degree of dental fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL	Based on the results in Tables 2, 3, and 4, a LOAEL for severe dental fluorosis cannot be identified from this study, because none of the children in any of the 3 villages showed severe dental fluorosis.

POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable ( ), Poor (x), Medium ( ), Strong ( ) This study seems to be poorly suited for dose-response modelling because even though a NOAEL was identified for dental fluorosis, a LOAEL was not identified, and no statistics were carried out on the data.
CRITICAL EFFECT(S):	Dental caries, dental fluorosis

Kumar, J.V. and Swango P.A. 1999. Fluoride exposure and dental fluorosis in Newburgh and Kingston, New York: policy implications. Community Dent. Oral Epidemiol. 27: 171-180.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Cross-sectional
POPULATION STUDIED:	U.S./New York/Newburgh City (fluoridated water supply): 7-14 yr-old school children (lifelong residents); 459 (47.9% male; 51.6% African-American) surveyed in 1986; 847 (49.0% male; 41.1% African-American) surveyed in 1995. U.S./New York/Newburgh Town (fluoridated water supply): 7-14 yr-old school children (lifelong residents); 289 (58.8% male; 8.3% African-American) surveyed in 1986; 289 (49.1% male, 10.4% African-American) surveyed in 1995.
CONTROL POPULATION:	U.S./New York/New Windsor (non-fluoridated water supply): 7-14 yr-old old school children (lifelong residents):-; 134 children (52.2% male, 5.2% African-American) surveyed in 1986; 237 (41.8% male, 6.8% African-American) surveyed in 1995. U.S./New York/ Kingston (non-fluoridated water supply): 7-14 yr-old school children (lifelong residents); 425 children (50.3% male; 16.0% African-American) surveyed in 1986; 646 (50.8% male, 19.2% African-American) surveyed in 1995. U.S./New York/Ulster (non-fluoridated water supply): 7-14 yr-old school children (lifelong residents), 174 children (50.0% male; 4.6% African-American) surveyed in 1995. PROFILER'S NOTE: Although the children in New Windsor, Kingston and Ulster did not have exposure to fluoridated water, some had exposure from fluoride supplements (tablets) and dentifrices with fluoride (see Table 1 under Exposure Groups).
EXPOSURE PERIOD:	Children from Newburgh City were exposed throughout their lifetime, except during a three year period from 1978 to 1981 (affecting children from the 1986 survey as follows: 7 year-olds from 0-2 years of age; 8 yr-olds from 0-3 years of age; 9 yr-olds from 1-4 years of age, etc., ranging up to 14 yr-olds affected from 6-9 years of age). Children from Newburgh Town surveyed in 1986 were exposed to fluoridation for 2 years. Those surveyed in 1995 were exposed beginning from birth up to age 3 for a maximum of 11 years. Children from New Windsor, Kingston, and Ulster were not exposed to fluoride in the drinking water supply.
EXPOSURE GROUPS:	Table 1 was copied directly from Kumar and Swango (1999) and summarizes the percent distribution of children in each study community according to age group, gender, race, and fluoride exposure. Males and females generally were equally represented in all areas, although there were differences in gender between 1986 and 1995 in Newburgh Town and New Windsor. In both 1986 and 1995, there were proportionally more African-American children in Newburgh City compared to other areas. The major (80-95%) race represented in each community was White or 'other', with 5 to 20% African-American; the exception was Newburgh City where African-Americans made up 52% and 41% in 1986 and 1995, respectively

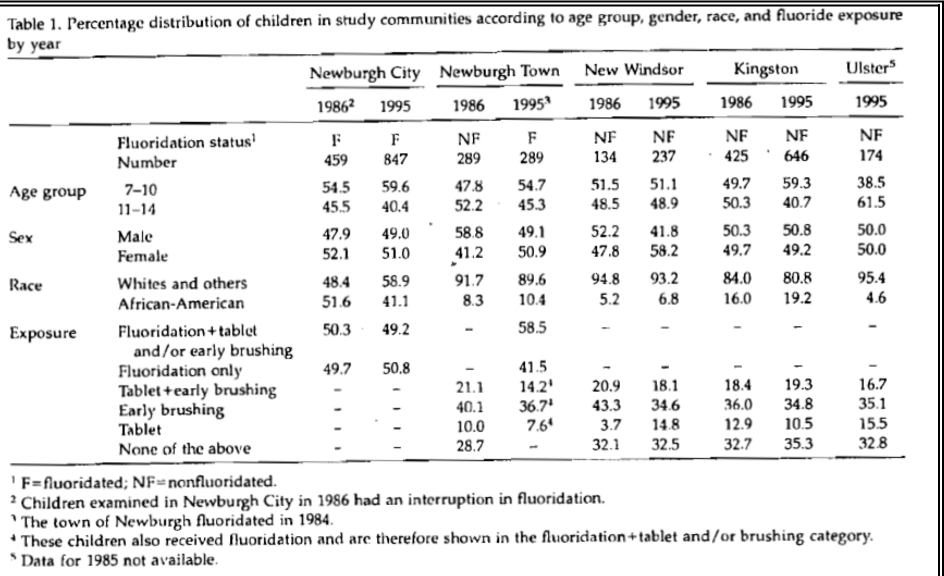


Table 1. Percentage distribution of children in study communities according to age group, gender, race, and fluoride exposure by year

		Newburgh City		Newburgh Town		New Windsor		Kingston		Ulster[5]
		1986[2]	1995	1986	1995[3]	1986	1995	1986	1995	1995
	Fluoridation status[1]	F	F	NF	F	NF	NF	NF	NF	NF
	Number	459	847	289	289	134	237	425	646	174
Age group	7–10	54.5	59.6	47.8	54.7	51.5	51.1	49.7	59.3	38.5
	11–14	45.5	40.4	52.2	45.3	48.5	48.9	50.3	40.7	61.5
Sex	Male	47.9	49.0	58.8	49.1	52.2	41.8	50.3	50.8	50.0
	Female	52.1	51.0	41.2	50.9	47.8	58.2	49.7	49.2	50.0
Race	Whites and others	48.4	58.9	91.7	89.6	94.8	93.2	84.0	80.8	95.4
	African-American	51.6	41.1	8.3	10.4	5.2	6.8	16.0	19.2	4.6
Exposure	Fluoridation + tablet and/or early brushing	50.3	49.2	–	58.5	–	–	–	–	–
	Fluoridation only	49.7	50.8	–	41.5	–	–	–	–	–
	Tablet + early brushing	–	–	21.1	14.2[4]	20.9	18.1	18.4	19.3	16.7
	Early brushing	–	–	40.1	36.7[4]	43.3	34.6	36.0	34.8	35.1
	Tablet	–	–	10.0	7.6[4]	3.7	14.8	12.9	10.5	15.5
	None of the above	–	–	28.7	–	32.1	32.5	32.7	35.3	32.8

[1] F = fluoridated; NF = nonfluoridated.

[2] Children examined in Newburgh City in 1986 had an interruption in fluoridation.

[3] The town of Newburgh fluoridated in 1984.

[4] These children also received fluoridation and are therefore shown in the fluoridation + tablet and/or brushing category.

[5] Data for 1985 not available.

EXPOSURE ASSESSMENT:

Some children in all the surveyed communities also were exposed to fluoride from other sources, including fluoride tablet supplements and early brushing (before age 2 years) with fluoridated toothpaste.

In the non-fluoridated communities 9see Table 1), approximately one third (29-35%) of the children were not exposed to fluoride from any source considered (water, tablet, early brushing); approximately another third (35-43%) were exposed only by early brushing; the remainder were exposed via tablet only (4-15%) or tablet plus early brushing (17-21%).

ANALYTICAL METHODS:

Data for measuring the fluoride concentrations were not included in the study report. Water quality parameters were not measured. The fluoride concentration in supplement tablets or toothpaste was not included.

STUDY DESIGN:

The purpose of the study was to determine whether the risk imposed by fluoride exposure has changed during the time period from 1986 to 1995, and to determine the effect of water fluoridation and other known fluoride sources (fluoride levels not reported) on dental fluorosis in participating children. Data were obtained from two cross-sectional surveys, conducted in 1986 and 1995 during the school years in the Newburgh and Kingston school districts. Analysis was limited to 3500, 7-14 year old lifelong residents of Newburgh City (fluoridated at 1±0.2 mg/L since 1945, with a 3 year interruption from 1978 to 1981), Newburgh Town (fluoridated since 1984—level not reported), and New Windsor, Kingston, or Ulster (all non-fluoridated).

The two surveys were similar in design except for the number of children studied (n=1307 in 1986; n=2193 in 1995). Dental fluorosis and caries were recorded using Dean’s criteria and the Decayed, Missing and Filled Tooth Surfaces (DMFS) index. Examination details were not reported, including the examiners, location where examinations occurred, lighting conditions, or equipment used. Examiners were blind to residential and fluoridation status of the children. Fluoride exposure data was collected by questionnaire. The questionnaire design differed between studies as follows:

1) The responses in the 1986 survey were primarily open-ended for the two questions related to the use of fluoride toothpaste and fluoride tablets. In the 1995 survey, categories for these two items were created.
2) Questions related to school lunch program participation, education of the head of the household, and breast-feeding were not included in the 1986 survey.
3) The response rate for participation was lower in 1995 (38%) than in 1986 (58%).

	4) Children from the town of Ulster could not be identified from the 1986 survey because a question regarding their place of residence was not included. 5) Different examiners were used in each survey, although they were trained by the same dentist. PROFILER'S NOTE: Dean's Index of Fluorosis is described in Section 2 of the report).
PARAMETERS MONITORED:	Dental fluorosis was measured using Dean's classification at the subject level. Fluorosis was scaled as none, questionable, very mild, mild, moderate or severe. Dental caries was recorded using the DMFS index (number of decayed, missing and filled permanent tooth surfaces) and visual-tactile examination.
STATISTICAL METHODS:	Regression procedures were used to estimate the effect of fluoridation, fluoride supplements, and early brushing on dental fluorosis. Analysis involved comparison of frequency distributions of Dean's fluorosis categories to examine changes over time, including a "ridit" analysis to examine the changes in severity. The proportion of children exposed to known fluoride sources was calculated for each category: a) fluoridation alone; b) fluoridation plus tablet and/or early brushing; c) tablet supplement alone; d) early tooth brushing alone; e) tablet supplement plus early brushing; f) none of the above exposures. Adjusted odds ratios and 95% confidence intervals were calculated for the variables associated with dental fluorosis in the bivariate analysis ($p<0.1$). This model included race and the categories for fluoride exposure variables. The fluoride exposure variable was introduced as an indicator variable and the reference group consisted of children from the non-fluoridated areas without known fluoride exposure. Logistic regression procedures were used to estimate the association between factors and dental fluorosis separately for the two surveys, and then were used to fit a generalized "logit" model for examining the effect of year, race and fluoride exposure and their interactions. Two separate regression models were constructed to compare categories of fluorosis: one to compare the questionable category with the normal, and another to compare the very mild to severe category (combined) with the normal. The examination of two-way and three-way interaction terms requires larger sample sizes, so exposure categories were combined as follows: a) fluoridation alone or fluoridation plus tablet and/or early brushing; b) tablet supplement alone or early tooth brushing alone or tablet supplement plus early brushing; c) reference group with none of the above exposures. The purpose of this analysis was to determine whether there were changes in the risk associated with fluoride exposure between the two surveys for African-American children and children of other racial groups. Analyses of crude, covariate-adjusted and ranked DMFS scores were performed to determine the relationship between caries and dental fluorosis. Four categories of fluorosis (normal, questionable, very mild, and mild to severe) were created for this analysis. Other variables included in the model were age, poverty status (based on participation in free-lunch program) in fluoridated and nonfluoridated areas, presence or absence of sealants, and education of the head of the household. The dependent variable (DMFS) was converted to a rank and the tests of significance were based on the rank of analysis of covariance.
RESULTS:	
Dental fluorosis	Tables were copied directly from Kumar and Swango (1999). Table 2 shows the distribution of dental fluorosis according to Dean's index by place of residence and year of examination. The highest prevalence of the very mild to severe categories was observed in Newburgh City in 1995 (18.6% combined, vs. 14.8% in Newburgh Town, 14.4% in New Windsor, 11.1% in Kingston, and 14.4% in Ulster). Between-survey comparisons show that neither the prevalence nor the severity of dental fluorosis increased after Newburgh Town was fluoridated. The case was the same for non-fluoridated areas. Changes were evident in Newburgh City (fluoridated), where a ridit analysis showed that the odds were 4 to 3 that a child examined in 1995 would have at

least questionable fluorosis, compared with a similar child in 1986.

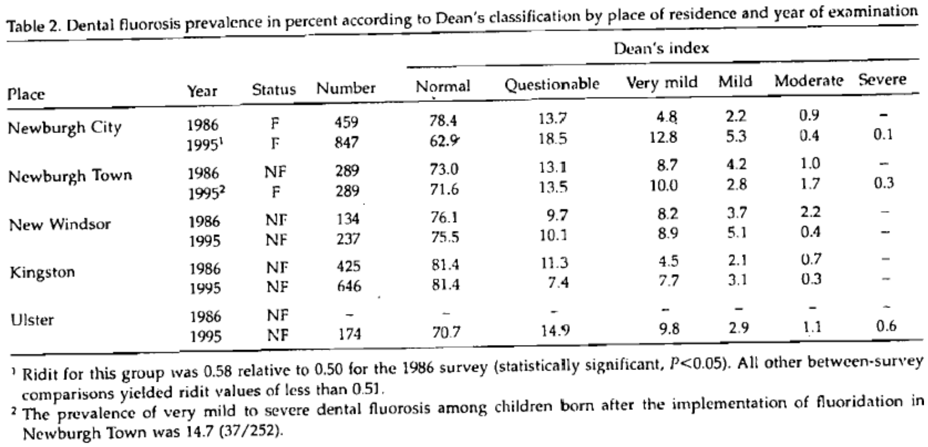


Table 2. Dental fluorosis prevalence in percent according to Dean's classification by place of residence and year of examination

				Dean's index					
Place	Year	Status	Number	Normal	Questionable	Very mild	Mild	Moderate	Severe
Newburgh City	1986	F	459	78.4	13.7	4.8	2.2	0.9	–
	1995[1]	F	847	62.9	18.5	12.8	5.3	0.4	0.1
Newburgh Town	1986	NF	289	73.0	13.1	8.7	4.2	1.0	–
	1995[2]	F	289	71.6	13.5	10.0	2.8	1.7	0.3
New Windsor	1986	NF	134	76.1	9.7	8.2	3.7	2.2	–
	1995	NF	237	75.5	10.1	8.9	5.1	0.4	–
Kingston	1986	NF	425	81.4	11.3	4.5	2.1	0.7	–
	1995	NF	646	81.4	7.4	7.7	3.1	0.3	–
Ulster	1986	NF	–	–	–	–	–	–	–
	1995	NF	174	70.7	14.9	9.8	2.9	1.1	0.6

[1] Ridit for this group was 0.58 relative to 0.50 for the 1986 survey (statistically significant, $P<0.05$). All other between-survey comparisons yielded ridit values of less than 0.51.

[2] The prevalence of very mild to severe dental fluorosis among children born after the implementation of fluoridation in Newburgh Town was 14.7 (37/252).

Table 3 summarizes the adjusted odds ratios associated with fluoride exposure and race by year of study. Children using fluoride tablets and early brushing had the highest odds ratios for very mild to severe fluorosis in both 1986 (OR: 5.0; CI: 2.5, 10.2) and 1995 (OR: 4.0; CI: 2.4, 6.9). Elevated odds ratios were observed for all the fluoride exposure variables in both years; however, exposure to fluoridation alone in 1986 was not statistically significant. African-American children studied in 1995 were at higher risk (OR: 2.3; CI: 1.8, 3.0) for dental fluorosis than children of other racial groups. While elevated odds ratios were observed for questionable fluorosis in 1995 (range: 1.6 to 4.4), they were not statistically significant in 1986 (range: 1.0 to 1.5).

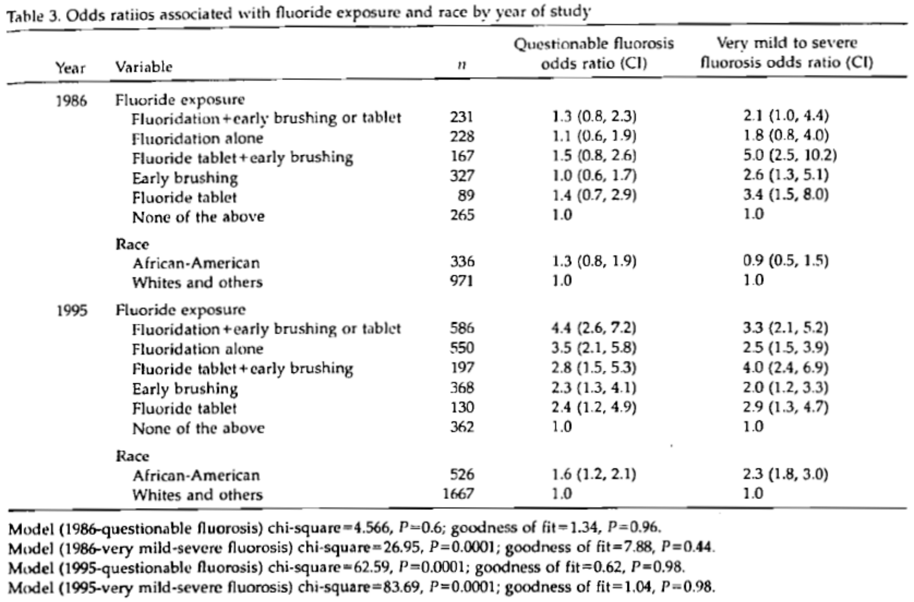


Table 3. Odds ratiios associated with fluoride exposure and race by year of study

Year	Variable	*n*	Questionable fluorosis odds ratio (CI)	Very mild to severe fluorosis odds ratio (CI)
1986	Fluoride exposure			
	Fluoridation + early brushing or tablet	231	1.3 (0.8, 2.3)	2.1 (1.0, 4.4)
	Fluoridation alone	228	1.1 (0.6, 1.9)	1.8 (0.8, 4.0)
	Fluoride tablet + early brushing	167	1.5 (0.8, 2.6)	5.0 (2.5, 10.2)
	Early brushing	327	1.0 (0.6, 1.7)	2.6 (1.3, 5.1)
	Fluoride tablet	89	1.4 (0.7, 2.9)	3.4 (1.5, 8.0)
	None of the above	265	1.0	1.0
	Race			
	African-American	336	1.3 (0.8, 1.9)	0.9 (0.5, 1.5)
	Whites and others	971	1.0	1.0
1995	Fluoride exposure			
	Fluoridation + early brushing or tablet	586	4.4 (2.6, 7.2)	3.3 (2.1, 5.2)
	Fluoridation alone	550	3.5 (2.1, 5.8)	2.5 (1.5, 3.9)
	Fluoride tablet + early brushing	197	2.8 (1.5, 5.3)	4.0 (2.4, 6.9)
	Early brushing	368	2.3 (1.3, 4.1)	2.0 (1.2, 3.3)
	Fluoride tablet	130	2.4 (1.2, 4.9)	2.9 (1.3, 4.7)
	None of the above	362	1.0	1.0
	Race			
	African-American	526	1.6 (1.2, 2.1)	2.3 (1.8, 3.0)
	Whites and others	1667	1.0	1.0

Model (1986-questionable fluorosis) chi-square = 4.566, $P = 0.6$; goodness of fit = 1.34, $P = 0.96$.
Model (1986-very mild-severe fluorosis) chi-square = 26.95, $P = 0.0001$; goodness of fit = 7.88, $P = 0.44$.
Model (1995-questionable fluorosis) chi-square = 62.59, $P = 0.0001$; goodness of fit = 0.62, $P = 0.98$.
Model (1995-very mild-severe fluorosis) chi-square = 83.69, $P = 0.0001$; goodness of fit = 1.04, $P = 0.98$.

Table 4 summarizes the results from the logistic regression analysis for fluorosis and the effect of year on race and fluoride exposure. In African-American children who received fluoride from sources other than water, the risk for very mild to severe fluorosis increased (OR 1.0 in 1986 vs. 10.5 in 1995), whereas for children of other racial groups there was a suggestion of slightly decreased risk (OR 0.9). Among those living in fluoridated areas, the risk for very mild to severe fluorosis increased for both racial groups and was slightly higher for African-American children (OR 3.9 for African-Americans vs. 2.5 for other racial groups). The risk for questionable fluorosis did not change from 1986 to 1995 in non-fluoridated areas for either racial category (OR 1.0); however, there was an increase in the OR from 1986 to 1995 for both racial categories (OR 1.7).

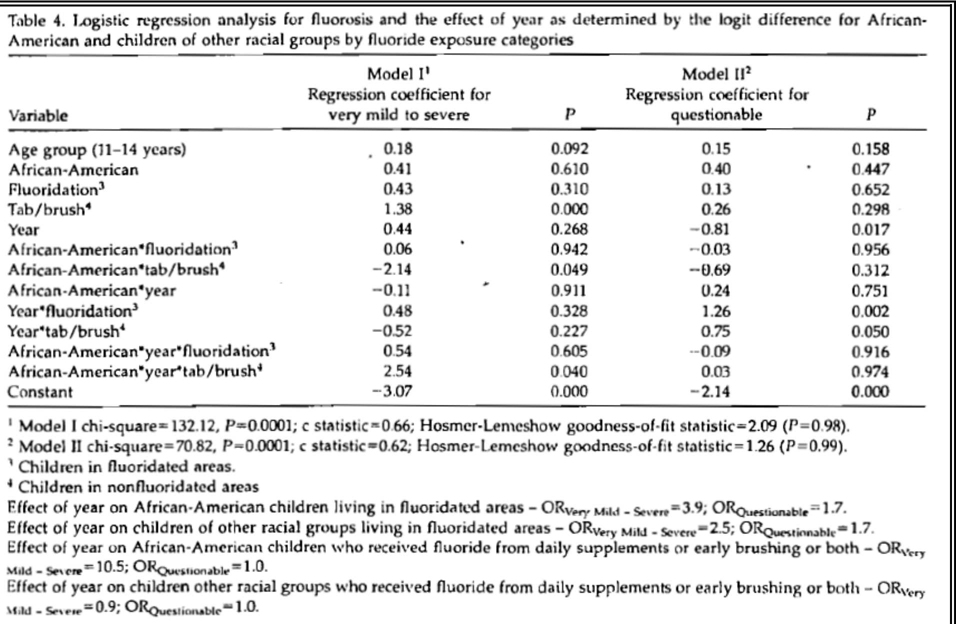


Table 4. Logistic regression analysis for fluorosis and the effect of year as determined by the logit difference for African-American and children of other racial groups by fluoride exposure categories

Variable	Model I^1 Regression coefficient for very mild to severe	P	Model II^2 Regression coefficient for questionable	P
Age group (11–14 years)	0.18	0.092	0.15	0.158
African-American	0.41	0.610	0.40	0.447
Fluoridation^3	0.43	0.310	0.13	0.652
Tab/brush^4	1.38	0.000	0.26	0.298
Year	0.44	0.268	−0.81	0.017
African-American*fluoridation^3	0.06	0.942	−0.03	0.956
African-American*tab/brush^4	−2.14	0.049	−0.69	0.312
African-American*year	−0.11	0.911	0.24	0.751
Year*fluoridation^3	0.48	0.328	1.26	0.002
Year*tab/brush^4	−0.52	0.227	0.75	0.050
African-American*year*fluoridation^3	0.54	0.605	−0.09	0.916
African-American*year*tab/brush^4	2.54	0.040	0.03	0.974
Constant	−3.07	0.000	−2.14	0.000

[1] Model I chi-square=132.12, P=0.0001; c statistic=0.66; Hosmer-Lemeshow goodness-of-fit statistic=2.09 (P=0.98).

[2] Model II chi-square=70.82, P=0.0001; c statistic=0.62; Hosmer-Lemeshow goodness-of-fit statistic=1.26 (P=0.99).

[3] Children in fluoridated areas.

[4] Children in nonfluoridated areas

Effect of year on African-American children living in fluoridated areas – $OR_{Very\ Mild\ -\ Severe}$=3.9; $OR_{Questionable}$=1.7.

Effect of year on children of other racial groups living in fluoridated areas – $OR_{Very\ Mild\ -\ Severe}$=2.5; $OR_{Questionable}$=1.7.

Effect of year on African-American children who received fluoride from daily supplements or early brushing or both – $OR_{Very\ Mild\ -\ Severe}$=10.5; $OR_{Questionable}$=1.0.

Effect of year on children other racial groups who received fluoride from daily supplements or early brushing or both – $OR_{Very\ Mild\ -\ Severe}$=0.9; $OR_{Questionable}$=1.0.

PROFILER'S NOTE: The profiler agrees that neither the prevalence nor the severity of fluorosis increased from 1986 to 1995 in Newburgh Town or in any of the non-fluoridated areas. In Newburgh City, there was a slightly higher prevalence of questionable, very mild, and mild fluorosis in 1995. For very mild to severe fluorosis, children using fluoride supplements and early brushing were at the highest risk. African-American children were at elevated risk compared to other racial groups in 1995.

Caries

Table 5 shows an inconsistent relationship between caries and fluorosis from the 1995 survey. The adjusted mean DMFS varied from a high of 1.39 among those with very mild fluorosis to a low of 0.65 among those with questionable fluorosis.

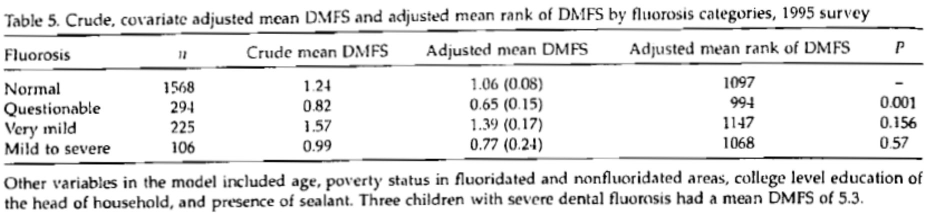


Table 5. Crude, covariate adjusted mean DMFS and adjusted mean rank of DMFS by fluorosis categories, 1995 survey

Fluorosis	n	Crude mean DMFS	Adjusted mean DMFS	Adjusted mean rank of DMFS	P
Normal	1568	1.24	1.06 (0.08)	1097	–
Questionable	294	0.82	0.65 (0.15)	994	0.001
Very mild	225	1.57	1.39 (0.17)	1147	0.156
Mild to severe	106	0.99	0.77 (0.24)	1068	0.57

Other variables in the model included age, poverty status in fluoridated and nonfluoridated areas, college level education of the head of household, and presence of sealant. Three children with severe dental fluorosis had a mean DMFS of 5.3.

PROFILER'S NOTE: No noteworthy information on the relationship between caries and fluorosis can be concluded from this data.

STUDY AUTHORS' CONCLUSIONS:

The two cross-sectional surveys conducted in 1986 and 1995 were considered sufficiently similar to allow a determination of the changes of risk over time. The risk of developing fluorosis did not decline over time in these communities. Water fluoridation affected fluorosis as evidenced by a significant increase in the prevalence and severity of fluorosis in Newburgh City. This increase was attributed primarily to the difference in duration of exposure to fluoridation between the two surveys. Residents of Newburgh City had continuous exposure since birth in the 1995 survey, but had a 3 year interruption in exposure in the 1986 survey. However, the increased risk associated with continuous exposure to water fluoridation may not result in an increase in fluorosis prevalence in every community after water fluoridation.

In Newburgh Town, fluoridated since 1984, neither the prevalence nor the severity of fluorosis changed between 1986 and 1995. It is likely that the total fluoride intake did not change since 71.3% of children in 1986 reported exposure to fluoride through supplements and/or early tooth brushing.

	A higher risk for fluorosis was observed in African-American children, consistent with other studies. In both surveys, the combined use of daily supplements and early brushing had the highest odds ratios for very mild to severe fluorosis. There was a significant association between the use of supplements or early brushing alone with mild to severe fluorosis. Although the three-way interaction term (year-race-fluoridation) was not statistically significant, the between survey risk increase for very mild to severe fluorosis among children in fluoridated areas was higher for African-Americans. The between survey change in the effect of fluoride supplements and/or early brushing was much more dramatic among African-American children. While African American children exposed to fluoride supplements and/or early brushing were more likely to develop fluorosis in 1995 compared to 1986, the reverse was true for children of other racial groups. No difference in risk was found for questionable fluorosis among racial groups.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	No references or definitions are cited.
PROFILER'S REMARKS ***Initials/date SJG/ 3/21/07***	Overall, the study was well-conducted and had adequate study design. However, the study was not designed for development of a dose response to fluoride; the emphasis was on the prevalence and severity of dental fluorosis in 7 to 14 year old children residing in fluoridated or non-fluoridated communities. Analysis of surveys conducted in 1986 and 1995 compared the effect of fluoride exposure (via water fluoridation, supplements and/or early brushing) on fluorosis with respect to year and racial group (i.e., Did the prevalence and/severity of fluorosis differ over time? Is there a different risk associated with various sources of fluoride exposure? Are African-American children at higher risk for developing fluorosis?). Neither the prevalence nor the severity of fluorosis increased from 1986 to 1995 in Newburgh Town (after fluoridation) or in any of the non-fluoridated areas. In Newburgh City (fluoridated), there was a slightly higher prevalence of questionable, very mild, and mild fluorosis in 1995; these children had lifelong exposure to fluoride in the water while those in the 1986 survey had a 3 year interruption. For very mild to severe fluorosis, children using fluoride supplements and early brushing were at the highest risk, although all fluoride exposures had elevated risk. African-American children were at elevated risk compared to other racial groups in 1995. No difference in risk was found for questionable fluorosis among racial groups. Although caries were evaluated (DMFS score), data was not presented in a clear manner to make any noteworthy conclusions regarding the relationship between fluorosis or fluoride exposure and caries. Factors that may affect the results, common to all cross-sectional studies, include: examiner variation, population differences, representativeness of the sample and recall of past events for exposure assessment. Fluoride level was not reported for Newburgh Town. The fluoride concentration in supplement tablets or toothpaste was not reported.
PROFILER'S ESTIM. NOEL/ NOAEL	Study design was not suitable for development of a NOAEL for dental fluorosis or caries.
PROFILER'S ESTIM. LOEL/ LOAEL	Study design was not suitable for development of a LOAEL for dental fluorosis or caries.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (X), Poor ( ), Medium ( ), Strong ( ) While the study was well-conducted, the study design was not conducive to provide data for a dose-response. The study indicated a higher risk (odds ratio) for mild to severe fluorosis with fluoride exposure (via water fluoridation, supplements and/or early brushing). African-American children were at higher risk than other racial groups. The

	study did not address any issues of plaque or gingivitis.
CRITICAL EFFECT(S):	Prevalence and severity of dental fluorosis

Kumar, J.V. and Swango P.A. 1999. Fluoride exposure and dental fluorosis in Newburgh and Kingston, New York: policy implications. Community Dent. Oral Epidemiol. 27: 171-180.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Cross-sectional
POPULATION STUDIED:	U.S./New York/Newburgh City (fluoridated water supply): 7-14 yr-old school children (lifelong residents); 459 (47.9% male; 51.6% African-American) surveyed in 1986; 847 (49.0% male; 41.1% African-American) surveyed in 1995. U.S./New York/Newburgh Town (fluoridated water supply): 7-14 yr-old school children (lifelong residents); 289 (58.8% male; 8.3% African-American) surveyed in 1986; 289 (49.1% male, 10.4% African-American) surveyed in 1995.
CONTROL POPULATION:	U.S./New York/New Windsor (non-fluoridated water supply): 7-14 yr-old old school children (lifelong residents):-; 134 children (52.2% male, 5.2% African-American) surveyed in 1986; 237 (41.8% male, 6.8% African-American) surveyed in 1995. U.S./New York/ Kingston (non-fluoridated water supply): 7-14 yr-old school children (lifelong residents); 425 children (50.3% male; 16.0% African-American) surveyed in 1986; 646 (50.8% male, 19.2% African-American) surveyed in 1995. U.S./New York/Ulster (non-fluoridated water supply): 7-14 yr-old school children (lifelong residents), 174 children (50.0% male; 4.6% African-American) surveyed in 1995. PROFILER'S NOTE: Although the children in New Windsor, Kingston and Ulster did not have exposure to fluoridated water, some had exposure from fluoride supplements (tablets) and dentifrices with fluoride (see Table 1 under Exposure Groups).
EXPOSURE PERIOD:	Children from Newburgh City were exposed throughout their lifetime, except during a three year period from 1978 to 1981 (affecting children from the 1986 survey as follows: 7 year-olds from 0-2 years of age; 8 yr-olds from 0-3 years of age; 9 yr-olds from 1-4 years of age, etc., ranging up to 14 yr-olds affected from 6-9 years of age). Children from Newburgh Town surveyed in 1986 were exposed to fluoridation for 2 years. Those surveyed in 1995 were exposed beginning from birth up to age 3 for a maximum of 11 years. Children from New Windsor, Kingston, and Ulster were not exposed to fluoride in the drinking water supply.
EXPOSURE GROUPS:	Table 1 was copied directly from Kumar and Swango (1999) and summarizes the percent distribution of children in each study community according to age group, gender, race, and fluoride exposure. Males and females generally were equally represented in all areas, although there were differences in gender between 1986 and 1995 in Newburgh Town and New Windsor. In both 1986 and 1995, there were proportionally more African-American children in Newburgh City compared to other areas. The major (80-95%) race represented in each community was White or 'other', with 5 to 20% African-American; the exception was Newburgh City where African-Americans made up 52% and 41% in 1986 and 1995, respectively

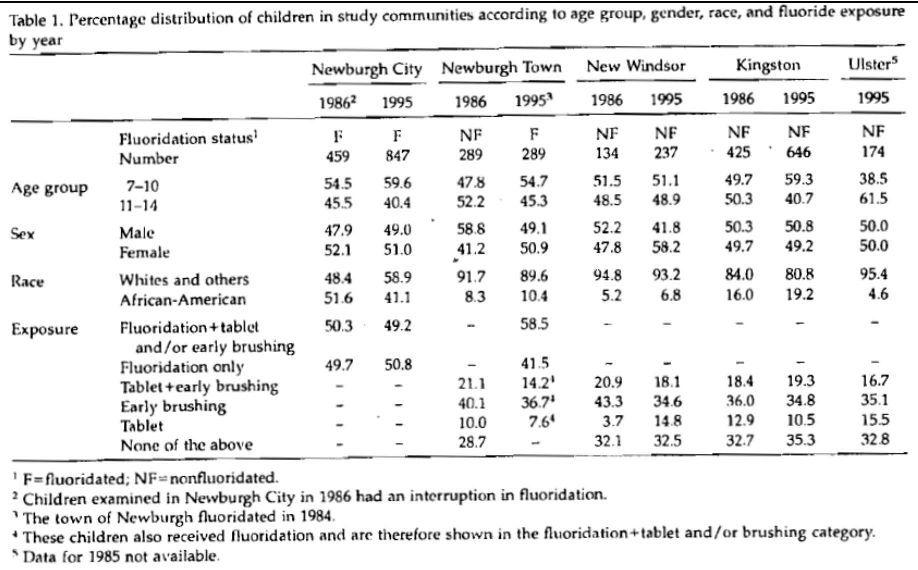


Table 1. Percentage distribution of children in study communities according to age group, gender, race, and fluoride exposure by year

		Newburgh City		Newburgh Town		New Windsor		Kingston		Ulster[5]
		1986[2]	1995	1986	1995[3]	1986	1995	1986	1995	1995
	Fluoridation status[1]	F	F	NF	F	NF	NF	NF	NF	NF
	Number	459	847	289	289	134	237	425	646	174
Age group	7–10	54.5	59.6	47.8	54.7	51.5	51.1	49.7	59.3	38.5
	11–14	45.5	40.4	52.2	45.3	48.5	48.9	50.3	40.7	61.5
Sex	Male	47.9	49.0	58.8	49.1	52.2	41.8	50.3	50.8	50.0
	Female	52.1	51.0	41.2	50.9	47.8	58.2	49.7	49.2	50.0
Race	Whites and others	48.4	58.9	91.7	89.6	94.8	93.2	84.0	80.8	95.4
	African-American	51.6	41.1	8.3	10.4	5.2	6.8	16.0	19.2	4.6
Exposure	Fluoridation+tablet and/or early brushing	50.3	49.2	–	58.5	–	–	–	–	–
	Fluoridation only	49.7	50.8	–	41.5	–	–	–	–	–
	Tablet+early brushing	–	–	21.1	14.2[4]	20.9	18.1	18.4	19.3	16.7
	Early brushing	–	–	40.1	36.7[4]	43.3	34.6	36.0	34.8	35.1
	Tablet	–	–	10.0	7.6[4]	3.7	14.8	12.9	10.5	15.5
	None of the above	–	–	28.7	–	32.1	32.5	32.7	35.3	32.8

[1] F=fluoridated; NF=nonfluoridated.

[2] Children examined in Newburgh City in 1986 had an interruption in fluoridation.

[3] The town of Newburgh fluoridated in 1984.

[4] These children also received fluoridation and are therefore shown in the fluoridation+tablet and/or brushing category.

[5] Data for 1985 not available.

EXPOSURE ASSESSMENT:

Some children in all the surveyed communities also were exposed to fluoride from other sources, including fluoride tablet supplements and early brushing (before age 2 years) with fluoridated toothpaste.

In the non-fluoridated communities 9see Table 1), approximately one third (29-35%) of the children were not exposed to fluoride from any source considered (water, tablet, early brushing); approximately another third (35-43%) were exposed only by early brushing; the remainder were exposed via tablet only (4-15%) or tablet plus early brushing (17-21%).

ANALYTICAL METHODS:

Data for measuring the fluoride concentrations were not included in the study report. Water quality parameters were not measured. The fluoride concentration in supplement tablets or toothpaste was not included.

STUDY DESIGN:

The purpose of the study was to determine whether the risk imposed by fluoride exposure has changed during the time period from 1986 to 1995, and to determine the effect of water fluoridation and other known fluoride sources (fluoride levels not reported) on dental fluorosis in participating children. Data were obtained from two cross-sectional surveys, conducted in 1986 and 1995 during the school years in the Newburgh and Kingston school districts. Analysis was limited to 3500, 7-14 year old lifelong residents of Newburgh City (fluoridated at 1±0.2 mg/L since 1945, with a 3 year interruption from 1978 to 1981), Newburgh Town (fluoridated since 1984—level not reported), and New Windsor, Kingston, or Ulster (all non-fluoridated).

The two surveys were similar in design except for the number of children studied (n=1307 in 1986; n=2193 in 1995). Dental fluorosis and caries were recorded using Dean's criteria and the Decayed, Missing and Filled Tooth Surfaces (DMFS) index. Examination details were not reported, including the examiners, location where examinations occurred, lighting conditions, or equipment used. Examiners were blind to residential and fluoridation status of the children. Fluoride exposure data was collected by questionnaire. The questionnaire design differed between studies as follows:

6) The responses in the 1986 survey were primarily open-ended for the two questions related to the use of fluoride toothpaste and fluoride tablets. In the 1995 survey, categories for these two items were created.
7) Questions related to school lunch program participation, education of the head of the household, and breast-feeding were not included in the 1986 survey.
8) The response rate for participation was lower in 1995 (38%) than in 1986 (58%).

	9) Children from the town of Ulster could not be identified from the 1986 survey because a question regarding their place of residence was not included. 10) Different examiners were used in each survey, although they were trained by the same dentist. PROFILER'S NOTE: Dean's Index of Fluorosis is described in Section 2 of the report).
PARAMETERS MONITORED:	Dental fluorosis was measured using Dean's classification at the subject level. Fluorosis was scaled as none, questionable, very mild, mild, moderate or severe. Dental caries was recorded using the DMFS index (number of decayed, missing and filled permanent tooth surfaces) and visual-tactile examination.
STATISTICAL METHODS:	Regression procedures were used to estimate the effect of fluoridation, fluoride supplements, and early brushing on dental fluorosis. Analysis involved comparison of frequency distributions of Dean's fluorosis categories to examine changes over time, including a "ridit" analysis to examine the changes in severity. The proportion of children exposed to known fluoride sources was calculated for each category: a) fluoridation alone; b) fluoridation plus tablet and/or early brushing; c) tablet supplement alone; d) early tooth brushing alone; e) tablet supplement plus early brushing; f) none of the above exposures. Adjusted odds ratios and 95% confidence intervals were calculated for the variables associated with dental fluorosis in the bivariate analysis ($p<0.1$). This model included race and the categories for fluoride exposure variables. The fluoride exposure variable was introduced as an indicator variable and the reference group consisted of children from the non-fluoridated areas without known fluoride exposure. Logistic regression procedures were used to estimate the association between factors and dental fluorosis separately for the two surveys, and then were used to fit a generalized "logit" model for examining the effect of year, race and fluoride exposure and their interactions. Two separate regression models were constructed to compare categories of fluorosis: one to compare the questionable category with the normal, and another to compare the very mild to severe category (combined) with the normal. The examination of two-way and three-way interaction terms requires larger sample sizes, so exposure categories were combined as follows: a) fluoridation alone or fluoridation plus tablet and/or early brushing; b) tablet supplement alone or early tooth brushing alone or tablet supplement plus early brushing; c) reference group with none of the above exposures. The purpose of this analysis was to determine whether there were changes in the risk associated with fluoride exposure between the two surveys for African-American children and children of other racial groups. Analyses of crude, covariate-adjusted and ranked DMFS scores were performed to determine the relationship between caries and dental fluorosis. Four categories of fluorosis (normal, questionable, very mild, and mild to severe) were created for this analysis. Other variables included in the model were age, poverty status (based on participation in free-lunch program) in fluoridated and nonfluoridated areas, presence or absence of sealants, and education of the head of the household. The dependent variable (DMFS) was converted to a rank and the tests of significance were based on the rank of analysis of covariance.
RESULTS:	
Dental fluorosis	Tables were copied directly from Kumar and Swango (1999). Table 2 shows the distribution of dental fluorosis according to Dean's index by place of residence and year of examination. The highest prevalence of the very mild to severe categories was observed in Newburgh City in 1995 (18.6% combined, vs. 14.8% in Newburgh Town, 14.4% in New Windsor, 11.1% in Kingston, and 14.4% in Ulster). Between-survey comparisons show that neither the prevalence nor the severity of dental fluorosis increased after Newburgh Town was fluoridated. The case was the same for non-fluoridated areas. Changes were evident in Newburgh City (fluoridated), where a ridit analysis showed that the odds were 4 to 3 that a child examined in 1995 would have at

least questionable fluorosis, compared with a similar child in 1986.

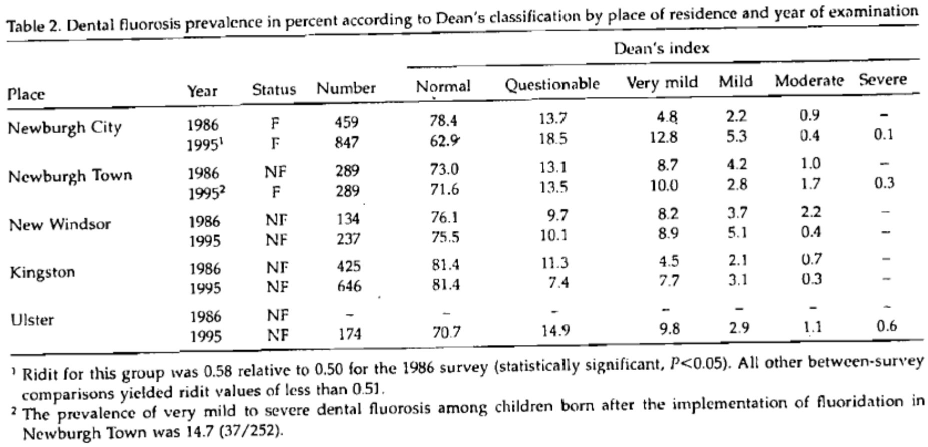


Table 2. Dental fluorosis prevalence in percent according to Dean's classification by place of residence and year of examination

				Dean's index					
Place	Year	Status	Number	Normal	Questionable	Very mild	Mild	Moderate	Severe
Newburgh City	1986	F	459	78.4	13.7	4.8	2.2	0.9	–
	1995[1]	F	847	62.9	18.5	12.8	5.3	0.4	0.1
Newburgh Town	1986	NF	289	73.0	13.1	8.7	4.2	1.0	–
	1995[2]	F	289	71.6	13.5	10.0	2.8	1.7	0.3
New Windsor	1986	NF	134	76.1	9.7	8.2	3.7	2.2	–
	1995	NF	237	75.5	10.1	8.9	5.1	0.4	–
Kingston	1986	NF	425	81.4	11.3	4.5	2.1	0.7	–
	1995	NF	646	81.4	7.4	7.7	3.1	0.3	–
Ulster	1986	NF	–	–	–	–	–	–	–
	1995	NF	174	70.7	14.9	9.8	2.9	1.1	0.6

[1] Ridit for this group was 0.58 relative to 0.50 for the 1986 survey (statistically significant, $P<0.05$). All other between-survey comparisons yielded ridit values of less than 0.51.

[2] The prevalence of very mild to severe dental fluorosis among children born after the implementation of fluoridation in Newburgh Town was 14.7 (37/252).

Table 3 summarizes the adjusted odds ratios associated with fluoride exposure and race by year of study. Children using fluoride tablets and early brushing had the highest odds ratios for very mild to severe fluorosis in both 1986 (OR: 5.0; CI: 2.5, 10.2) and 1995 (OR: 4.0; CI: 2.4, 6.9). Elevated odds ratios were observed for all the fluoride exposure variables in both years; however, exposure to fluoridation alone in 1986 was not statistically significant. African-American children studied in 1995 were at higher risk (OR: 2.3; CI: 1.8, 3.0) for dental fluorosis than children of other racial groups. While elevated odds ratios were observed for questionable fluorosis in 1995 (range: 1.6 to 4.4), they were not statistically significant in 1986 (range: 1.0 to 1.5).

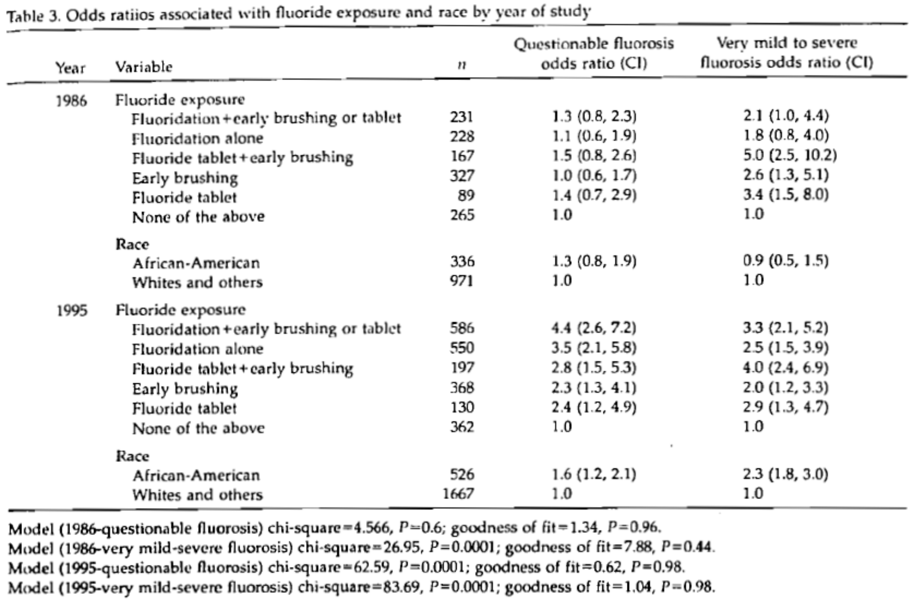


Table 3. Odds ratiios associated with fluoride exposure and race by year of study

Year	Variable	n	Questionable fluorosis odds ratio (CI)	Very mild to severe fluorosis odds ratio (CI)
1986	Fluoride exposure			
	Fluoridation + early brushing or tablet	231	1.3 (0.8, 2.3)	2.1 (1.0, 4.4)
	Fluoridation alone	228	1.1 (0.6, 1.9)	1.8 (0.8, 4.0)
	Fluoride tablet + early brushing	167	1.5 (0.8, 2.6)	5.0 (2.5, 10.2)
	Early brushing	327	1.0 (0.6, 1.7)	2.6 (1.3, 5.1)
	Fluoride tablet	89	1.4 (0.7, 2.9)	3.4 (1.5, 8.0)
	None of the above	265	1.0	1.0
	Race			
	African-American	336	1.3 (0.8, 1.9)	0.9 (0.5, 1.5)
	Whites and others	971	1.0	1.0
1995	Fluoride exposure			
	Fluoridation + early brushing or tablet	586	4.4 (2.6, 7.2)	3.3 (2.1, 5.2)
	Fluoridation alone	550	3.5 (2.1, 5.8)	2.5 (1.5, 3.9)
	Fluoride tablet + early brushing	197	2.8 (1.5, 5.3)	4.0 (2.4, 6.9)
	Early brushing	368	2.3 (1.3, 4.1)	2.0 (1.2, 3.3)
	Fluoride tablet	130	2.4 (1.2, 4.9)	2.9 (1.3, 4.7)
	None of the above	362	1.0	1.0
	Race			
	African-American	526	1.6 (1.2, 2.1)	2.3 (1.8, 3.0)
	Whites and others	1667	1.0	1.0

Model (1986-questionable fluorosis) chi-square=4.566, $P=0.6$; goodness of fit=1.34, $P=0.96$.
Model (1986-very mild-severe fluorosis) chi-square=26.95, $P=0.0001$; goodness of fit=7.88, $P=0.44$.
Model (1995-questionable fluorosis) chi-square=62.59, $P=0.0001$; goodness of fit=0.62, $P=0.98$.
Model (1995-very mild-severe fluorosis) chi-square=83.69, $P=0.0001$; goodness of fit=1.04, $P=0.98$.

Table 4 summarizes the results from the logistic regression analysis for fluorosis and the effect of year on race and fluoride exposure. In African-American children who received fluoride from sources other than water, the risk for very mild to severe fluorosis increased (OR 1.0 in 1986 vs. 10.5 in 1995), whereas for children of other racial groups there was a suggestion of slightly decreased risk (OR 0.9). Among those living in fluoridated areas, the risk for very mild to severe fluorosis increased for both racial groups and was slightly higher for African-American children (OR 3.9 for African-Americans vs. 2.5 for other racial groups). The risk for questionable fluorosis did not change from 1986 to 1995 in non-fluoridated areas for either racial category (OR 1.0); however, there was an increase in the OR from 1986 to 1995 for both racial categories (OR 1.7).

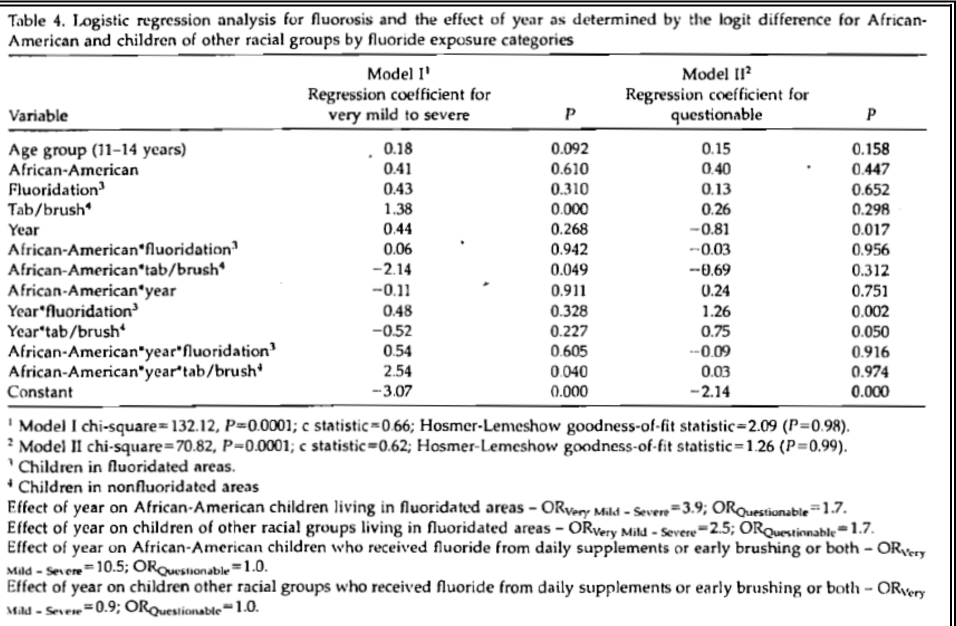


Table 4. Logistic regression analysis for fluorosis and the effect of year as determined by the logit difference for African-American and children of other racial groups by fluoride exposure categories

Variable	Model I[1] Regression coefficient for very mild to severe	P	Model II[2] Regression coefficient for questionable	P
Age group (11–14 years)	0.18	0.092	0.15	0.158
African-American	0.41	0.610	0.40	0.447
Fluoridation[3]	0.43	0.310	0.13	0.652
Tab/brush[4]	1.38	0.000	0.26	0.298
Year	0.44	0.268	−0.81	0.017
African-American*fluoridation[3]	0.06	0.942	−0.03	0.956
African-American*tab/brush[4]	−2.14	0.049	−0.69	0.312
African-American*year	−0.11	0.911	0.24	0.751
Year*fluoridation[3]	0.48	0.328	1.26	0.002
Year*tab/brush[4]	−0.52	0.227	0.75	0.050
African-American*year*fluoridation[3]	0.54	0.605	−0.09	0.916
African-American*year*tab/brush[4]	2.54	0.040	0.03	0.974
Constant	−3.07	0.000	−2.14	0.000

[1] Model I chi-square=132.12, P=0.0001; c statistic=0.66; Hosmer-Lemeshow goodness-of-fit statistic=2.09 (P=0.98).

[2] Model II chi-square=70.82, P=0.0001; c statistic=0.62; Hosmer-Lemeshow goodness-of-fit statistic=1.26 (P=0.99).

[3] Children in fluoridated areas.

[4] Children in nonfluoridated areas

Effect of year on African-American children living in fluoridated areas – $OR_{Very\ Mild\ -\ Severe}$=3.9; $OR_{Questionable}$=1.7.

Effect of year on children of other racial groups living in fluoridated areas – $OR_{Very\ Mild\ -\ Severe}$=2.5; $OR_{Questionable}$=1.7.

Effect of year on African-American children who received fluoride from daily supplements or early brushing or both – $OR_{Very\ Mild\ -\ Severe}$=10.5; $OR_{Questionable}$=1.0.

Effect of year on children other racial groups who received fluoride from daily supplements or early brushing or both – $OR_{Very\ Mild\ -\ Severe}$=0.9; $OR_{Questionable}$=1.0.

PROFILER'S NOTE: The profiler agrees that neither the prevalence nor the severity of fluorosis increased from 1986 to 1995 in Newburgh Town or in any of the non-fluoridated areas. In Newburgh City, there was a slightly higher prevalence of questionable, very mild, and mild fluorosis in 1995. For very mild to severe fluorosis, children using fluoride supplements and early brushing were at the highest risk. African-American children were at elevated risk compared to other racial groups in 1995.

Caries

Table 5 shows an inconsistent relationship between caries and fluorosis from the 1995 survey. The adjusted mean DMFS varied from a high of 1.39 among those with very mild fluorosis to a low of 0.65 among those with questionable fluorosis.

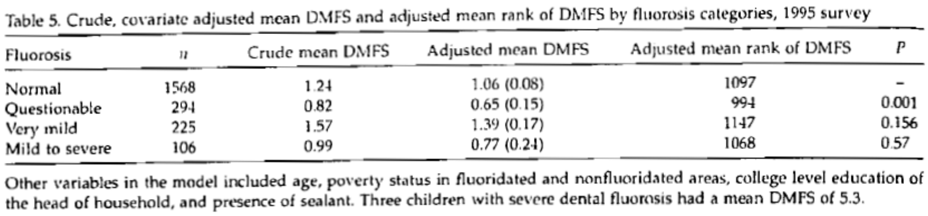


Table 5. Crude, covariate adjusted mean DMFS and adjusted mean rank of DMFS by fluorosis categories, 1995 survey

Fluorosis	n	Crude mean DMFS	Adjusted mean DMFS	Adjusted mean rank of DMFS	P
Normal	1568	1.24	1.06 (0.08)	1097	–
Questionable	294	0.82	0.65 (0.15)	994	0.001
Very mild	225	1.57	1.39 (0.17)	1147	0.156
Mild to severe	106	0.99	0.77 (0.24)	1068	0.57

Other variables in the model included age, poverty status in fluoridated and nonfluoridated areas, college level education of the head of household, and presence of sealant. Three children with severe dental fluorosis had a mean DMFS of 5.3.

PROFILER'S NOTE: No noteworthy information on the relationship between caries and fluorosis can be concluded from this data.

STUDY AUTHORS' CONCLUSIONS:

The two cross-sectional surveys conducted in 1986 and 1995 were considered sufficiently similar to allow a determination of the changes of risk over time. The risk of developing fluorosis did not decline over time in these communities. Water fluoridation affected fluorosis as evidenced by a significant increase in the prevalence and severity of fluorosis in Newburgh City. This increase was attributed primarily to the difference in duration of exposure to fluoridation between the two surveys. Residents of Newburgh City had continuous exposure since birth in the 1995 survey, but had a 3 year interruption in exposure in the 1986 survey. However, the increased risk associated with continuous exposure to water fluoridation may not result in an increase in fluorosis prevalence in every community after water fluoridation.

In Newburgh Town, fluoridated since 1984, neither the prevalence nor the severity of fluorosis changed between 1986 and 1995. It is likely that the total fluoride intake did not change since 71.3% of children in 1986 reported exposure to fluoride through supplements and/or early tooth brushing.

		A higher risk for fluorosis was observed in African-American children, consistent with other studies. In both surveys, the combined use of daily supplements and early brushing had the highest odds ratios for very mild to severe fluorosis. There was a significant association between the use of supplements or early brushing alone with mild to severe fluorosis. Although the three-way interaction term (year-race-fluoridation) was not statistically significant, the between survey risk increase for very mild to severe fluorosis among children in fluoridated areas was higher for African-Americans. The between survey change in the effect of fluoride supplements and/or early brushing was much more dramatic among African-American children. While African American children exposed to fluoride supplements and/or early brushing were more likely to develop fluorosis in 1995 compared to 1986, the reverse was true for children of other racial groups. No difference in risk was found for questionable fluorosis among racial groups.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		No references or definitions are cited.
PROFILER'S REMARKS	***Initials/date SJG/ 3/21/07***	Overall, the study was well-conducted and had adequate study design. However, the study was not designed for development of a dose response to fluoride; the emphasis was on the prevalence and severity of dental fluorosis in 7 to 14 year old children residing in fluoridated or non-fluoridated communities. Analysis of surveys conducted in 1986 and 1995 compared the effect of fluoride exposure (via water fluoridation, supplements and/or early brushing) on fluorosis with respect to year and racial group (i.e., Did the prevalence and/severity of fluorosis differ over time? Is there a different risk associated with various sources of fluoride exposure? Are African-American children at higher risk for developing fluorosis?). Neither the prevalence nor the severity of fluorosis increased from 1986 to 1995 in Newburgh Town (after fluoridation) or in any of the non-fluoridated areas. In Newburgh City (fluoridated), there was a slightly higher prevalence of questionable, very mild, and mild fluorosis in 1995; these children had lifelong exposure to fluoride in the water while those in the 1986 survey had a 3 year interruption. For very mild to severe fluorosis, children using fluoride supplements and early brushing were at the highest risk, although all fluoride exposures had elevated risk. African-American children were at elevated risk compared to other racial groups in 1995. No difference in risk was found for questionable fluorosis among racial groups. Although caries were evaluated (DMFS score), data was not presented in a clear manner to make any noteworthy conclusions regarding the relationship between fluorosis or fluoride exposure and caries. Factors that may affect the results, common to all cross-sectional studies, include: examiner variation, population differences, representativeness of the sample and recall of past events for exposure assessment. Fluoride level was not reported for Newburgh Town. The fluoride concentration in supplement tablets or toothpaste was not reported.
PROFILER'S ESTIM. NOEL/ NOAEL		Study design was not suitable for development of a NOAEL for dental fluorosis or caries.
PROFILER'S ESTIM. LOEL/ LOAEL		Study design was not suitable for development of a LOAEL for dental fluorosis or caries.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( ) While the study was well-conducted, the study design was not conducive to provide data for a dose-response. The study indicated a higher risk (odds ratio) for mild to severe fluorosis with fluoride exposure (via water fluoridation, supplements and/or early brushing). African-American children were at higher risk than other racial groups. The

	study did not address any issues of plaque or gingivitis.
CRITICAL EFFECT(S):	Prevalence and severity of dental fluorosis

Leake, J., F. Goettler, B. Stahl-Quinlan and H. Stewart. 2002. Has the level of dental fluorosis among Toronto children changed? J Can Dent Assoc 68(1):21-5.

ENDPOINT STUDIED:	Dental caries and fluorosis (maxillary permanent anterior teeth)
TYPE OF STUDY:	Prevalence study of dental caries and fluorosis.
POPULATION STUDIED:	Canada/Toronto: The current study reports results for 2435 children aged 7 to 13 years out of an overall total of 3657 children (number of males and females not specified) aged 5, 7 or 13 years from high-, medium- and low-risk schools in each of four health regions (3 x 3 x 4 cells) of Toronto, Canada. (According to Toronto standards, a school is at medium risk if between 9.5% and 14.0% of junior and senior kindergarten children have decay on 2 or more teeth. Definitions for low- and high-risk schools were not provided in the study report.)
CONTROL POPULATION:	None.
EXPOSURE PERIOD:	Study was conducted in 1999-2000 with 7 and 13 yr-old children (N = 2435 in these age classes).
EXPOSURE GROUPS:	The study population was not divided into groups based on fluoride levels in the drinking water. Fluoride concentrations in drinking water were not measured, although the authors report that the Toronto water system has been fluoridated since 1963, and the F concentration was gradually reduced from 1.2 ppm to 0.8 ppm in 1999 to meet revised Canadian water standards (Health Canada 1996).
EXPOSURE ASSESSMENT	No estimates of fluoride intake were provided.
ANALYTICAL METHODS:	None
STUDY DESIGN	The purpose of the study was to obtain valid estimates of the oral health status of a probability sample of children in 4 regions of the newly amalgamated city of Toronto, Ontario, Canada. An overall total of 3657 children (number of males and females not provided) were enrolled in the parent study, of which 2435 between the ages of 7-13 were evaluated in the current report. The current study was conducted during the 1999-2000 school year and included examinations for caries in all children and for fluorosis of the maxillary permanent anterior teeth in 7- and 13-year-old children. One of two specially trained dental hygienists examined each child's teeth and periodontal tissues. The two examiners were trained during separate, day-long sessions by the senior investigator (J.L.L.). Compliance with the criteria of the protocol was rechecked approximately biweekly by the senior investigator, who independently examined children enrolled in the study and compared his results to those of the 2 examiners.] A two-stage sampling process was used. During the first stage, 6 schools for each cell (age, risk category and region) were selected. Then a random start and cell-specific sampling ratio (age-specific enrolment in the 6 schools divided by 100) was used to select the children to be included in each cell. Informed consent was obtained from parents. The survey examination followed the protocol issued by the Ontario Ministry of Health (Ontario Ministry of Health, 1998), as described under PARAMETERS MONITORED. The protocol also calls for examiners to indicate whether the child has urgent treatment needs; criteria include the presence of pain, infection, hemorrhage, trauma, large open lesions and acute periodontal conditions.
PARAMETERS MONITORED:	The survey examination followed the protocol issued by the Ontario Ministry of Health. The protocol states that only dentinal caries are to be scored at the level of the tooth, i.e., surface scores are not recorded. Fluorosis was measured on the maxillary permanent anterior teeth of 2435 children aged 7 and 13 years according to the Tooth Surface Index of

Fluorosis (TSIF; see Section 2). The ministry protocol states that TSIF be scored, in terms of the highest score on bilateral pairs of teeth, as none (TSIF=0); parchment white patches visible on less than one-third of the tooth surface (TSIF=1); parchment white color visible on at least one-third but less than two-thirds of the tooth surface (TSIF=2); parchment white color visible on two-thirds or more of the tooth surface (TSIF=3); and staining or pitting (or both) in conjunction with a TSIF score of 1, 2 or 3 (TSIF=4).

STATISTICAL METHODS:

Data were transferred to the Statistical Package for Social Sciences (SPSS). The descriptive findings were weighted according to the city's population in each age group. Tests for associations with potential determinants were conducted on the unweighted data. Basic findings were recorded according to the O'Keefe template (O'Keefe, 1995). For fluorosis, the reporting cut-off of a score of 2 or more reflects the untested hypothesis that most parents and children would not be aware of a condition scoring 1. No fluorosis findings were reported in 5-year-olds since only permanent teeth were examined for this condition.

RESULTS:

Results of the study in Tables 1 through 4 are shown directly from Leake, et al. (2002) and are limited to findings of fluorosis on maxillary permanent anterior teeth and its relationship to prevalence/severity of caries. The authors state that "a score of 1…is by convention assumed to be aesthetically unimportant" (p. 23).

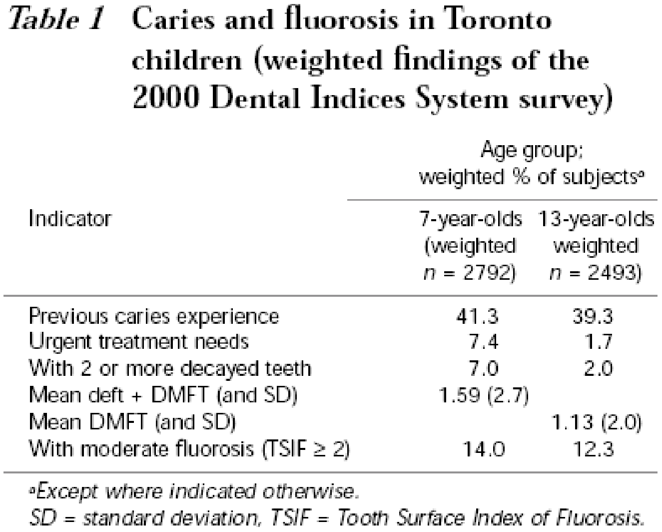


Table 1 **Caries and fluorosis in Toronto children (weighted findings of the 2000 Dental Indices System survey)**

Indicator	Age group; weighted % of subjects[a]	
	7-year-olds (weighted n = 2792)	13-year-olds weighted n = 2493)
Previous caries experience	41.3	39.3
Urgent treatment needs	7.4	1.7
With 2 or more decayed teeth	7.0	2.0
Mean deft + DMFT (and SD)	1.59 (2.7)	
Mean DMFT (and SD)		1.13 (2.0)
With moderate fluorosis (TSIF ≥ 2)	14.0	12.3

[a]Except where indicated otherwise.
SD = standard deviation, TSIF = Tooth Surface Index of Fluorosis.

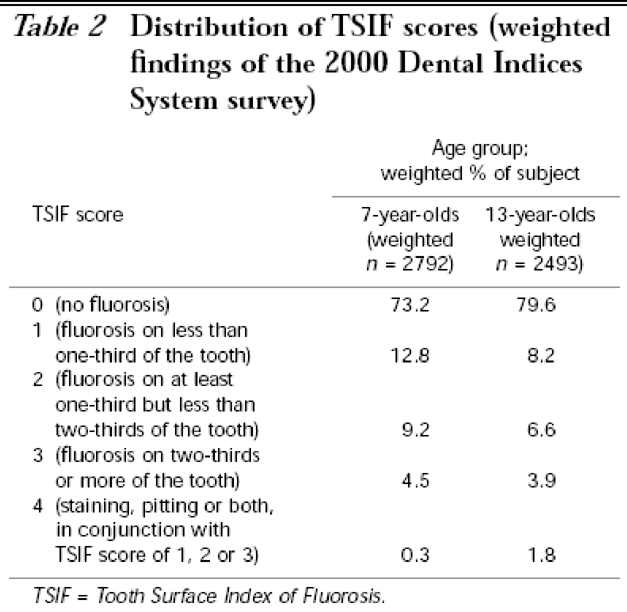


Table 2 **Distribution of TSIF scores (weighted findings of the 2000 Dental Indices System survey)**

TSIF score	Age group; weighted % of subject 7-year-olds (weighted *n* = 2792)	13-year-olds weighted *n* = 2493)
0 (no fluorosis)	73.2	79.6
1 (fluorosis on less than one-third of the tooth)	12.8	8.2
2 (fluorosis on at least one-third but less than two-thirds of the tooth)	9.2	6.6
3 (fluorosis on two-thirds or more of the tooth)	4.5	3.9
4 (staining, pitting or both, in conjunction with TSIF score of 1, 2 or 3)	0.3	1.8

TSIF = Tooth Surface Index of Fluorosis.

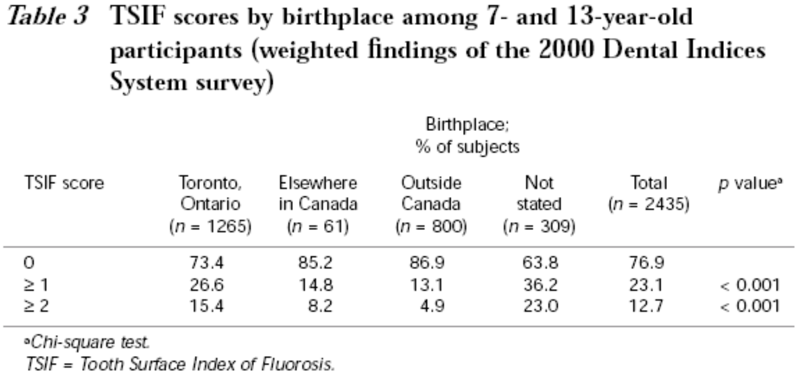


Table 3 **TSIF scores by birthplace among 7- and 13-year-old participants (weighted findings of the 2000 Dental Indices System survey)**

TSIF score	Birthplace; % of subjects Toronto, Ontario (*n* = 1265)	Elsewhere in Canada (*n* = 61)	Outside Canada (*n* = 800)	Not stated (*n* = 309)	Total (*n* = 2435)	*p* value[a]
0	73.4	85.2	86.9	63.8	76.9	
≥ 1	26.6	14.8	13.1	36.2	23.1	< 0.001
≥ 2	15.4	8.2	4.9	23.0	12.7	< 0.001

[a]*Chi-square test.*
TSIF = Tooth Surface Index of Fluorosis.

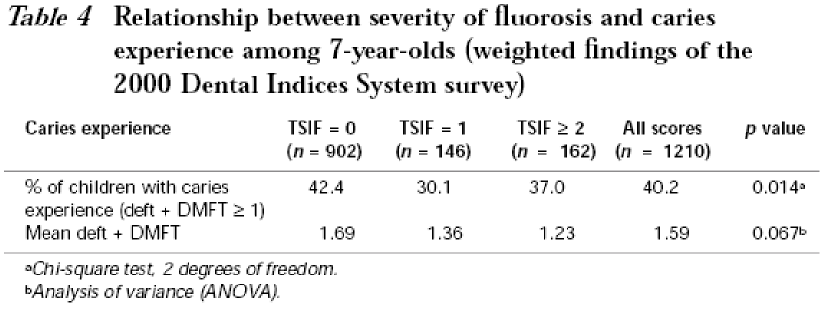


Table 4 **Relationship between severity of fluorosis and caries experience among 7-year-olds (weighted findings of the 2000 Dental Indices System survey)**

Caries experience	**TSIF = 0 (*n* = 902)**	**TSIF = 1 (*n* = 146)**	**TSIF ≥ 2 (*n* = 162)**	**All scores (*n* = 1210)**	***p* value**
% of children with caries experience (deft + DMFT ≥ 1)	42.4	30.1	37.0	40.2	0.014[a]
Mean deft + DMFT	1.69	1.36	1.23	1.59	0.067[b]

[a]*Chi-square test, 2 degrees of freedom.*
[b]*Analysis of variance (ANOVA).*

NOTE: "deft" refers to decayed, extracted due to caries and filled **primary** teeth
"DEFT" refers to decayed, missing and filled **permanent** teeth

STUDY AUTHORS' CONCLUSIONS:

Caries continues to be found in about 40% of children. Moderate fluorosis (TSIF approximately 2) was evident in 14% of children at age 7. The prevalence and severity of dental fluorosis among those identified as being born in Toronto support the 1999 decision to reduce Toronto's water fluoride concentration to 0.8 ppm.

Levels of fluoride exposure at time of crown formation (see TSIF scores and Table 4) continue to be related to prevalence of caries among 7 year-olds.

		Interpretation of results was limited by the Dental Indices System protocol, which provided information only on place of birth and age to be used as possible variables for levels of fluorosis. Examiner biases could have resulted because examiners may have under-reported caries in children they previously identified as having fluorosis since fluorosis incidence was recorded before caries incidence in the protocol.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Ontario Ministry of Health. 1998. Dental index system. Toronto, Canada: Public Health Branch. O'Keefe, J.P. 1995. A template dental health status report for Ontario public health units. Can J Community Dent 10(1)18-24. Health Canada. 1996. Guidelines for Canadian Drinking Water Quality—Supporting Documents. Ottawa, Canada. (http://www.hc-sc.gc.ca/ehp/catalogue/bch_pubs/dwgsup_doc/fluoride.pdf)
PROFILER'S REMARKS	***Initials/Date*** VAD/01-01-07	The reported study was a good measure of the prevalence of caries and fluorosis in Toronto children aged 7 and 13 during the 1999-2000 school term. Birthplace information was not available for all children and if available, may not have provided accurate exposure information during the susceptible period for fluorosis development on the permanent teeth. One hygienist examined 90% of the children, which could have biased the results. Although the results indicated that a small percentage of the study group exhibited severe fluorosis, the effect of severe fluorosis on caries prevalence was not evaluated, other than to document that of 37% of the 7 yr olds with "moderate" fluorosis (TSIF ≥ 2) had caries vs. 30.1% for those with only "mild" fluorosis (TSIF = 1; Table 4). Only 0.3% of the 7 yr-olds and 1.8% of the 13 yr-olds had TSIF scores of 4 (Table 2). REVIEWER'S REMARKS: Although not reported in the current study, it is presumed that the drinking water to which study participants were exposed was in compliance with Health Canada (1996) requirements (e.g., 1.2 ppm prior to 1999 [See the previous page.] and reduced to 0.8 ppm in 1999).
PROFILER's ESTIM. NOAEL		The study design did not estimate fluoride intake and the association with fluorosis.
PROFILER'S ESTIM. LOAEL		The study design did not estimate fluoride intake and the association with fluorosis.
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable (X_); Poor (_); Medium (); Strong (_)
CRITICAL EFFECTS:		Dental caries and fluorosis (maxillary permanent anterior teeth)

Levy, S.M., Warren, J.J., Broffitt, B., Hillis, S.L. and Kanellis, M.J. 2003. Fluoride, beverages and dental caries in the primary dentition. Caries Res. 37:157-165.

ENDPOINT STUDIED:	Dental caries in children up to 6 years
TYPE OF STUDY:	Longitudinal cohort of children whose parents were recruited at the time of the child's birth during 1992-1995. PROFILER'S NOTE: There are 4 articles that report on different findings but all use the population of children that originally were part of the Iowa Fluoride Study (IFS) that occurred during 1992 to 1995 and was a birth cohort study of fluoride exposures and intake, fluorosis and caries. The profiler did not put all assessments on the same profile as the data were sufficiently different to combine. The reports were as follows: Levy et al., 2003; Marshall et al., 2004; Levy et al., 2006a and Levy et al., 2006b.
POPULATION STUDIED:	US/Iowa: 291 individuals were recruited from eight Iowa hospitals to participate in the Iowa Fluoride Study.
CONTROL POPULATION:	No control population was included.
EXPOSURE PERIOD:	Children were followed until between the ages of 4 and 6 years.
EXPOSURE GROUPS:	The participants were not divided into exposure groups. Although weighted average fluoride levels in water sources were placed in 3 groups: < 0.3 ppm (10.9%); 0.3-0.6 ppm (16%) and >0.6 ppm (73.1%); groups were not compared for fluorosis prevalence. Using questionnaires at scheduled intervals, dietary and non-dietary sources of fluoride were assessed to estimate intake.
EXPOSURE ASSESSMENT:	Daily fluoride exposure, fluoride intake and categories of dietary intake were determined at the age of the child for each questionnaire response. Linear interpolation was used to obtain daily estimates of values for intervals between returned questionnaires. Finally, yearly summaries of fluoride and dietary intake for each subject were obtained by averaging the daily values (observed and interpolated) over each of the first 4 years of life. The questionnaires asked parents to summarize their child's dietary intake for the previous week. Dietary intake was partitioned into eleven broad categories: water, formula, breast milk, cow's milk, juices and juice drinks, non-juice beverages as purchased, beverages made from frozen concentrates, beverages made from powdered concentrates, ready-to-feed baby food, infant cereal made from powder, and other foods made with water (Jell-O®, soup, etc.). Formula and juice drink questions contained additional detail to ascertain the amount of personal water that was added to each beverage since subjects sometimes used ready-to-feed juice or formula but at other times used products made from powder or liquid concentrate. Fluoride from dentifrice was estimated by combining frequency of use, brand-specific fluoride concentration and estimates of the amounts of dentifrice used and ingested at each brushing for each time period beginning at 6 months of age. Estimated daily fluoride intake from dietary fluoride supplements similarly was determined by combining frequency of use with brand-specific dosage information separately for each time period. Estimates of fluoride intake from water incorporated both the daily amount of water consumed by the child and an estimate of the fluoride concentration (parts per million) in each of the major water sources used by the child (e.g. home, child care).
ANALYTICAL METHODS:	The method for analyzing fluoride levels was not described. Water fluoride levels were determined through assay of individual wells or filtered public water supplies, assays of commercial bottled waters, and documentation of fluoride levels for public water supplies.
STUDY DESIGN	Parents were recruited at the time of their child's birth from eight Iowa hospitals. Demographic information was obtained at the time of recruitment. Using questionnaires sent at scheduled intervals, parents also provided information about the children's water

	sources, beverage and selected food intake, use of dietary fluoride supplements, and toothbrushing habits. Questionnaires were sent out at regular intervals starting at 6 weeks of age, with the greatest frequency during the child's first year of life (5 times) and with decreasing frequency thereafter. Dental examinations were conducted on primary dentition when the children were between 4 and 6 years.
PARAMETERS MONITORED:	Oral examinations of children were conducted to determine dental caries in the primary dentition according to the criteria of Warren et al. (2002). Children were examined at age 4–6 years, using $d_1d_{2–3}f$ criteria that differentiated between non-cavitated (d_1) and cavitated ($d_{2–3}$) carious lesions with each surface scored as sound, filled, or as a cavitated or non-cavitated lesion.
STATISTICAL METHODS:	The Statistical Analysis System (SAS) Version 8 was used for data analysis. All predictor variables (except gender) were transformed to 3-level ordinal variables having the following values: 0 = low, 1 = medium, and 2 = high. Assignment to the low, medium, and high levels was based on distribution percentiles, so that roughly equal numbers of subjects fell into each level for each transformed variable. The 3-level variables were then used as linear predictors in logistic regression models. Odds ratio estimates in the logistic regressions should be interpreted as the estimated change in the odds ratio resulting from an increase to the next higher category (low to medium, or medium to high) in the corresponding variable. The association between certain variables and caries experience was determined by computer model. Subsets of variables included in the model were none, age and gender, water consumption, and sugar beverages/milk consumption.
RESULTS:	
Dental caries	Only 23% of the children had caries experience and approximately 73% had weighted average fluoride levels in water sources that exceeded 0.6 ppm (Table 1). A logistic regression model was used to calculate odd ratios in order to show relationships between the parameter variables used in the model. Water consumption (36-48 months), more frequent toothbrushing (36-48 months), and milk consumption (24-36 months) were statistically significantly associated with decreased odds ratios for caries. In contrast, consumption of sugar beverages or milk (6 weeks to 12 months) was statistically significantly associated with an increased odds ratio for caries.

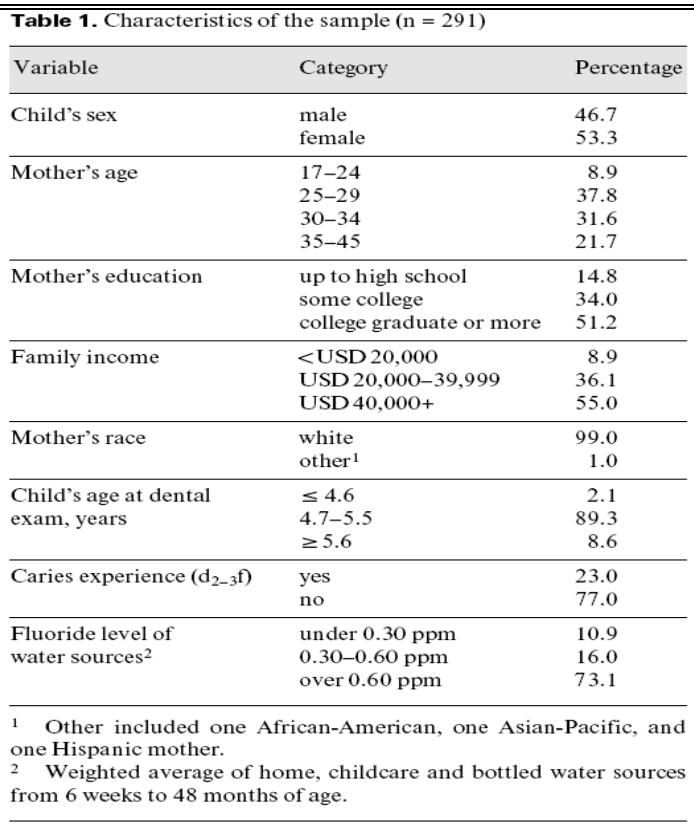


Table 1. Characteristics of the sample (n = 291)

Variable	Category	Percentage
Child's sex	male	46.7
	female	53.3
Mother's age	17–24	8.9
	25–29	37.8
	30–34	31.6
	35–45	21.7
Mother's education	up to high school	14.8
	some college	34.0
	college graduate or more	51.2
Family income	<USD 20,000	8.9
	USD 20,000–39,999	36.1
	USD 40,000+	55.0
Mother's race	white	99.0
	other[1]	1.0
Child's age at dental exam, years	≤ 4.6	2.1
	4.7–5.5	89.3
	≥ 5.6	8.6
Caries experience ($d_{2-3}f$)	yes	23.0
	no	77.0
Fluoride level of water sources[2]	under 0.30 ppm	10.9
	0.30–0.60 ppm	16.0
	over 0.60 ppm	73.1

[1] Other included one African-American, one Asian-Pacific, and one Hispanic mother.
[2] Weighted average of home, childcare and bottled water sources from 6 weeks to 48 months of age.

STUDY AUTHORS' CONCLUSIONS:	Water consumption (36–48 months), milk consumption (24–36 months), and fluoridated toothpaste brushings (36–48 months) were negatively associated with caries; sugared beverages and milk (6 weeks to 12 months) were positively associated. Although fluoride exposure is important, sugared beverages contribute substantially to caries risk, while water and milk consumption and frequent toothbrushing early can have protective effects.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Warren, J.J., Levy, S.M., and Kanellis, M.J. 2002. Dental caries in the primary dentition: Assessing prevalence of cavitated and non-cavitated lesions. J. Publ. Health Dent. 62:109-114.
PROFILER'S REMARKS ***Initials/date CSW 1/9/2007***	This study was an analysis of data collected as part of the Iowa Fluoride Study. The main conclusions were that consumption of fluoridated water early in life and toothbrushing may reduce caries while consumption of sugared beverages contributes to the development of caries. Doses could not be reconstructed because these data were not collected.
PROFILER'S ESTIM. NOEL/NOAEL	Could not be determined.
PROFILER'S ESTIM. LOEL/ LOAEL	Could not be determined.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (X), Poor (_), Medium (_), Strong (_) Although extensive data were collected on beverage consumption and dietary intake of fluoride, no doses could be calculated.
CRITICAL EFFECT(S):	Dental caries

Levy, S.M., J.J. Warren, B. Broffitt, and M.J. Kanellis. 2006a. Associations between dental fluorosis of the permanent and primary dentitions. Journal of Public Health Dentistry. Vol. 66, No. 3, p. 180-185.

ENDPOINT STUDIED:	Dental fluorosis in primary and permanent dentition
TYPE OF STUDY:	Birth cohort; longitudinal study. PROFILER'S NOTE: There are 4 articles (Levy et al., 2003; Marshall et al., 2004; Levy et al., 2006a and Levy et al., 2006b) that report on different findings but all use the same population of children that were originally part of the Iowa Fluoride Study (IFS) during 1992 to 1995. The IFS was a birth cohort study of fluoride exposures and intake, fluorosis and caries. The profiler did not place all assessments on the same profile, as the individually reported data were sufficiently different.
POPULATION STUDIED:	US/Iowa: 601 children who participated in the Iowa Fluoride Study; their parents were recruited in the hospital at each child's birth during 1992-1995. Institutional Review Board approval, parental consent and child assent were all obtained. PROFILER'S NOTE: The applicability of this study population for the general United States is somewhat limited as the subjects and their families were mostly Caucasian, middle-income and the majority of the parents had a college education.
CONTROL POPULATION:	None described
EXPOSURE PERIOD:	Parents of the children were recruited at birth from 8 Iowa hospitals during 1992-1995. The children were given dental examinations to identify fluorosis at ages 4-6 (mean age 5.2) and 7-12 (mean age 9.2).
EXPOSURE GROUPS:	The IFS database was used to determine all possible routes of fluoride exposure. Information in the database included drinking water fluoride levels; filtration sources; water, beverage and selected food intake; use of fluoride supplements and fluoride dentifrice; and body weight. PROFILER'S NOTE: Although this study stated that fluoride from all the above mentioned sources were collected, no quantitative values were provided.
EXPOSURE ASSESSMENT:	All possible sources of fluoride exposure, including food and drink, were evaluated by questionnaire.
ANALYTICAL METHODS:	Analytical methods for determining fluoride concentrations were not described in the report.
STUDY DESIGN	The population was a birth cohort of children participating in the Iowa Fluoride Study. Children were given two dental examinations for fluorosis. One occurred between 4-6 years old and the second between 7-12 years old. Examinations were performed by two trained, calibrated dentists with portable equipment and halogen headlights. Additional examinations were conducted by both examiners on a subset to assess inter-examiner reliability. Parents were sent questionnaires five times during the first year and then 2-3 times per year, thereafter, to assess fluoride intake. Questionnaires addressed water sources, filtration status, water, beverage, and selected food intake, use of dietary fluoride supplements and dentifrice and body weight. Total dietary fluoride intake was divided by body weight for each questionnaire. Average daily fluoride intake (mgF/kg bw) was estimated from birth to 36 months and again from 36 to 72 months using the trapezoidal method of calculation for area-under-the-curve (AUC).

	PROFILER’S NOTE: Although the paper describes the sources of fluoride, no quantitative data on the actual concentration of fluoride from each source were included.
PARAMETERS MONITORED:	At the first examination at ages 4-6, primary teeth were assessed for fluorosis using the Tooth Surface Index of Fluorosis (TSIF), adapted for primary teeth (Warren et al., 2001). For the second examination, the Fluorosis Risk Index (FRI) (Pendrys, 1990) was used to evaluate the early erupting permanent teeth (8 permanent incisors and 4 first molars) and the TSIF was used for primary second molars. The FRI was selected by the study authors, as it scores fluorosis on four zones of the tooth. For this study, three FRI zones of each buccal surface (incisal edge/cusp tip, incisal/occlusal third and middle third, with gingival zones excluded due to less full eruption) were included. The permanent teeth were categorized as follows: 1) definitive cases: at least one FRI score of 2 (white striations) or 3 (staining/pitting/deformity) on more than one-half of a surface zone; 2) questionable: with a maximum FRI score of 1 for less than half of a zone clearly or possibly affected by white striations; and 3) none: all zones scored as FRI=0 (no indications of fluorosis) or 7 (non-fluoride opacity). PROFILER’S NOTE: The NRC (2006) states that the FRI index by Pendrys (1990) was specifically designed for use in case-control studies, of which there are very few.
STATISTICAL METHODS:	Statistical analysis was performed using SAS version 9 (SAS 2003). Both permanent incisor and permanent first molar fluorosis results were separately assessed at age 5 and at age 9 using relative risks and logistic regression. Relative risks and 95% confidence intervals were calculated according to the SAS cohort study method. Two separate logistic regressions predicting definitive permanent incisor fluorosis used 0-36 and 36-72 month AUC fluoride intake, respectively, in addition to primary second molar fluorosis at age 5. Two additional logistic regressions predicting definitive permanent first molar fluorosis also used primary second molar fluorosis assessed at age 5, as well as 0-36 and 36-72 month AUC fluoride intake, respectively.
RESULTS:	
Dental fluorosis	Tables 1 and 2 are copied directly from Levy et al. (2006a). The tables provide the relationships between permanent incisors and molars as compared to primary molar fluorosis. Table 1 shows a significant relationship between age 5 and age 9 primary tooth and permanent incisor fluorosis, although they were stronger for age 9 primary second molars. The age 5 primary tooth fluorosis prevalence rates were 2.2% for the first molars and 9.8% for the second molars. Prevalence rates for fluorosis of the permanent incisors (age 9) were 36.3% definitive, 27.3% questionable and 36.4% none, while fluorosis prevalence for the permanent first molars was 20.0% definitive, 25.5% questionable and 54.6% none. Almost all dental fluorosis was mild, with only 8 individuals (1%) with moderate (dark staining)/severe (pitting) permanent tooth fluorosis (FRI score of 3) and only 2 (0.3%) with severe primary tooth fluorosis (TSIF score of 5).

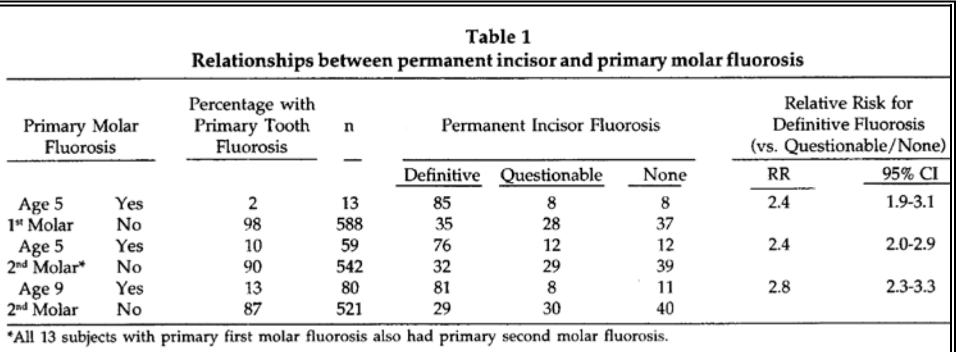


Table 1
Relationships between permanent incisor and primary molar fluorosis

Primary Molar Fluorosis		Percentage with Primary Tooth Fluorosis	n	Permanent Incisor Fluorosis			Relative Risk for Definitive Fluorosis (vs. Questionable/None)	
				Definitive	Questionable	None	RR	95% CI
Age 5	Yes	2	13	85	8	8	2.4	1.9-3.1
1st Molar	No	98	588	35	28	37		
Age 5	Yes	10	59	76	12	12	2.4	2.0-2.9
2nd Molar*	No	90	542	32	29	39		
Age 9	Yes	13	80	81	8	11	2.8	2.3-3.3
2nd Molar	No	87	521	29	30	40		

*All 13 subjects with primary first molar fluorosis also had primary second molar fluorosis.

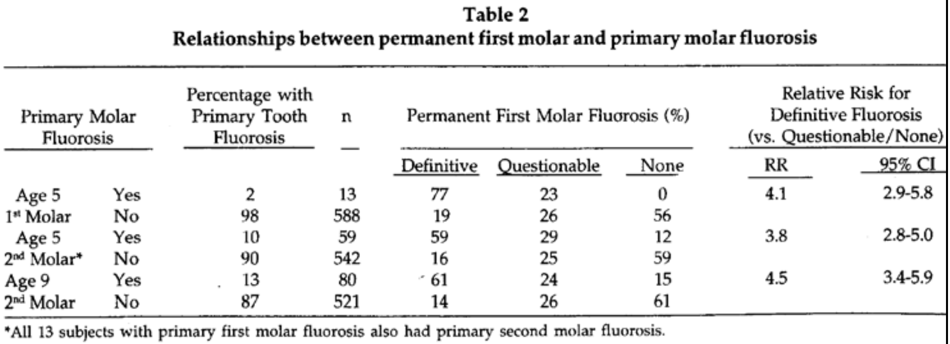


Table 2
Relationships between permanent first molar and primary molar fluorosis

Primary Molar Fluorosis		Percentage with Primary Tooth Fluorosis	n	Permanent First Molar Fluorosis (%)			Relative Risk for Definitive Fluorosis (vs. Questionable/None)	
				Definitive	Questionable	None	RR	95% CI
Age 5	Yes	2	13	77	23	0	4.1	2.9-5.8
1st Molar	No	98	588	19	26	56		
Age 5	Yes	10	59	59	29	12	3.8	2.8-5.0
2nd Molar*	No	90	542	16	25	59		
Age 9	Yes	13	80	61	24	15	4.5	3.4-5.9
2nd Molar	No	87	521	14	26	61		

*All 13 subjects with primary first molar fluorosis also had primary second molar fluorosis.

PROFILER'S NOTE: While the tables do support that fluorosis in primary teeth can be a good predictor that fluorosis will be observed in permanent incisors, the degree of fluorosis observed is not provided. There is no reported evidence to support any dose-related trend (i.e. as fluorosis in primary teeth was more severe, the fluorosis in permanent teeth was also). The study states only that a majority of the children had mild fluorosis, which is not considered adverse. Although the study collected data on the sources of fluoride (i.e. food, water, beverages, supplements), data are not included to identify which sources are most important, or to establish relative source contribution.

Fluoride intake and prediction of fluorosis

Figures 1 and 2 are copied directly from Levy et al. (2006a) and show logistic regression predictions of permanent incisor and molar fluorosis based on primary 2nd molar incidence of fluorosis and the intake of fluoride from 0-36 months. The graphs show that those children with primary molar fluorosis were much more likely to have permanent incisor fluorosis (76% vs. 32%) and permanent molar fluorosis (59% vs. 16%) at all levels of fluoride intake. Similar results were found when the 36-72 months results were plotted, but the data were not provided in the reported study.

Figure 1
Logistic Regression Prediction of Permanent Incisor Fluorosis
Using Primary 2nd Molar Fluorosis Indicator
and AUC Fluoride Intake from Age 0 to 36 Months
N=349

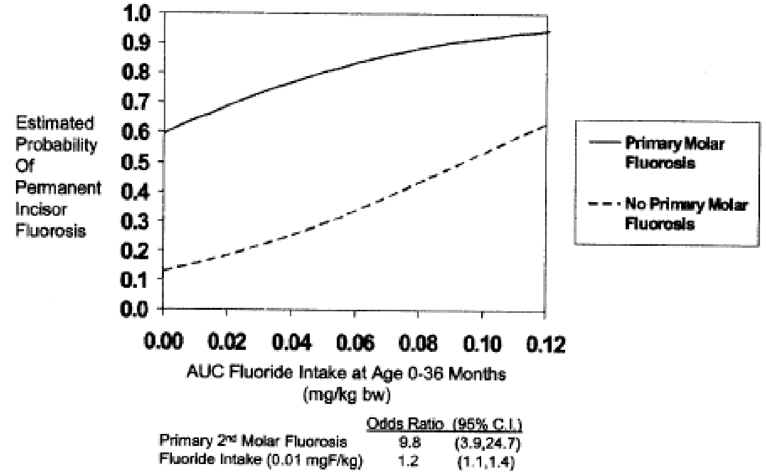
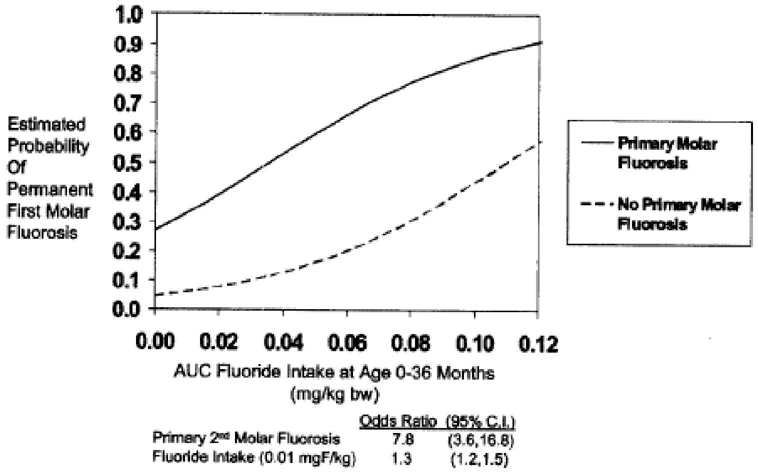


Figure 2
Logistic Regression Prediction of Permanent First Molar Fluorosis
Using Primary 2nd Molar Fluorosis Indicator
and AUC Fluoride Intake from Age 0 to 36 months
N=349



PROFILER'S NOTE: Although fluoride intake levels were provided, the parameters for the degree of fluorosis were not included on the chart; the study only states that the majority of the children had mild fluorosis, which is not considered adverse. Although the study collected data on the sources of fluoride (i.e. food, water, beverages, supplements), data are not included to identify which sources are most important.

STUDY AUTHORS' CONCLUSIONS:		There is a strong association between primary and permanent tooth fluorosis that is independent of the level of fluoride intake. The detection of primary tooth fluorosis in pre-school children should alert clinicians and parents to the high likelihood of subsequent fluorosis in the permanent dentition.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Warren, J.J., S.M. Levy and M.J. Kanellis. 2001. Prevalence of dental fluorosis in the primary dentition. Journal Public Health Dent. Vol. 61(2), p. 87-91.
PROFILER'S	***Initials/date***	While the Iowa Fluoride Study appears to be a thorough study, this paper does not include

REMARKS	***DFG/1-07***	data critical for determining a dose-response. Levy et al. (2006a) provided limited data on the fluoride concentration intake levels to which the children were exposed, but did not provide any quantitative data on the sources of fluoride or relative source contribution. Limited data on the degree of fluorosis observed indicate that very few children experienced severe (adverse) fluorosis. The authors also use a Fluorosis Risk Index (Pendrys, 1990) that is of limited applicability according to the NRC (2006). The study population was not a true reflection of the majority of children in the United States as most were from families within the middle-income bracket with parents having a 4-year college degree which tends to indicate better preventative dental care was available.
PROFILER'S ESTIM. NOEL/NOAEL		Data are unsuitable for determining a dose-response for fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL		Data are unsuitable for determining a dose-response for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor (_), Medium (_), Strong (_)
CRITICAL EFFECT(S):		Dental fluorosis in permanent dentition as related to its presence in primary dentition.

Levy, S.M., L. Hong, J.J. Warren and B. Broffitt. 2006b. Use of the fluorosis risk index in a cohort study: the Iowa fluoride study. Journal of Public Health Dentistry. Vol. 66, No. 2, p. 92-96.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Cohort PROFILER'S NOTE: There are 4 articles that report on different findings but all use the population of children that originally were part of the Iowa Fluoride Study (IFS) that occurred during 1992 to 1995 and was a birth cohort study of fluoride exposures and intake, fluorosis and caries. The profiler did not put all assessments on the same profile as the data were sufficiently different and provided different information. The reports are inter-related, however, and will be grouped together. The reports include: Levy et al., 2003; Marshall et al., 2004; Levy et al., 2006a and Levy et al., 2006b.
POPULATION STUDIED:	US/Iowa: 443 children who participated in the Iowa Fluoride Study; parents were recruited in the hospital at their birth during 1992-1995. PROFILER'S NOTE: The applicability of this study population for the general United States is somewhat limited as the subjects and their families were mostly Caucasian, middle-income and the majority of the parents had a college education.
CONTROL POPULATION:	None described
EXPOSURE PERIOD:	Parents of the children were recruited at birth. The children were given dental examinations to identify fluorosis around age 9.
EXPOSURE GROUPS:	Children were part of the original Iowa Fluoride Study.
EXPOSURE ASSESSMENT:	The study reported that the majority of the children were exposed to drinking water with fluoride levels of 0.7-1.2 ppm. PROFILER'S NOTE: Although the original IFS assessed fluoride levels from various sources including, drinking water, foods, beverages, and the use of fluoride supplements and dentifrices, this study only provided drinking water fluoride levels.
ANALYTICAL METHODS:	Analytical methods for evaluating the fluoride concentration in the drinking water were not provided.
STUDY DESIGN	Children originally recruited into the Iowa Fluoride Study were examined at approximately 9 years old for dental fluorosis on early-erupting permanent teeth by two trained and calibrated dentists using the Fluorosis Risk Index (Pendrys 1990). Twelve teeth were examined for each subject: 4 mandibular incisors, 4 maxillary incisors and 4 first molars. After being dried slightly with gauze, teeth were examined using a mouth mirror and exam light. Fluorosis was differentiated from non-fluorosis opacities based on the criteria of Russell (Russell 1961 and Warren et al., 2001) and from "white spot' carious lesions based on color, texture, demarcation and relationship to gingival margin.
PARAMETERS MONITORED:	The Fluorosis Risk Index (FRI) by Pendrys (1990) was used to assess fluorosis. The FRI was developed to improve researchers' ability to relate the risk of fluorosis to the developmental stage of the permanent dentition at the time of exposure to fluoride. The FRI assesses fluorosis on four enamel zones classified according to the age at which fluoride enamel is initiated. Ten early developing zones are defined as FRI-I zones (occlusal cusp areas of first molars and incisal edges of 6 of the 8 incisors) while there are 24 FRI-II zones (that develop and erupt later). Therefore, it has more potential to show accurate identification between age-specific ingestion of fluoride and the development of permanent tooth enamel fluorosis.

Using this index, three zones (incisal edge, incisal third and middle third) of facial surfaces were assessed separately for these early erupting permanent teeth with the FRI scoring criteria as follows: **no fluorosis**: FRI of 0; **questionable fluorosis**: FRI of 1, 50% or less of zone with white striations; **definitive fluorosis**: FRI of 2, greater than 50% of zone with white striations and **severe fluorosis**: FRI of 3, zone displays pitting, staining and/or deformity. Cervical zones were excluded from the analysis because of incomplete eruption of the teeth. Teeth that were unable to be scored were given a score of 9 and a tooth without fluorosis was defined as having all zones with FRI of 0 (or 7).

PROFILER'S NOTE: The NRC (2006) states that the index by Pendrys (1990) was specifically designed for use in case-control studies, of which there are very few. Levy et al. (2006b) agree that this index was designed for case-control analytical studies of age-related fluoride exposure risk factors for fluorosis with the purpose to maximize the contrast of the identified case and control groups. The study authors also state that this method creates a large number of scores being within the "questionable" category.

STATISTICAL METHODS: The only statistical analysis reported in the article was Kappa methods used to assess inter-examiner reliability which ranged from 77% to 94% agreement.

RESULTS:

Dental fluorosis

Tables 1 and 2 are copied directly from Levy et al. (2006b). Tooth specific fluorosis prevalence varied with the maxillary central incisor most affected and the mandibular incisors least affected. With the three zones of the teeth, 40.6% overall had at least one tooth with mild or more involved fluorosis, 30.2% had questionable fluorosis and 29.1% had no fluorosis. When only FRI zone I were considered, the percentages were 33.2%, 29.3% and 37.5%, for mild or more, questionable and no fluorosis, respectively. Using different combinations of teeth, the prevalence using 3 zones were usually 1-9% points higher than those estimated using FRI zone 1 only. Most fluorosis was mild with only 7 individuals (1.6%) having FRI scores indicating severe fluorosis.

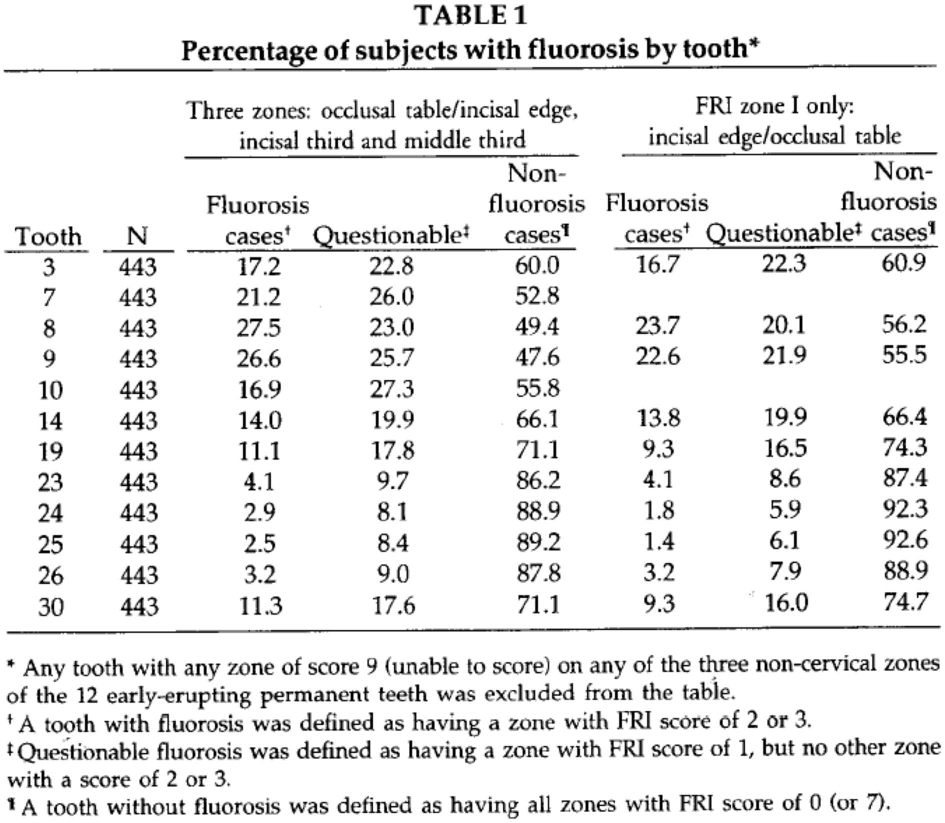


TABLE 1
Percentage of subjects with fluorosis by tooth*

		Three zones: occlusal table/incisal edge, incisal third and middle third			FRI zone I only: incisal edge/occlusal table		
Tooth	N	Fluorosis cases†	Questionable‡	Non-fluorosis cases¶	Fluorosis cases†	Questionable‡	Non-fluorosis cases¶
3	443	17.2	22.8	60.0	16.7	22.3	60.9
7	443	21.2	26.0	52.8			
8	443	27.5	23.0	49.4	23.7	20.1	56.2
9	443	26.6	25.7	47.6	22.6	21.9	55.5
10	443	16.9	27.3	55.8			
14	443	14.0	19.9	66.1	13.8	19.9	66.4
19	443	11.1	17.8	71.1	9.3	16.5	74.3
23	443	4.1	9.7	86.2	4.1	8.6	87.4
24	443	2.9	8.1	88.9	1.8	5.9	92.3
25	443	2.5	8.4	89.2	1.4	6.1	92.6
26	443	3.2	9.0	87.8	3.2	7.9	88.9
30	443	11.3	17.6	71.1	9.3	16.0	74.7

* Any tooth with any zone of score 9 (unable to score) on any of the three non-cervical zones of the 12 early-erupting permanent teeth was excluded from the table.

† A tooth with fluorosis was defined as having a zone with FRI score of 2 or 3.

‡ Questionable fluorosis was defined as having a zone with FRI score of 1, but no other zone with a score of 2 or 3.

¶ A tooth without fluorosis was defined as having all zones with FRI score of 0 (or 7).

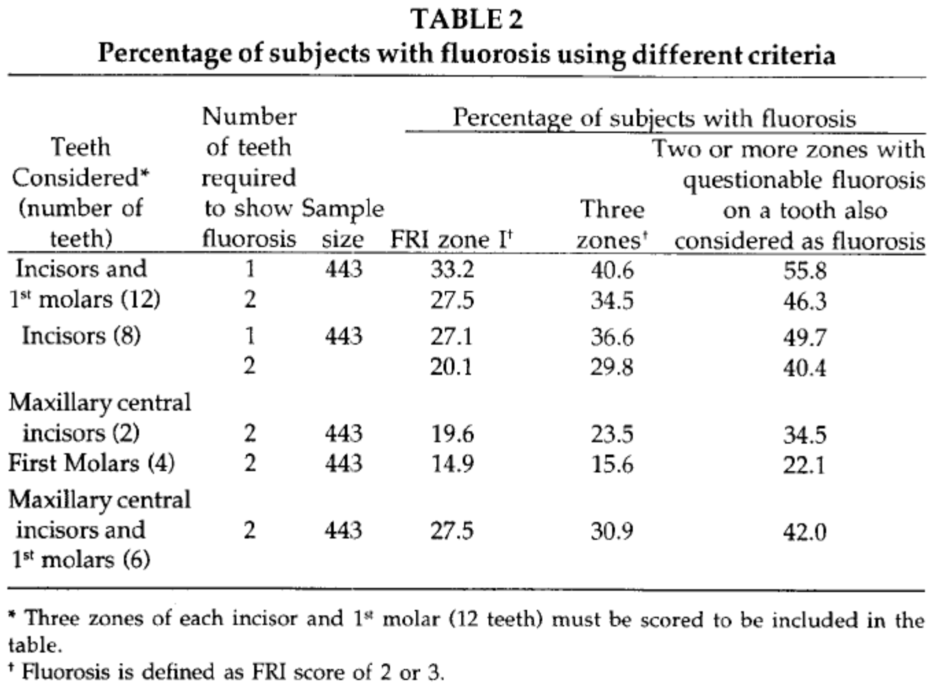


TABLE 2
Percentage of subjects with fluorosis using different criteria

Teeth Considered* (number of teeth)	Number of teeth required to show fluorosis	Sample size	Percentage of subjects with fluorosis: FRI zone I†	Percentage of subjects with fluorosis: Three zones†	Percentage of subjects with fluorosis: Two or more zones with questionable fluorosis on a tooth also considered as fluorosis
Incisors and 1st molars (12)	1	443	33.2	40.6	55.8
	2		27.5	34.5	46.3
Incisors (8)	1	443	27.1	36.6	49.7
	2		20.1	29.8	40.4
Maxillary central incisors (2)	2	443	19.6	23.5	34.5
First Molars (4)	2	443	14.9	15.6	22.1
Maxillary central incisors and 1st molars (6)	2	443	27.5	30.9	42.0

* Three zones of each incisor and 1st molar (12 teeth) must be scored to be included in the table.
† Fluorosis is defined as FRI score of 2 or 3.

PROFILER'S NOTE: The study did not provide details on the individual fluoride intakes as related to the amount of fluorosis. For Table 1, there is no information identifying the tooth number with the type of tooth, maxillary or mandibular incisors or the first molars (i.e. is tooth number 3 an incisor or molar?). The data do not distinguish between a fluorosis score of 2 or 3 which indicate definitive (2) or severe (3); the study only states that 7 individuals had severe fluorosis which would be considered an adverse effect.

STUDY AUTHORS' CONCLUSIONS:

The FRI has advantages if used for analytical epidemiology studies for dental fluorosis; however, the population prevalence varies depending on the index and case definition used. The authors recommend that consideration be given to concurrent use of another index (i.e. Dean's, TSIF) if prevalence estimates are an important study outcome.

In this study, the majority of the children drank water with the optimal fluoride level (0.7-1.2 ppm) and overall 34.5% had definitive fluorosis (FRI score of 2 or 3) on at least two teeth.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

Russell, A.L. 1961. The differential diagnosis of fluoride and non-fluoride enamel opacities. J Public Health Dent. 21:143-6.

Warren, J.J., S.M. Levy and M.J. Kanellis. 2001. Prevalence of dental fluorosis in the primary dentition. Journal Public Health Dent. Vol. 61(2), p. 87-91.

PROFILER'S REMARKS ***DFG/1-07***

The study interpreted data from the Iowa Fluoride Study and used the FRI to assess for fluorosis, making the study not useful in determining a dose response. Quantitative data were not included in regards to actual fluoride exposures and the number of children within each fluorosis scoring group. The only quantitative data provided was the percentage of children with "severe" fluorosis and this was only 7/443 (1.6%) indicating very few had an adverse effect from fluoride. Data on statistical methods used and how fluoride levels in the water were derived were incomplete. The study population was not a true reflection of the majority of children in the United States as most were from families within the middle-income bracket with parents having a 4-year college degree which tends to indicate better preventative dental care was available.

PROFILER'S ESTIM. NOEL/NOAEL

Data are not suitable for development of a NOAEL for fluorosis.

PROFILER'S ESTIM. LOEL/ LOAEL	Data are not suitable for development of a LOAEL for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (X), Poor (_), Medium (_), Strong (_)
CRITICAL EFFECT(S):	The use of the fluorosis risk index in identifying fluorosis in children.

Mann, J., M. Tibi, H.D. Sgan-Cohen. 1987. Fluorosis and caries prevalence in a community drinking above-optimal fluoridated water. Community Dent Oral Epidemiol 15:293-5.

ENDPOINT STUDIED:	Dental caries and fluorosis (permanent teeth)
TYPE OF STUDY:	Prevalence study of dental caries and fluorosis.
POPULATION STUDIED:	Israel administered Gaza Strip: adolescents (15-16 years old) residing in one small village. All 182 (90 boys and 92 girls) of this age group participated in the study. All children resided in the area since birth and had access to the same drinking water source (two local wells) since birth No information was provided about written consent by the children's parents.
CONTROL POPULATION:	None.
EXPOSURE PERIOD:	Birth to 15-16 years; the dates of the study conduct were not provided.
EXPOSURE GROUPS:	The concentration of fluoride in the well water was 5 ppm.
EXPOSURE ASSESSMENT	A questionnaire was administered to determine smoking, dietary patterns, drinking habits and oral hygiene routines, but fluoride intake from these practices was not estimated.
ANALYTICAL METHODS:	Three samples of drinking water were analyzed for fluoride concentration (in ppm) on different non-consecutive days using a combined activity electrode.
STUDY DESIGN	The objectives of the study were to assess the prevalence and severity of dental caries and fluorosis in a community characterized by naturally above-optimal fluoridated water (5 ppm). The study population consisted of 182 (90 boys and 92 girls) adolescents (15-16 years old) residing since birth in a small village in the Israeli administered Gaza Strip. All children of this age group in the village participated in the study. Dental caries levels and the severity of fluorosis were determined in all children. One study author conducted all the examinations using artificial light, dental mirrors and sickle-shaped explorers. A questionnaire was administered to determine smoking, dietary patterns, drinking habits and oral hygiene routines, but fluoride intake from these practices was not estimated.
PARAMETERS MONITORED:	Dental fluorosis was determined according to Dean's index (see NRC, 2006, pages 88-89). Dental caries were evaluated using the DMFS (decayed, missing or filled surfaces) index according to the recommendations of WHO (1977). WHO criteria for classifying decayed teeth were followed: only surfaces with detectable softened floor, undermined enamel, softened wall or temporary fillings were recorded as DS (decayed untreated teeth).
STATISTICAL METHODS:	Student's t-test, chi-square and analysis of variance were employed to analyze the results. The level of significance was $p<0.05$.
RESULTS:	Study results in Tables 1-4 are shown directly from Mann, 1987.

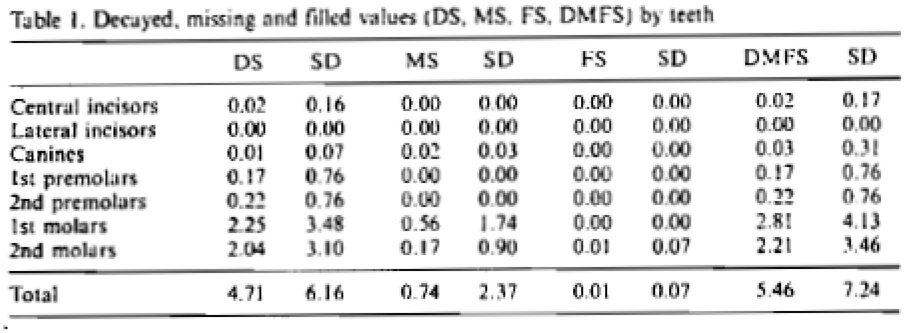


Table 1. Decayed, missing and filled values (DS, MS, FS, DMFS) by teeth

	DS	SD	MS	SD	FS	SD	DMFS	SD
Central incisors	0.02	0.16	0.00	0.00	0.00	0.00	0.02	0.17
Lateral incisors	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Canines	0.01	0.07	0.02	0.03	0.00	0.00	0.03	0.31
1st premolars	0.17	0.76	0.00	0.00	0.00	0.00	0.17	0.76
2nd premolars	0.22	0.76	0.00	0.00	0.00	0.00	0.22	0.76
1st molars	2.25	3.48	0.56	1.74	0.00	0.00	2.81	4.13
2nd molars	2.04	3.10	0.17	0.90	0.01	0.07	2.21	3.46
Total	4.71	6.16	0.74	2.37	0.01	0.07	5.46	7.24

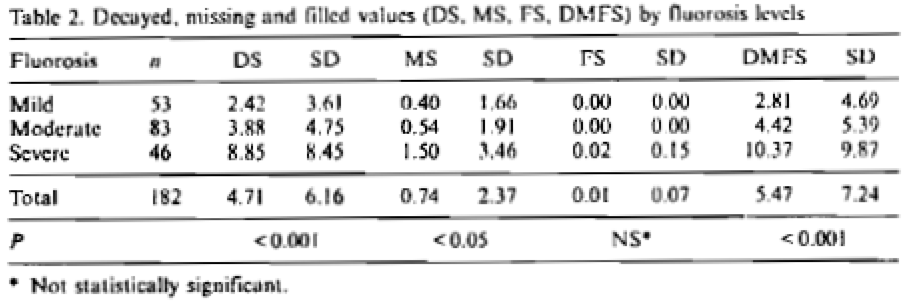


Table 2. Decayed, missing and filled values (DS, MS, FS, DMFS) by fluorosis levels

Fluorosis	*n*	DS	SD	MS	SD	FS	SD	DMFS	SD
Mild	53	2.42	3.61	0.40	1.66	0.00	0.00	2.81	4.69
Moderate	83	3.88	4.75	0.54	1.91	0.00	0.00	4.42	5.39
Severe	46	8.85	8.45	1.50	3.46	0.02	0.15	10.37	9.87
Total	182	4.71	6.16	0.74	2.37	0.01	0.07	5.47	7.24
P		< 0.001		< 0.05		NS*		< 0.001	

* Not statistically significant.

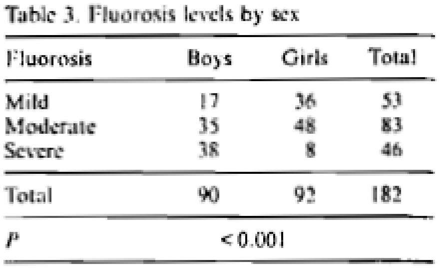


Table 3. Fluorosis levels by sex

Fluorosis	Boys	Girls	Total
Mild	17	36	53
Moderate	35	48	83
Severe	38	8	46
Total	90	92	182
P	< 0.001		

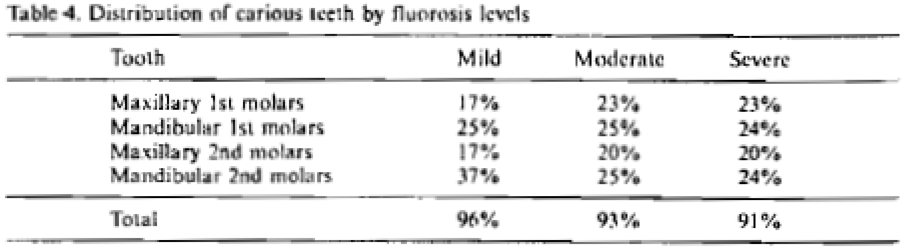


Table 4. Distribution of carious teeth by fluorosis levels

Tooth	Mild	Moderate	Severe
Maxillary 1st molars	17%	23%	23%
Mandibular 1st molars	25%	25%	24%
Maxillary 2nd molars	17%	20%	20%
Mandibular 2nd molars	37%	25%	24%
Total	96%	93%	91%

STUDY AUTHORS' CONCLUSIONS:

The study authors concluded that a statistically significant positive association was found between caries prevalence and fluorosis; the more caries experienced, the more severe the fluorosis level. Boys experienced significantly higher fluorosis levels than girls.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

World Health Organization. Oral health surveys: basic methods. Geneva: WHO, 1977.

PROFILER'S REMARKS	***Initials/Date*** VAD/03-08-07	The material and methods for the study conduct were not described in detail. The study results are not representative of the U.S. population since the study was conducted in the Israeli administered Gaza Strip. Fluoride intake from other sources, in addition to the

<table>
<tr><td></td><td></td><td>drinking water, was not estimated and could have explained the higher fluorosis levels in boys. Analyses of drinking water for fluoride concentration were conducted three times, but only one value (5 ppm) was reported. The range of levels should have been reported since fluoride concentrations in water are known to fluctuate.
The incidence of severe fluorosis was about 25% for a drinking water fluoride concentration of 5 ppm. Although other sources of fluoride exposure are possible, the incidence of severe fluorosis is not inconsistent with the data of Dean (1942) for similar drinking water fluoride levels.</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td colspan="2">PROFILER’s ESTIM. NOAEL</td><td>The study design did not identify a no-fluorosis intake dose.</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td colspan="2">PROFILER’S ESTIM. LOAEL</td><td>Study participants were exposed to only one concentration of fluoride in the water (5 ppm). At this level, all the adolescents had caries and either mild, moderate or severe fluorosis.</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td colspan="2">SUITABILITY FOR DOSE RESPONSE MODELING</td><td>Not suitable,(_); Poor (X_); Medium (_); Strong (__)
Only a single exposure level was evaluated</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td colspan="2">CRITICAL EFFECTS:</td><td>Dental caries and fluorosis (permanent teeth)</td></tr>
<tr><td colspan="2"></td><td></td></tr>
</table>

Mann, J., W. Mahmoud, M. Ernest, et al. 1990. Fluorosis and dental caries in 5-8 year-old children in a 5 ppm fluoride area. Community Dent. Oral Epidemiol. 18:77-79.

ENDPOINT STUDIED:	Dental fluorosis; dental caries
TYPE OF STUDY:	Survey
POPULATION STUDIED:	Gaza Strip: 152 children (72 boys and 80 girls), 6-8 yrs old, residing in a village in the Gaza Strip. Comparisons were made with 16-18 yr old children from the same region who had been evaluated in a previous study (Mann et al., 1987).
CONTROL POPULATION:	None
EXPOSURE PERIOD:	Six to 8 years (the date the examinations took place was not reported).
EXPOSURE GROUPS:	All children in the study population drank water from two local wells having fluoride levels of 4.7, 5.3 and 5.1 ppm (three samples taken on non-consecutive days).
EXPOSURE ASSESSMENT:	Fluoride levels in well water were documented and the study authors noted that an earlier study (Mann et al., 1985) had shown that tea consumed by the population in this region had high levels of fluoride (levels and consumption patterns not reported), and that boys drank more (unquantified amounts) tea than girls. Presumed (but unstated) assumption is that monitored wells were the sole source of drinking water for examined children.
ANALYTICAL METHODS:	Combined F activity electrode (Orion Research of Cambridge, MA). Limits of detection not provided by authors.
STUDY DESIGN	Dental fluorosis and caries in primary and permanent dentition were evaluated in a population of children (72 boys and 80 girls, 6-8 yrs old), residing in a village in the Gaza Strip who were exposed to fluoride in well water used as drinking water (4.7, 5.3 and 5.1 ppm). Dean's index was used for scoring fluorosis and DMFS and defs for scoring caries incidence. Data were analyzed statistically using Chi-square and ANOVA.
PARAMETERS MONITORED:	Severity of fluorosis was monitored in primary and permanent dentition according to Dean's index (Dean, 1942), with a range from normal enamel (score 0) to severe fluorosis (score 4). Dental caries levels were also evaluated using the "DMFS and defs" indices according to WHO (1987) recommendations. All clinical exams were conducted by one examiner.
STATISTICAL METHODS:	Chi-square was used to evaluate the prevalence of dental fluorosis in primary and permanent dentition. DMFS and defs scores were evaluated with ANOVA. Level of significance of $p<0.05$ was used for both methods. A Kappa statistic (of 0.83) established a high level of inter-examiner reliability (92%).
RESULTS:	
Dental fluorosis	For primary dentition, 45 of the 152 children (29.6%) had moderate fluorosis, but none had severe fluorosis, and more females than males were fluorosis free (see Table 3, copied directly from Mann et al., 1990):

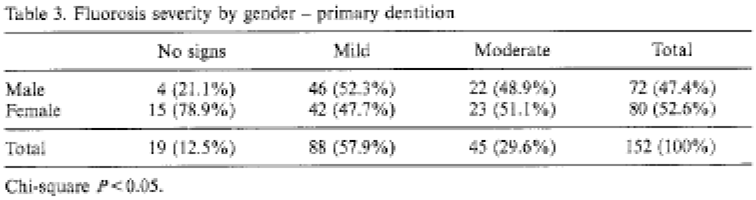


Table 3. Fluorosis severity by gender – primary dentition

	No signs	Mild	Moderate	Total
Male	4 (21.1%)	46 (52.3%)	22 (48.9%)	72 (47.4%)
Female	15 (78.9%)	42 (47.7%)	23 (51.1%)	80 (52.6%)
Total	19 (12.5%)	88 (57.9%)	45 (29.6%)	152 (100%)

Chi-square $P < 0.05$.

For the permanent dentition, 6 children had severe fluorosis and 55 had moderate fluorosis (composite of moderate + severe was 40.1%), and females and males had similar levels of fluorosis. (see Table 2, copied directly from Mann et al., 1990):

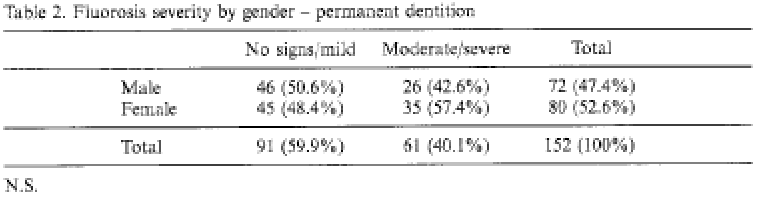


Table 2. Fluorosis severity by gender – permanent dentition

	No signs/mild	Moderate/severe	Total
Male	46 (50.6%)	26 (42.6%)	72 (47.4%)
Female	45 (48.4%)	35 (57.4%)	80 (52.6%)
Total	91 (59.9%)	61 (40.1%)	152 (100%)

N.S.

Other effects

The decay rate gradually increased in the permanent dentition with increasing fluorosis severity, but the same pattern was not seen in the primary dentition.

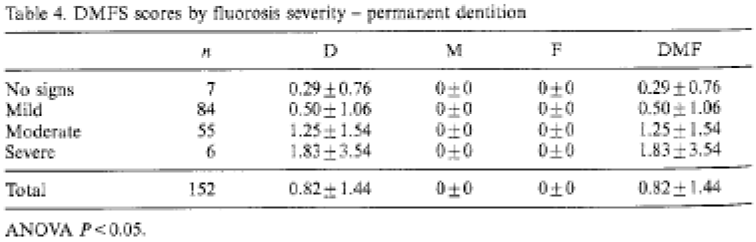


Table 4. DMFS scores by fluorosis severity – permanent dentition

	n	D	M	F	DMF
No signs	7	0.29±0.76	0±0	0±0	0.29±0.76
Mild	84	0.50±1.06	0±0	0±0	0.50±1.06
Moderate	55	1.25±1.54	0±0	0±0	1.25±1.54
Severe	6	1.83±3.54	0±0	0±0	1.83±3.54
Total	152	0.82±1.44	0±0	0±0	0.82±1.44

ANOVA $P < 0.05$.

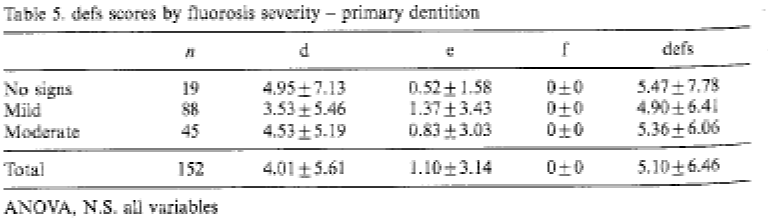


Table 5. defs scores by fluorosis severity – primary dentition

	n	d	e	f	defs
No signs	19	4.95±7.13	0.52±1.58	0±0	5.47±7.78
Mild	88	3.53±5.46	1.37±3.43	0±0	4.90±6.41
Moderate	45	4.53±5.19	0.83±3.03	0±0	5.36±6.06
Total	152	4.01±5.61	1.10±3.14	0±0	5.10±6.46

ANOVA, N.S. all variables

STUDY AUTHORS' CONCLUSIONS:

The study authors discuss several reasons for the observed lower severity of fluorosis in the primary teeth: (1) the shorter duration of enamel formation and maturation of primary teeth (and their much thinner enamel layer) allows a smaller amount of fluoride to be deposited in the developing enamel (when compared to permanent teeth), (2) primary teeth formed during the prenatal period do not receive the same level of fluoride exposure from the mother as the permanent teeth from fluoride in drinking water, and (3) higher exchange of fluoride during development of primary dentition as compared to permanent dentition. The study authors note that the incidence of moderate to severe fluorosis in the permanent teeth in the 16-18 yr olds [data from previous study (Mann et al., 1985)] was higher in boys than in girls and may have been due in part to higher levels of consumption (unquantified amounts) of tea by boys in this age group.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

WHO. 1987. Oral Health Surveys; basic methods. World Health Organization, Geneva.

For description of Dean's Index of Fluorosis see Section 2, for definition of DMFS and defs scores, see List of Acronyms.

PROFILER'S ***DMO***

Study not useful for defining NOAEL/LOAELS, but it does identify an adverse effect

REMARKS	***11/22/06 and 12/15/2006***	level.
PROFILER'S ESTIM. NOEL/NOAEL		Not possible from the data presented (all children are reported to drink from the same 2 local wells).
PROFILER'S ESTIM. LOEL/ LOAEL		The exposure level of 5.1 ppm is considered an adverse effect level due to the high incidence of moderate to severe fluorosis in the studied population; however, a LOAEL cannot be identified.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor (_), Medium (X), Strong (_) Total fluoride intake due to consumption of drinking water and tea is not documented.
CRITICAL EFFECT(S):		Dental fluorosis and caries incidence

Marshall, T.A., S.M. Levy, J.J. Warren, B. Broffitt, J.M. Eichenberger-Gilmore and P.J. Stumbo. 2004. Associations between intakes of fluoride from beverages during infancy and dental fluorosis of primary teeth. Journal of American College of Nutrition. Vol. 23 (2): 108-116.

ENDPOINT STUDIED:	Dental fluorosis in primary dentition (and contributing variables).
TYPE OF STUDY:	Longitudinal cohort study PROFILER'S NOTE: There are 4 articles (Levy et al., 2003; Marshall et al., 2004; Levy et al., 2006a and Levy et al., 2006b) that report on different findings but all use the same population of children that were originally part of the Iowa Fluoride Study (IFS) during 1992 to 1995. This IFS population was a birth cohort study of fluoride exposures and intake, fluorosis and caries. The profiler did not place all assessments on the same profile as the data presented in each report were sufficiently different.
POPULATION STUDIED:	US/Iowa: 677, 4.5-6.9 year old children (48.3% males and 51.7% females) participating in the Iowa Fluoride Study (IFS). PROFILER'S NOTE: Marshall et al. (2004) questioned the applicability of this study population for the general United States, as the subjects and their families were mostly Caucasian, middle-income and the majority of the parents had a college education.
CONTROL POPULATION:	None described
EXPOSURE PERIOD:	Birth to 4.5-6.9 years
EXPOSURE GROUPS:	Of the 690 children that received dental examinations at age 4.5-6.9 years old, only 677 adequately completed a questionnaire and could be used as the study population.
EXPOSURE ASSESSMENT:	The study measured F in water, food, beverages and estimated F exposure from fluoride supplements and dentifrices by the method of 3-day food and beverage diaries every 3-4 months(from age 6 wks to 3 yrs) and then every 6 months.
ANALYTICAL METHODS:	As part of the IFS, non-municipal home and childcare water, filtered municipal water and beverages were analyzed for fluoride. Concentrations of F from the public water systems were obtained from the Iowa State Health Department. Fluoride levels of foods were assayed as well. The method used to analyze for F was not described.
STUDY DESIGN	The Iowa Fluoride Study took place during 1992 to 1995; parents were first asked to participate in the study during the hospital stay at the time of their child's birth. Parents of the children were sent questionnaires on the children's diet and beverage intakes when the child was 6 weeks old and 3, 6, 9, and 12 months old. After 12 months of age, each child was examined every 4 months until the age of 3 years, and then every 6 months thereafter. Children underwent dental examinations on the primary dentition between ages 4.5 and 6.9 years of age, conducted at The university of Iowa General Clinical Research Center. Examinations were visual, conducted using a portable chair and exam light and performed by two trained examiners. Dental fluorosis was determined using the Tooth Surface Index of Fluorosis (Warren et al., 2001; Horowitz et al., 1984). For the diet/beverage information, parents recorded their child's intake for 3 days and all entries were compiled into a Food and Beverage Intake Table. A Nutrient Table was created from nutrient data obtained from the U.S.D.A. A Fluoride Concentration table was also compiled based on data from the water fluoride concentrations obtained and analysis of food in the laboratory. A regional database then combined the data from the Food and Beverage Intake Table, Nutrient Table and Fluoride Concentration Table to calculate the total daily fluoride intake. Data were also collected on the usage of fluoride supplements and/or

dentifrices.

PARAMETERS MONITORED:

The criteria used for identifying fluorosis in primary teeth were adapted from the Tooth Surface Index of Fluorosis (Warren et al., 2001; Horowitz et al., 1984). Fluorosis was distinguished from non-fluoride opacities based on differences in shape, demarcation and color (Russell 1961).

PROFILER’S NOTE: Details of the TSIF index (Horowitz et al., 1984) are provided in Section 2 of this report.

STATISTICAL METHODS:

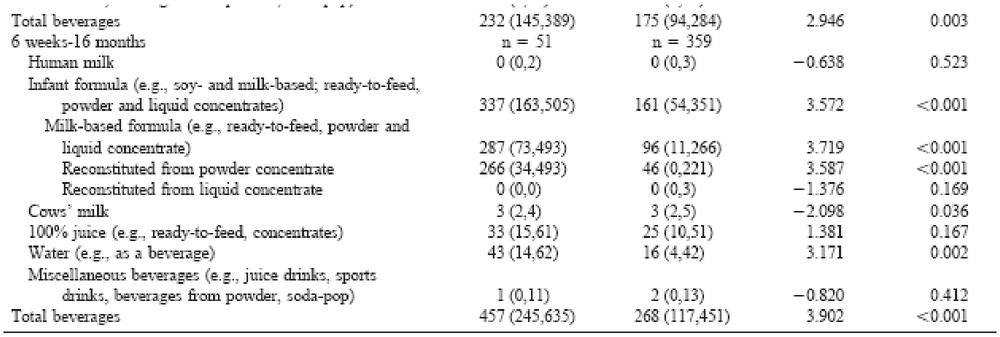
Statistical analysis was conducted using SAS (SAS, Version 8: Cary, N.C.). Subject characteristics were categorized and presented as percentages. The Wilcoxon rank-sum test compared distributions of beverage and fluoride intakes between subjects with and without fluorosis. Statistical significance occurred at p<0.05. The categories making up the variables were used to develop statistical models to predict fluorosis since not all of the relationships between beverage and fluoride intakes and fluorosis were linear. Intakes were categorized into three levels: none (nonconsumers), low and high intakes. Low and high intakes were defined as below or above the median level of consumers. Each three-category variable was represented by two indicator variables in fluorosis predication models using the LOGIST procedure in SAS. Multiple logistic regression models were developed to predict fluorosis status separately from beverage and fluoride intakes. Backward elimination was used to reduce the number of variables and final models only included variables significant at p<0.05.

RESULTS:

Variables as related to presence of fluorosis

Estimated mean total fluoride intakes were 285, 396, 497, 539, 392 and 476 µg/day at 6 weeks, 3, 6, 9, 12 and 16 months, respectively. Estimated fluoride intakes from dentifrices or supplements did not differ between subjects at any timepoint.

Part of Table 2 from Marshall et al. (2004) is copied directly below. Consumption of milk-based formulas reconstituted from powder was associated with risk of fluorosis; quantities consumed by subjects with fluorosis were higher and the fluoride concentration of water used for reconstitution by subjects with fluorosis was higher. Multiple logistic regression models developed to predict primary tooth fluorosis using categories of beverage intakes indicated that high intakes of milk for 6 weeks through 16 months (p<0.05) were negatively associated with fluorosis and high intakes of water used to reconstitute formula for 6 weeks through 16 months (p<0.05) were positively associated . Multiple logistic regression models developed to predict primary tooth fluorosis from fluoride intakes from various categories indicated that high intakes of fluoride from water used to reconstitute formulas (p<0.001) and from water as a beverage (p<0.05) and any fluoride from supplements from 6 weeks through 16 months were positively associated with fluorosis.



Beverage	**Fluorosis**	**No fluorosis**	**Wilcoxon Z- score**	**p-value**
Total beverages	232 (145,389)	175 (94,284)	2.946	0.003
6 weeks-16 months	n = 51	n = 359		
Human milk	0 (0,2)	0 (0,3)	−0.638	0.523
Infant formula (e.g., soy- and milk-based; ready-to-feed, powder and liquid concentrates)	337 (163,505)	161 (54,351)	3.572	<0.001
Milk-based formula (e.g., ready-to-feed, powder and liquid concentrate)	287 (73,493)	96 (11,266)	3.719	<0.001
Reconstituted from powder concentrate	266 (34,493)	46 (0,221)	3.587	<0.001
Reconstituted from liquid concentrate	0 (0,0)	0 (0,3)	−1.376	0.169
Cows’ milk	3 (2,4)	3 (2,5)	−2.098	0.036
100% juice (e.g., ready-to-feed, concentrates)	33 (15,61)	25 (10,51)	1.381	0.167
Water (e.g., as a beverage)	43 (14,62)	16 (4,42)	3.171	0.002
Miscellaneous beverages (e.g., juice drinks, sports drinks, beverages from powder, soda-pop)	1 (0,11)	2 (0,13)	−0.820	0.412
Total beverages	457 (245,635)	268 (117,451)	3.902	<0.001

PROFILER’S NOTE: Individual fluoride concentration levels were not provided in the study. Also, the degree of fluorosis observed based on TSIF scores was not provided; fluorosis was only stated as being present or absent.

<table>
<tr><td colspan="2">STUDY AUTHORS' CONCLUSIONS:</td><td>Infant beverages, particularly infant formulas prepared with fluoridated water, can increase the risk of fluorosis in primary teeth.</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td colspan="2">DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)</td><td>Russell, A.L. 1961. The differential diagnosis of fluoride and nonfluoride enamel opacities. J. Public Health Dent., 21:143-146.

Warren, J.J., S.M. Levy and M.J. Kanellis. 2001. Prevalence of dental fluorosis in primary dentition. J. Public Health Dent., 61:87-91.</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td>PROFILER'S REMARKS</td><td><i>Initials/date DFG/1-07</i></td><td>The study cannot be used for dose-response modelling as no quantitative data was provided. The study did not provide the degree of fluorosis identified (i.e. mild, moderate, severe) or the amount of fluoride the children were exposed to in relationship to the fluorosis. Data on the primary dentition for evidence of fluorosis were reported only as present or absent. The study population was not a true reflection of the majority of children in the United States as most were from families within the middle-income bracket with parents having a 4-year college degree which tends to indicate better preventative dental care was available.

Some of the tabulated data may assist the relative source contribution analysis.</td></tr>
<tr><td colspan="2"></td><td></td></tr>
<tr><td colspan="2">PROFILER'S ESTIM. NOEL/NOAEL</td><td>Data are unsuitable for development of a NOAEL for fluorosis.</td></tr>
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<tr><td colspan="2">POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:</td><td>Not suitable (X), Poor ( ), Medium ( ), Strong ( )</td></tr>
<tr><td colspan="2"></td><td></td></tr>
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<tr><td colspan="2"></td><td></td></tr>
</table>

Maupomé, G., J.D. Shulman, D.C. Clark and S.M. Levy. 2003. Socio-demographic features and fluoride technologies contributing to higher fluorosis scores in permanent teeth of Canadian children. Caries Res 37:327-334.

ENDPOINT STUDIED:	Dental fluorosis (maxillary anterior permanent teeth)
TYPE OF STUDY:	Canada/British Columbia: Prevalence study of dental fluorosis in male and female children in grades 2, 3, 8 and 9 in two communities during 1996-1997. Data were from British Columbia (BC) Fluoridation Cessation Study, a longitudinal evaluation of the effects of removing fluoride from water supplies that were previously fluoridated in British Columbia. The community of Comox/Courtenay/ Campbell River stopped fluoridating water supplies in 1992 and was designated "FE" (fluoridation ended). The second community, Kamloops continued fluoridation and was designated "SF" (still fluoridated). All children included in the study were lifelong residents in these communities and had permanent anterior teeth mineralized at the time water supplies were optimally fluoridated.
POPULATION STUDIED:	A total of 8,277 subjects were examined in 1996-1997, 49.6% from FE and 50.4% from SF. Of these, 49.8% were female; 50.1% were in grades 2 and 3 and 49.9% in grades 8 and 9. Two dental examiners determined dental fluorosis in the children during 1996-1997 using the Thylstrup-Fejerskov Index (TFI; see NRC, 2006, pages 88-89 and Section 2 of this report). Informed consent was obtained from parents and children, as approved by the Ethical Review Board of the University of British Columbia.
CONTROL POPULATION:	None.
EXPOSURE PERIOD:	From birth until time of dental exam.
EXPOSURE GROUPS:	Children in grades 2, 3, 8 and 9 in two communities with differing F concentrations in British Columbia, Canada.
EXPOSURE ASSESSMENT	Exposure measurements for the monthly fluoridated water levels (means ± SD) for 1985-1992 in Comox/Courtenay and Campbell River, and for 1982-1993 in Kamloops were 0.92 ± 0.21, 0.88 ± 0.28 and 0.95 ± 0.27 mg F/L, respectively. Neither the analytical protocol nor the water monitoring equipment used was reported in Maupomé, et al (2003). Based on data from questionnaires completed by parents, fluoride exposure histories (supplements, rinses, toothpaste amount, tooth brushing frequency and tooth brushing starting age) were developed.
ANALYTICAL METHODS:	None.
STUDY DESIGN	The present study used epidemiological data and fluoride and diet histories from follow-up surveys and questionnaires previously described (Clark and Berkowitz, 1997a, b; Maupomé et al, 2001a, b) to examine levels of fluorosis among children from two Canadian communities exposed to fluoride. Maxillary anterior permanent teeth of children from these communities (grades 2, 3, 8 and 9 in 1996-97) were ranked with the TFI scoring system (see NRC, 2006, pages 88-89 and Section 2 of this report). Questionnaires completed by parents included information characterizing frequency of dental attendance, use of bottled water or formula in the first year of life, frequency of tooth brushing with home products containing fluoride, starting age of tooth brushing, when self-brushing began, and the amount of toothpaste used during the first four years of life (as a proxy measure for swallowing toothpaste and fluoride supplement use).
PARAMETERS MONITORED:	One of two trained dental examiners determined dental fluorosis for subject children. The TFI intra-examiner reliability k coefficient 0.72 and inter-examiner reliability was 0.63 (on

a per-child basis). Examiners viewed all teeth both with and without the use of the dental light, and a score was assigned to each tooth. CDC standard procedures for epidemiological dental examinations were followed (Summers et al, 1994).

STATISTICAL METHODS:

Basic descriptive statistics were obtained and the relationships between TFI and the independent variables using a multivariate regression model were assessed. The variables obtained by questionnaires from the parents included age, gender and whether the children lived in either SF or FE communities.

Generated variables derived from questionnaire data included: 1) a composite measure of the socio-economic level (SES), frequency of dental attendance and parental education; 2) pre- and post-eruptive exposure to fluorides through the use of fluoride supplements; 3) use of bottled water or formula during the first year of life; 4) post-eruptive exposure to fluorides from the frequency of tooth brushing with home care products containing fluoride; and 5) estimation of the amount of toothpaste used in the first four years of life as a proxy measure for swallowing toothpaste, together with tooth brushing frequency and starting age. Since TFI scores were heavily skewed with a mode of zero, a multivariate Poisson regression model was used. A fully saturated model was first fitted using TFI as a dependent variable and the previously described covariates. Using the Wald X^2 tests, the least significant covariates were sequentially eliminated. All two-way interactions between the covariates were tested and those that were significant ($p<0.05$) were added to the model. If the two-way interactions were significant, three-way interactions were tested, and those meeting the $p<0.05$ criterion were added to the model.

RESULTS:

Study results are included in Tables 3 and 4 shown directly from Maupomé et al (2003).

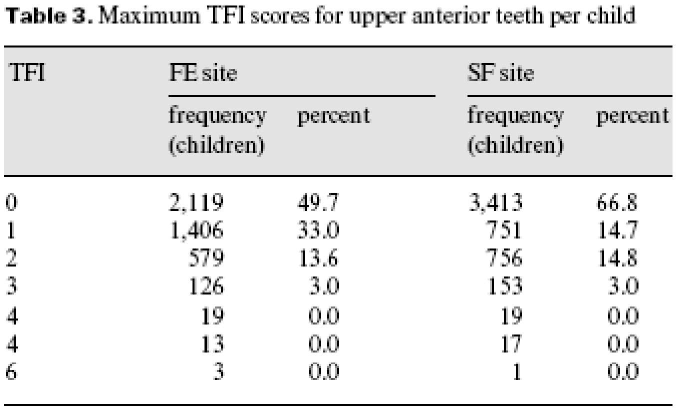


Table 3. Maximum TFI scores for upper anterior teeth per child

TFI	FE site		SF site	
	frequency (children)	percent	frequency (children)	percent
0	2,119	49.7	3,413	66.8
1	1,406	33.0	751	14.7
2	579	13.6	756	14.8
3	126	3.0	153	3.0
4	19	0.0	19	0.0
4	13	0.0	17	0.0
6	3	0.0	1	0.0

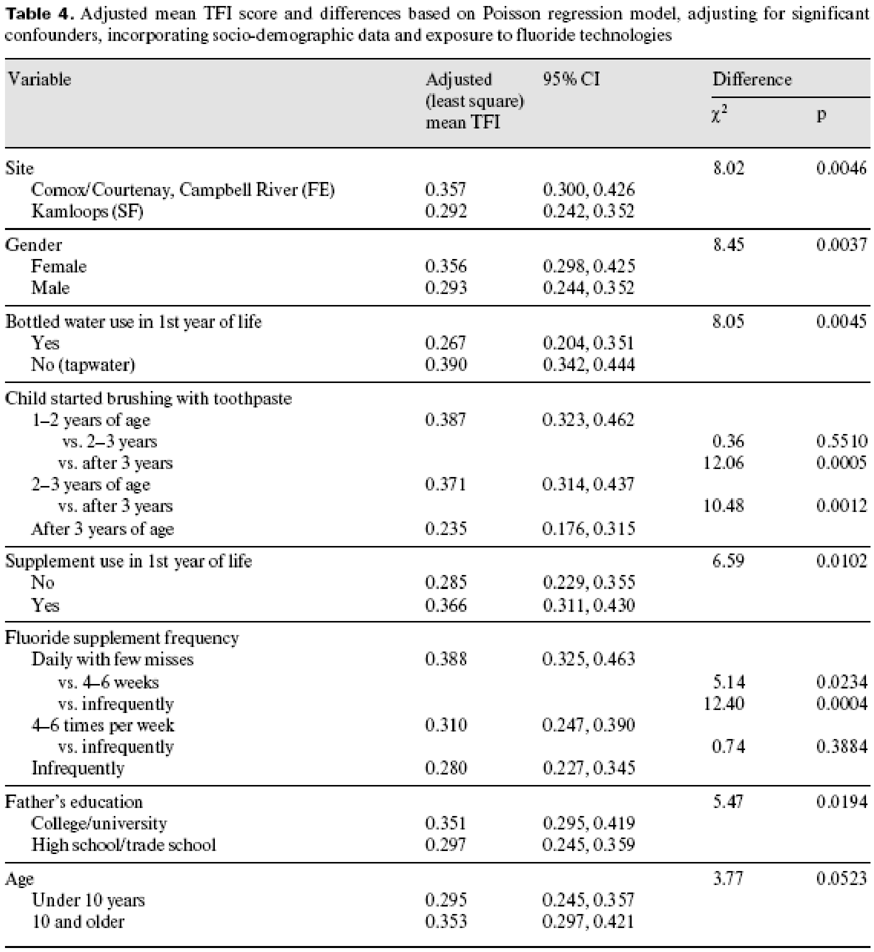


Table 4. Adjusted mean TFI score and differences based on Poisson regression model, adjusting for significant confounders, incorporating socio-demographic data and exposure to fluoride technologies

Variable	Adjusted (least square) mean TFI	95% CI	Difference	
			χ^2	p
Site			8.02	0.0046
Comox/Courtenay, Campbell River (FE)	0.357	0.300, 0.426		
Kamloops (SF)	0.292	0.242, 0.352		
Gender			8.45	0.0037
Female	0.356	0.298, 0.425		
Male	0.293	0.244, 0.352		
Bottled water use in 1st year of life			8.05	0.0045
Yes	0.267	0.204, 0.351		
No (tapwater)	0.390	0.342, 0.444		
Child started brushing with toothpaste				
1–2 years of age	0.387	0.323, 0.462		
vs. 2–3 years			0.36	0.5510
vs. after 3 years			12.06	0.0005
2–3 years of age	0.371	0.314, 0.437		
vs. after 3 years			10.48	0.0012
After 3 years of age	0.235	0.176, 0.315		
Supplement use in 1st year of life			6.59	0.0102
No	0.285	0.229, 0.355		
Yes	0.366	0.311, 0.430		
Fluoride supplement frequency				
Daily with few misses	0.388	0.325, 0.463		
vs. 4–6 weeks			5.14	0.0234
vs. infrequently			12.40	0.0004
4–6 times per week	0.310	0.247, 0.390		
vs. infrequently			0.74	0.3884
Infrequently	0.280	0.227, 0.345		
Father's education			5.47	0.0194
College/university	0.351	0.295, 0.419		
High school/trade school	0.297	0.245, 0.359		
Age			3.77	0.0523
Under 10 years	0.295	0.245, 0.357		
10 and older	0.353	0.297, 0.421		

STUDY AUTHORS' CONCLUSIONS:

REVIEWER'S NOTE: Residents of FE (fluoridation-ended in 1992; historical F concentration <1ppm) communities exhibited marginally higher TFI scores than SF (still fluoridated at 0.95 ppm). Observed levels of dental fluorosis were low to mild. The consumption of bottled water between birth and 6 month of age was protective against dental fluorosis in the subject population (for maxillary anterior permanent teeth).

Study authors concluded that higher fluoride exposure slightly increased the likelihood that a child exhibited a higher TFI score, especially when more fluoridation technologies (e.g., fluoride tooth paste and F supplements) were used at home.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

Clark, D.C. and J. Berkowitz. 1997a. The relationship between the number of sound, decayed, and filled permanent tooth surfaces and the number of sealed surfaces in children and adolescents. J Public Health Dent 57:171-175.

Clark, D.C. and J. Berkowitz. 1997b. The influence of various fluoride exposures on the prevalence of esthetic problems resulting from dental fluorosis. J Public Health Dent 57:144-149.

Maupomé, G., D.C. Clark, S.M. Levy and J. Berkowitz. 2001a. Patterns of dental caries following the cessation of water fluoridation. Community Dent Oral Epidemiol 29:36-46.

Maupomé, G., J.D. Shulman, D.C. Clark, S.M. Levy and J. Berkowitz. 2001b. Tooth-surface progression and reversal changes in fluoridated and no-longer-fluoridated communities over a three-year period. Caries Res 35:95-105.

Summers, C.J., B.F. Gooch, D.W. Malvitz, and W.W. Bond 1994. Practical infection control in oral health surveys and screenings. J Am Dent Assoc 125:1213-1217.

PROFILER'S ***Initials/***

The Materials and Methods for the study were brief because they have been described in

REMARKS	***Date*** VAD/01-02-07	other publications. The study was conducted in British Columbia, Canada, so the cohort may not be representative of the U.S. general population. Recall biases could have occurred since parents were asked to remember events that occurred many years prior to completing the questionnaires and may have been confounded by memories of other children. The examiners were different for each study site and were not blinded to site fluoridation status; however, good k values suggested appropriate levels of examiner consistency. Fluorosis results were generally limited to the low to mild category; 234 of 8,277 children (2.8%) had TFI scores of ≥ 3. This paper also contains information useful to analysis of relative source contribution. Fluoridation status of study communities was in the range considered optimal for North America North of Mexico (approximately 1 mg F/L). As a consequence, variation in TFI scores between the study communities would not be expected to be large. It appears that insufficient contrast in F concentrations between study communities was incorporated into the study protocol. Further, fluoridation terminated in one study community in 1992, 4-5 years prior to dental exam. Thus, some confounding of collected dental fluorosis data is likely.
PROFILER's ESTIM. NOAEL		The study design did not estimate a NOAEL.
PROFILER'S ESTIM. LOAEL		The study design did not estimate a LOAEL.
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable,(X); Poor (X); Medium (); Strong (_)
CRITICAL EFFECTS:		Dental fluorosis (maxillary anterior permanent teeth)

Meneghim, M.C., Tagliaferrro, E.P.S., Tengan, C., Meneghim, Z.M.A.P., Pereira, A.C., Ambrosano, G.M.B., and Assaf, A.V. 2006. Trends in Caries Experience and Fluorosis Prevalence in 11- to 12-Year Old Brazilian Children between 1991 and 2004. Oral Health Prev Dent. 4(3): 193-198.

ENDPOINT STUDIED:	Dental caries and fluorosis
TYPE OF STUDY:	Retrospective.
POPULATION STUDIED:	Brazil/Sao Paulo State/Iracemapolis: 236 male and female public school children, ages 11- and 12- years old; individuals were born in the town or lived there since the age of two, did not use fixed orthodontic appliances, and did not present severe dental hypoplasia. This was a follow-up in a series of surveys conducted in the same city (Pereira et al., 2000; Kozlowski, 2001).
CONTROL POPULATION:	Comparisons were made with previous surveys of 11-12 year old children carried out in Iracemapolis in 1991 (n=200); 1995 (n= 160); 1997 (n= 314); and 2000 (n= 244).
EXPOSURE PERIOD:	The study was conducted in 2004 on a group of children born in 1992 and 1993. Fluoride was added to the water supply beginning in 1997 (7 years prior to the current study). Fluoridated dental products became available in 1989. The study authors state that children in all public schools performed tooth brushing under the supervision of their teachers, and were instructed to brush twice per day; however, the report does not indicate when the school-supervised program began. Caries decline and fluorosis increase have been verified since 1991 (6 years prior to water fluoridation).
EXPOSURE GROUPS:	Fluoride was added to the water at 0.7 ppm beginning in 1997. At the initiation of this fluoridation program, the children in this study were already 4-5 yrs old. Fluoridated dentifrices were commercially available since 1989, and there was a tooth-brushing program at the public schools; consequently, children may have been using fluoridated dentifrices since beginning school; however, the exact date when the school program began was not indicated. The study authors state that no oral health program based on fluoride therapy was available, and presumably this meant therapies such as non-invasive application of fluoride in gel, solution, or varnish.
EXPOSURE ASSESSMENT:	Dental caries and fluorosis prevalence were measured. No radiographs were taken during the surveys.
ANALYTICAL METHODS:	Data on how fluoride concentrations in the water supply were measured were not included in the study report. The fluoride concentration in the dentifrices also was not included.
STUDY DESIGN	In the study, 236 schoolchildren (both genders), ages 11 to 12 years old, made up the study population. All study participants were born in the town of Iracemapolis, Brazil or lived there since the age of two, did not use fixed orthodontic appliances, and did not present severe dental hypoplasia. The prevalence rates of dental caries and fluorosis in the current study population (surveyed in 2004) was compared to prevalence rates from previous surveys carried out in 1991 (n=200), 1995 (n=160), 1997 (n=314), and 2001 (n=244). The same protocol was followed in each survey. Examinations: The decayed, missing, and filled permanent teeth (DMFT) index was used for caries examination following the World Health Organization criteria, and the Thylstrup-Fejerskov (T-F) index was used for fluorosis examination with the highest score being registered for each child. Prior to the examination, each individual received

a toothbrush with fluoridated dentifrice and performed tooth-brushing supervised by a dental hygienist. All schoolchildren were examined under natural light in an outdoor setting, using a dental probe, buccal mirror, and air-drying. No radiographs were taken during the surveys. For the DMFT index all permanent teeth were examined and for the T-F index all the buccal surfaces of all permanent teeth that showed more than two-thirds of erupted crown, and no fillings, were examined. The differential diagnosis between very mild signs of dental fluorosis and nonfluorotic enamel opacities followed the Russel's criteria.

Two dentists, aided by two recorders, performed the examinations in all the surveys. One dentist examined dental caries and the other dental fluorosis. Duplicate examinations were conducted in 10% of the sample to assess intra-examiner consistency. Kappa values were greater then 0.81 for both examiners in all surveys.

PARAMETERS MONITORED:

Dental caries and fluorosis were measured using the mean number of decayed, missing, and filled permanent teeth (DMFT) and Thylstrup-Fejerskov (T-F) indices, respectively. No radiographs were taken during the surveys.

STATISTICAL METHODS:

The variation of the DMFT index over time (1991 to 2004) was assessed by analysis of regression at 1% significance level ($p<0.01$). Comparison of fluorosis prevalence (T-F>1) according to the year of survey was performed using the Chi-square test ($p<0.05$).

RESULTS:

Caries

Table 1 was copied directly from Meneghim et al. (2006) and summarizes the results of dental caries experience obtained in all surveys carried out between 1991 and 2004. In 2004, 50% of schoolchildren were caries-free. The mean DMFT was 1.2, 82.1% lower than the results obtained in 1991 (DMFT=6.7). Seven years after fluoridation of the water supply (2004), the DMFT was 58.6% lower (versus 1997 DMFT=2.9). In the 1991-1997 period, with no fluoride in the drinking water, the DMFT was lowered 56.7%. A significant decrease of DMFT over time for 12 year old schoolchildren could be demonstrated by analysis of regression that showed a linear effect for DMFT and year of survey ($R^2=0.92$; figure 1, copied directly from Meneghim et al. (2006)).

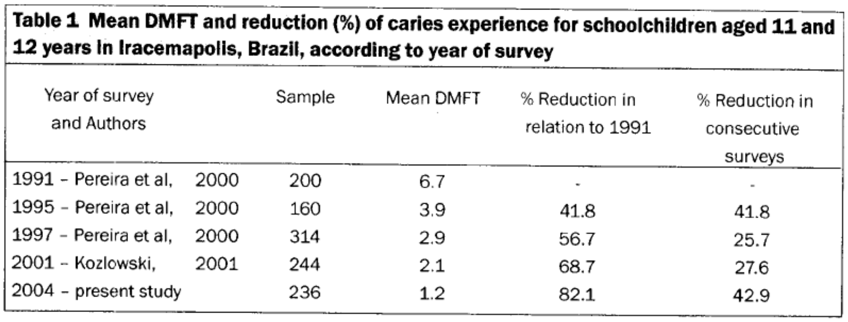


Table 1 Mean DMFT and reduction (%) of caries experience for schoolchildren aged 11 and 12 years in Iracemapolis, Brazil, according to year of survey

Year of survey and Authors		Sample	Mean DMFT	% Reduction in relation to 1991	% Reduction in consecutive surveys
1991 – Pereira et al,	2000	200	6.7	-	-
1995 – Pereira et al,	2000	160	3.9	41.8	41.8
1997 – Pereira et al,	2000	314	2.9	56.7	25.7
2001 – Kozlowski,	2001	244	2.1	68.7	27.6
2004 – present study		236	1.2	82.1	42.9

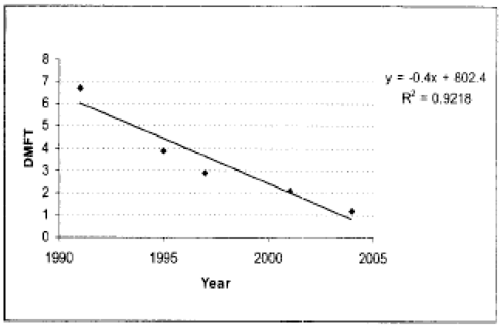


Fig 1 DMFT variation for 11- to 12-year-old schoolchildren in function of time.

PROFILER'S NOTE: The profiler agrees that there was a reduction in the mean DMFT index over time from 1991 to 2004.

Dental fluorosis

Table 2 was copied directly from Meneghim et al. (2006) and summarizes the prevalence of fluorosis (T-F>1) from 1991-2004. Statistically significant increases ($p<0.01$) were found between 1991 and 1997 as well as 1997 and 2004. In 2004, 15.7% of children presented with fluorosis, T-F>1. A total of 59.7%, 24.6%, 10.6%, and 5.1% of the children were scored as T-F=0, T-F=1, T-F=2, and T-F≥3, respectively.

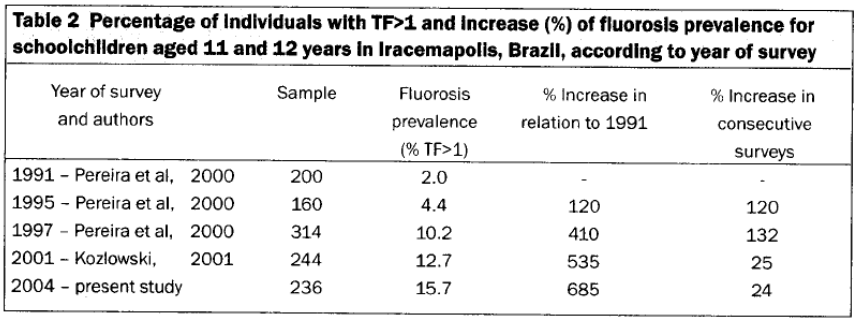


Table 2 Percentage of individuals with TF>1 and increase (%) of fluorosis prevalence for schoolchildren aged 11 and 12 years in Iracemapolis, Brazil, according to year of survey

Year of survey and authors	Sample	Fluorosis prevalence (% TF>1)	% Increase in relation to 1991	% Increase in consecutive surveys
1991 – Pereira et al, 2000	200	2.0	-	-
1995 – Pereira et al, 2000	160	4.4	120	120
1997 – Pereira et al, 2000	314	10.2	410	132
2001 – Kozlowski, 2001	244	12.7	535	25
2004 – present study	236	15.7	685	24

PROFILER’S NOTE: The profiler agrees that the prevalence of fluorosis (T-F>1) increased over time.

STUDY AUTHORS’ CONCLUSIONS:

A significant decrease in dental caries and a significant increase in dental fluorosis prevalence could be verified from five epidemiological studies carried out from 1991 to 2004 in Iracemapolis, Brazil. The expansion of preventative programs at schools (date of initiation not reported), the presence of fluoride in the water supply (since 1997), and fluoridated dentifrices (available since 1989) are recognized as the main factors for caries decline in Brazil.

Most of the individuals with fluorosis presented with T-F scores of 1 or 2 (T-F≥3 =5.1%) which does not affect aesthetics or function. Water fluoridation can not be claimed as the responsible factor in the increase of fluorosis prevalence observed from 1997 to 2004. The significant increase in fluorosis prevalence is possibly due to the inappropriate use of fluoridated dentifrices by young children.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

Kozlowski, F.C. (2001). Relacao entre o fator socioeconomico e a prevalencia e severidade de fluorose e carie dentaria. [Dissertacao]. Piracicaba: Universidade Estadual de Campinas, Faculdade de Odontologia de Piracicaba.

Pereira A.C., Cunha F.L., Meneghim M.C., Werner C.W. (2000). Dental caries and fluorosis prevalence study in a nonfluoridated Brazilian community: trend analysis and toothpaste association. *ASDC J Dent Child*. **67**, 132-135.

Russell, A.L. (1961). The differential diagnosis of fluoride and non-fluoride enamel opacities. *Journal of Public Health Dentistry* **21**, 143-146.

World Health Organization (1987). Oral Health Surveys: Basic Methods. 3rd ed. WHO, Geneva.

World Health Organization (1997). Oral Health Surveys: Basic Methods. 4th ed. WHO, Geneva.

PROFILER’S REMARKS — ***Initials/date SJG/ 3/7/07***

The study was well-conducted and had adequate study design. However, the study was not designed for development of a dose-response to fluoride as the emphasis was on monitoring dental caries and fluorosis in children before and after the addition of fluoride in the water supply (1997). Based on the study design, the observed decrease in caries and increase in fluorosis from 1991 to 2004 can not be attributed to any one cause. A limitation of the article is that a description of the preventative program in schools (i.e., brushing under teacher supervision) was not described fully, including

		when it was initiated. The increase in fluorosis prevalence can not be attributed to water fluoridation because: 1) A significant increase in fluorosis was observed from 1991 to 1997, prior to the addition of fluoride to the water in 1997 (other sources of fluoride exposure, besides fluoridated denitricies, were not mentioned). 2) The percent increase was higher before 1997 (120% between 1991 and 1995 and 132% between 1995 and 1997) than after1997 (25% between 1997 and 2001 and 24% between 2001 and 2004); and 3) Examinations were conducted on children after the critical period for developing fluorosis. Children examined in 2004 were 4-5 years old in 1997 and the critical period for developing manifest fluorosis in the upper central incisors is from 2-3 years old PROFILER'S NOTE: The study authors state that the critical period for developing manifest fluorosis in the upper central incisors is from 2-3 years old, but upon further inspection of the reference (Ishii and Suckling, J Dent Res 1991; 70: 952-956), this is a questionable time frame. Ishii and Suckling concluded that children were "at-risk" for fluorosis development if exposure to high fluoride in the water (7.8 ppm) started after 11 months and ended before 7 years of age, and this time frame was dependent on tooth type (i.e., pre-molars, upper central incisors, molars). Although estimates for critical periods were reported, limitations in their study preclude conclusions for "at-risk" periods of susceptibility to fluorosis from being used without caution. Therefore, the children examined in the current study still may have been vulnerable to fluorosis in 1997 when water fluoridation was initiated (they were less than 7 years old).
PROFILER'S ESTIM. NOEL/NOAEL		Study design was not suitable for development of a NOAEL for caries or fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL		Study design was not suitable for development of a LOAEL for caries or fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( ) While the study was well-conducted, the study design was not conducive to provide data for a dose-response. The study only indicated an increased incidence of dental caries and decreased prevalence of fluorosis in the public school population of 11- to 12- year old children in Iracemapolis, Brazil from 1991 to 2004. The study did not address any issues of plaque or gingivitis.
CRITICAL EFFECT(S):		Prevalence of dental caries and fluorosis

Olsson, B. 1979. Dental findings in high-fluoride areas in Ethiopia. Community Dent. Oral Epidemiol, 7:51-56.

ENDPOINT STUDIED:	Dental fluorosis, dental caries and gingivitis in schoolchildren
TYPE OF STUDY:	Cross-sectional survey
POPULATION STUDIED:	Ethiopia/Rift Valley. 478 children aged 6-7 years old and 13-14 years old from either Wonji, a sugar plantation area in the Shoa province or Awassa, the capital of the Sidamo province, were used in the study. 60 boys and 60 girls in each age group for each area were randomly selected for the study; however, data from 2 children were lost.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	The exact duration of exposure to the drinking water was not stated, however, the older children were questioned on the place of their birth, thus assuming the children were exposed to drinking water in the area since birth. An exact date on when the study took place was not provided. PROFILER'S NOTE: There was no information regarding whether or not the 6-7 year old group were asked the place of their birth; the profiler assumes Olsson (1979) thought they would have been native to the area.
EXPOSURE GROUPS:	The schoolchildren were from either Wonji or Awassa which are in the Rift Valley area of Ethiopia. Fluoride levels in Wonji, taken from six wells, ranged from 6.0 ppm to 17 ppm (mean of 12.4 ppm). In Awassa, fluoride levels taken from seven wells ranged from 1.2 ppm to 7.4 ppm (mean of 3.5 ppm). Dates for well water sample collections were not reported.
EXPOSURE ASSESSMENT:	The children in the 13-14 year old group were asked whether they were born in the area to determine if exposure to the drinking water had been since birth. The study did not state if the younger children were asked this information. No information was included in the study on other possible sources of fluoride besides the drinking water.
ANALYTICAL METHODS:	Water samples were analyzed for fluoride content from six wells in the Wonji area and seven wells in the Awassa area. The method of fluoride analysis was according to that of Frant and Ross (1966).
STUDY DESIGN	478 schoolchildren aged 6-7 years old and 13-14 years old from either Wonji, a sugar plantation area in the Shoa province; or Awassa, the capital of the Sidamo province were evaluated. Subjects were selected from schools in the community from randomly chosen classes until 60 boys and 60 girls in each age group were identified. Water samples from wells in both areas were collected and analyzed for fluoride. Olsson served as the single dental examiner for the subjects; thorough dental examinations were performed under natural light using plane mouth mirrors and explorers for dental fluorosis, oral hygiene assessment, periodontal condition, and dental caries.
PARAMETERS MONITORED:	Dental fluorosis was scored according to the criteria of Dean (1934), as modified by Moller (1965). The severe score was reserved for teeth with extensive loss of enamel while teeth with some confluent pits only were scored as moderate. Each individual child was assigned a fluorosis rating according to the two teeth with the highest fluorosis score. Also, a community index of dental fluorosis (F_{ci}) (Dean 1942) was determined for each area using the formula below. Frequency was the actual number of cases in each dental fluorosis score category times the weights for each score, which were as follows: very mild, 1; mild, 2; moderate, 3; and severe, 4. The total numerator was divided by the total number of children examined. A similar severity index of fluorosis was determined for tooth groups (F_{ti}) (Moller et al. 1970). $F_{ci} = \frac{\text{frequency x weight}}{\text{No. of individuals}}$

Oral hygiene was assessed by the Simplified Oral Hygiene Index (OHI-S) as presented in Greene and Vermillion (1964). Periodontal condition was assessed as sound ("sound" was not defined) presence of gingivitis only, or presence of destructive periodontal disease, following the criteria of WHO for field surveys (1971).

Dental caries was diagnosed for the tooth surface only when definite cavitation existed "with sticking on probing" occurred. Assessments were made on the number of decayed and filled primary teeth (dft) and the number of decayed, missing and filled permanent teeth (DMFT).

Duplicate examinations were performed on 18 of the 13-14 year olds. In duplicate examinations, caries assessments were reproduced in all instances but one and the fluorosis scoring was consistent in 89% of the examinations. The different scorings occurred mostly in the very mild and mild groups.

PROFILER'S NOTE: Olsson (1979) rated the fluorosis according to Dean (1934). Dean's Index of Fluorosis is described in Section 2 of this report. The difference between the two indexes was that the 1934 fluorosis scoring by Dean (1934) included a category of "moderately severe and severe," and the modified 1942 Dean index combined these categories into one, calling it "severe" (NRC 2006). The profiler is unsure what is meant by "…as modified by Moller (1965)," but has ordered an open-literature paper by Moller et al (1970) to investigate the issue.

STATISTICAL METHODS: No information characterizing the type of statistical analysis used was included in the study report. However, Olsson stated that statistical analysis was performed on the score frequencies.

RESULTS:

Dental fluorosis

Tables 1 and 2 are directly copied from Olsson (1979) and provide data on the fluorosis scoring and incidence. Olsson (1979) stated that no gender-related differences were observed in any of the parameters examined. In Table 1, in both cities, moderate and severe fluorosis was more prevalent in the permanent dentition compared to the primary dentition, and both communities of Wonji and Awassa had a similar number of participants with moderate and severe fluorosis scores. Tables (not copied below) were also provided indicating the tooth severity index and identified the second molars as the teeth most affected by dental fluorosis in both the primary and permanent teeth in the children born in Wonji and Awassa.

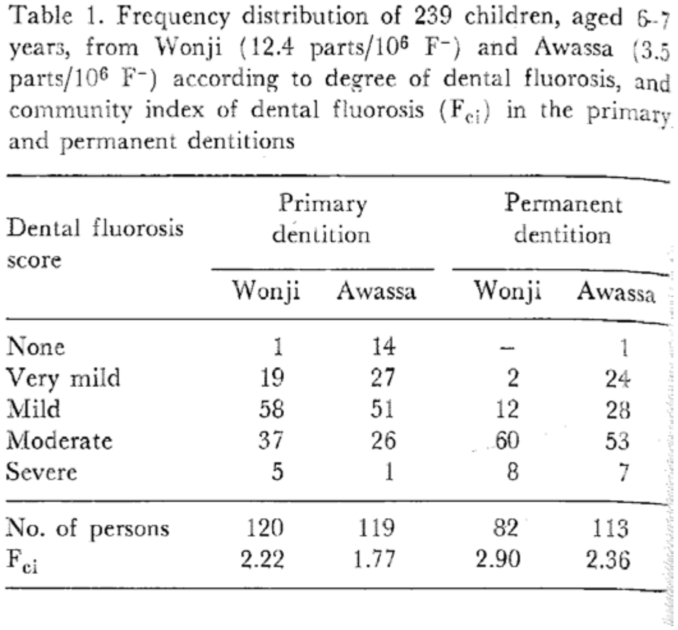


Table 1. Frequency distribution of 239 children, aged 6-7 years, from Wonji (12.4 parts/10^6 F^-) and Awassa (3.5 parts/10^6 F^-) according to degree of dental fluorosis, and community index of dental fluorosis (F_{ci}) in the primary and permanent dentitions

Dental fluorosis score	Primary dentition		Permanent dentition	
	Wonji	Awassa	Wonji	Awassa
None	1	14	–	1
Very mild	19	27	2	24
Mild	58	51	12	28
Moderate	37	26	60	53
Severe	5	1	8	7
No. of persons	120	119	82	113
F_{ci}	2.22	1.77	2.90	2.36

Table 2 provides similar information for those children ages 13-14; however, it is only for permanent dentition and indicates the difference between those native to the area and those not native to the area. All of the 13-14 year old children born in Wonji and Awassa had dental fluorosis with most having a moderate score. For those not born in the areas, 84% had dental fluorosis with the majority scoring as very mild.

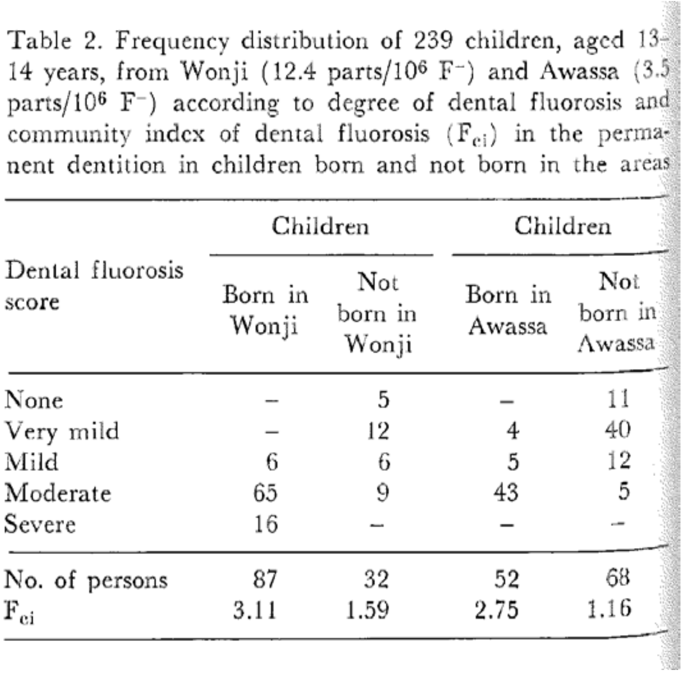


Table 2. Frequency distribution of 239 children, aged 13–14 years, from Wonji (12.4 parts/10^6 F^-) and Awassa (3.5 parts/10^6 F^-) according to degree of dental fluorosis and community index of dental fluorosis (F_{ci}) in the permanent dentition in children born and not born in the areas

Dental fluorosis score	Children		Children	
	Born in Wonji	Not born in Wonji	Born in Awassa	Not born in Awassa
None	–	5	–	11
Very mild	–	12	4	40
Mild	6	6	5	12
Moderate	65	9	43	5
Severe	16	–	–	–
No. of persons	87	32	52	68
F_{ci}	3.11	1.59	2.75	1.16

PROFILER’S NOTE: A confounder was identified for the data from Wonji as Olsson (1979) stated at the end of the paper that some wells located in Wonji had a fluoride concentration of 2 ppm, and defluoridated water was distributed to the living quarters of the management of the sugar factory and also to some of the plantation villages. Data are unclear regarding whether this occurred during the duration of the study or if all or any children included in the study were either living in the management quarters or within the plantation villages receiving the defluoridated water. These data must be considered when applying the study to use for a dose-response. Children in Wonji did have severe fluorosis but if they were exposed to some water with lower fluoride concentrations, the number of children with reported scores of moderate or severe may be lower than if they had been exposed only to the water in Wonji with the reported fluoride levels.

Dental caries

Table 5 was copied directly from Olsson (1979) and shows how the fluorosis scores correlate with the incidence of caries in both the 6-7 year old children’s primary teeth and the 13-14 year old children’s permanent teeth with further breakdown into first and second molars. Caries was diagnosed in 24% of all teeth with severe fluorosis.

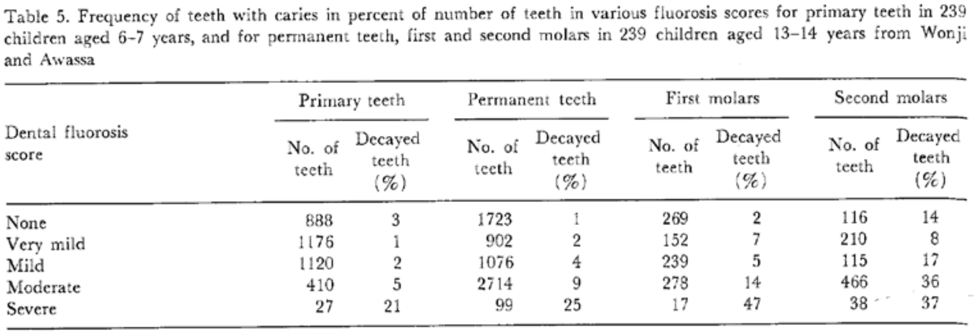


Table 5. Frequency of teeth with caries in percent of number of teeth in various fluorosis scores for primary teeth in 239 children aged 6–7 years, and for permanent teeth, first and second molars in 239 children aged 13–14 years from Wonji and Awassa

Dental fluorosis score	Primary teeth		Permanent teeth		First molars		Second molars	
	No. of teeth	Decayed teeth (%)	No. of teeth	Decayed teeth (%)	No. of teeth	Decayed teeth (%)	No. of teeth	Decayed teeth (%)
None	888	3	1723	1	269	2	116	14
Very mild	1176	1	902	2	152	7	210	8
Mild	1120	2	1076	4	239	5	115	17
Moderate	410	5	2714	9	278	14	466	36
Severe	27	21	99	25	17	47	38	37

PROFILER’S NOTE: In both primary and permanent teeth, the number of decayed teeth increased when the dental fluorosis score was severe.

Other findings

Olsson (1979) also reported that gingivitis was observed in 99% of the 6-7 year old children and 95% of the 13-14 year old children. The OHI-S was 1.99 ± 0.75 for the 6-7 year olds and 1.89 ± 0.67 for the 13-14 year olds.

STUDY AUTHORS' CONCLUSIONS:	From the study, it was concluded that severely disfiguring fluorosis was very common in the surveyed areas, causing an increase in both caries and gingivitis in addition to the obvious aesthetic disadvantages. Olsson (1979) stated that his results were probably lower than other comparable studies because he did not score questionable fluorosis and that only teeth with extensive loss of enamel were given the severe score. He also noted that high water consumption in the dry season, frequent tea drinking and malnutrition could have attributed to the fluorosis present. Olsson (1979) stated that data indicated conclusive evidence of placental transfer of fluoride in high-fluoride areas due to moderate fluorosis in the enamel of primary incisors.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Frant, S.M. and J.W. Ross, Jr. 1966. Electrode for sensing fluoride ion activity in solution. Science, 154: 1553-1554. Greene, J.C. and J.R. Vermillion. 1964. The simplified oral hygiene index. J. Am. Dent. Assoc., 68: 25-31. Moller, I.J. 1965. Dental fluorose og caries. Thesis. Rhodos, Copenhagen. Moller, I.J. , J.J. Pindborg, I Gedalia and B. Roed-Petersen. 1970. The prevalence of dental fluorosis in the people of Uganda. Arch. Oral. Biol. 15: 213-225. WHO (World Health Organization). 1971. Oral health surveys: basic methods. Geneva.
PROFILER'S REMARKS ***DFG 11/30/2006 and 12/14/2006***	Moderate and severe fluorosis was observed in this study mostly in the permanent dentition of children native to the area. While Olsson (1979) recognizes that other factors could be contributing to the high scores besides the fluoride in the drinking water, i.e. tea drinking, malnutrition, those factors were not addressed further in this study. Some confounding information was identified at the end of the report. Olsson (1979) stated that some areas around Wonji had wells with lower amounts of fluoride (2 ppm) and that defluoridated water had been distributed for several years to some residential areas and villages (not separately analyzed) in the study area. Because it is not clear if the children in the study were included in this population given the lower fluoride water for several years, this creates a possible confounder that could make the reported data for the community of Wonji actually lower than if the children had been exposed to the measured quantities of fluoride continuously. Adequate data concerning the statistical analysis used, if any, were lacking.
PROFILER'S ESTIM. NOEL/NOAEL	Data are not suitable for development of a NOAEL for fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL	Data are not suitable for development of a LOAEL for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (_), Poor (_), Medium (X), Strong (X) While the study does provide adequate study numbers and follows the standard indexes of measurement for fluorosis, data gaps (i.e. other sources of fluoride, lack of statistical analysis) and confounding information (the possibility of some children being introduced to defluoridated water in Wonji for an undetermined duration) makes this study of medium use for dose-response. There were adequate data to correlate a severe fluorosis score with a high level of decay in teeth when children were exposed to high levels of fluoride for some period of time. Data for Awassa was not affected by the confounding data.
CRITICAL EFFECT(S):	Dental fluorosis, dental caries and gingivitis in schoolchildren

Retief et al., 1979. Relationships among fluoride concentrations in enamel, degree of fluorosis and caries incidence in a community residing in a high fluoride area. Journal of Oral Pathology 8: 224-236.

ENDPOINT STUDIED:	Dental fluorosis and dental caries
TYPE OF STUDY:	Cross-sectional study of fluorosis and caries incidence and fluoride levels in teeth enamel
POPULATION STUDIED:	South Africa/Kenhardt: 85 children, 14-16 yrs old (37 boys and 48 girls) of mixed racial background (Caucasian, Negroid and Malayan). The town drinking water is obtained from boreholes. No further information on the study population was reported. Rainfall in the study area was reported to be 12.5-25 cm per year; the mean maximum annual temperature was not reported.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	Not stated
EXPOSURE GROUPS:	The fluoride content of the water supply was 3.2 ppm
EXPOSURE ASSESSMENT:	Fluoride exposures from non-drinking water sources were not evaluated.
ANALYTICAL METHODS:	The fluoride content in the teeth enamel was determined with a Model 96-09 Orion combination fluoride electrode coupled to an Orion Model 801A pH/mv meter.
STUDY DESIGN	The relationship between fluoride concentrations in teeth enamel and dental fluorosis and dental caries was investigated in a South African children, ages 14 -16, who lived in an area with approximately 3.2 ppm fluoride in the drinking water. The children were examined by a dental surgeon and the caries incidence (DMFT), and the degree of fluorosis, measured by Dean's Index of Fluorosis (see Section 2) were assessed. The fluoride content of the children's teeth enamel was analyzed and the fluoride concentrations were corrected to a uniform depth of 10 µm. The association between the degree of dental caries, dental fluorosis, and fluoride content in the teeth enamel was assessed.
PARAMETERS MONITORED:	The DMFT index and the percentage of children free from caries was used to measure the incidence of dental caries and Dean's Index of Fluorosis was used to evaluate the grade of dental fluorosis
STATISTICAL METHODS:	The data were transformed from mass fluoride in picograms to log mass fluoride and from mass enamel in micrograms to log mass enamel. Preliminary t-tests were carried out to determine the significance level of the differences between log mass fluoride and log mass enamel for the left and right incisors of the children. A covariance analysis was run to test the differences between sexes for log mass fluoride using log mass enamel as the covariate. The adjusted log mass fluoride mean values were obtained by correcting the unadjusted log mass fluoride values to a standardized depth of 10 µm. In order to determine the association between the degree of dental caries, the degree of dental fluorosis, and log mass fluoride, correlations between the various pairs of variables were calculated adjusting for the sex of the children.
RESULTS:	
Caries	See Table 2, copied directed from Retief et al. (1979), for the incidence of dental caries (DMFT) and the percentage of children caries free:

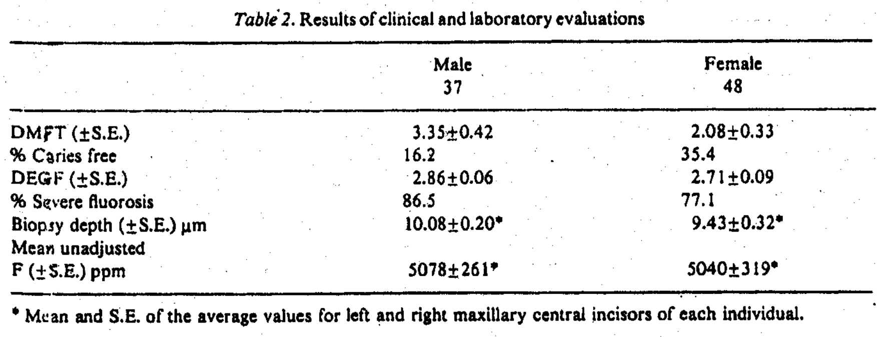


Table 2. Results of clinical and laboratory evaluations

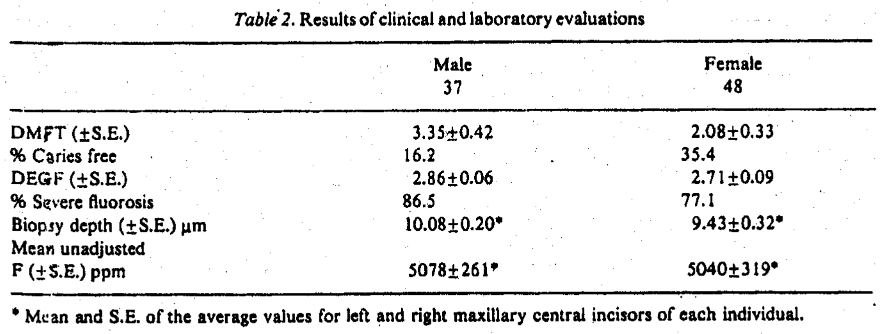
	Male 37	Female 48
DMFT (±S.E.)	3.35±0.42	2.08±0.33
% Caries free	16.2	35.4
DEGF (±S.E.)	2.86±0.06	2.71±0.09
% Severe fluorosis	86.5	77.1
Biopsy depth (±S.E.) µm	10.08±0.20*	9.43±0.32*
Mean unadjusted F (±S.E.) ppm	5078±261*	5040±319*

* Mean and S.E. of the average values for left and right maxillary central incisors of each individual.

DMFT vs. log mass fluoride, r = .415, P<0.0001

Dental fluorosis

The degree of dental fluorosis (DEGF) in the children is shown below in Table 2 copied directly from Retief et al. (1979:



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Mean unadjusted F (±S.E.) ppm	5078±261*	5040±319*

* Mean and S.E. of the average values for left and right maxillary central incisors of each individual.

DEGF vs. log mass fluoride, r = 0.389, P<0.005
DMFT vs. DEGF, r = 0.251, P<0.02

STUDY AUTHORS' CONCLUSIONS:

The exposure to drinking water with a high fluoride concentration (3.2 ppm) resulted in 86.5% of the males and 77.1% of the females showing severe fluorosis associated with marked pitting of enamel. A highly significant positive correlation between the degree of dental fluorosis and the fluoride enamel levels was seen, as well as a significant association between the incidence of dental caries and fluoride concentrations in the teeth enamel.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

None

PROFILER'S REMARKS

Initials/date SBG 3/28/07

This study was in South Africa and there was no control group with exposure to lower levels of fluoride in the drinking water.

Confounding factors which may have contributed to total fluoride intake, such as dietary habits, were not addressed and only one exposure level was considered. Nevertheless, the results might be useful when compared with data from other studies.

PROFILER'S ESTIM. NOEL/NOAEL

A NOAEL for severe dental fluorosis was not identified in the study

PROFILER'S ESTIM. LOEL/ LOAEL

Based on the results from Table 2, the fluoride concentration of 3.2 ppm was associated with a high incidence of severe dental fluorosis; therefore, the lowest effect level would be expected to be less than 3.2 ppm.

POTENTIAL SUITABILITY

Not suitable ( ), Poor (x), Medium ( ), Strong ( )

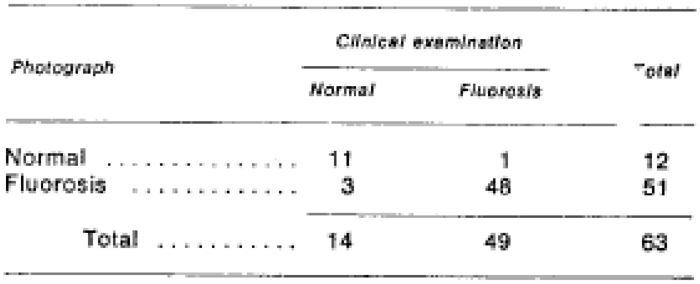
FOR DOSE-RESPONSE MODELING:	This study itself is poorly suited for dose-response modelling because only one dose was evaluated.
CRITICAL EFFECT(S):	Dental caries, dental fluorosis

Rozier, R.G. and G.G. Dudney. 1981. Dental fluorosis in children exposed to multiple sources of fluoride: Implications for school fluoridation programs. Public Health Rep 96(8):542-48.

ENDPOINT STUDIED:	Dental fluorosis (permanent teeth)
TYPE OF STUDY:	Prevalence study of dental fluorosis.
POPULATION STUDIED:	North Carolina (rural area, exact location not stated): The study population originally included 307 children, ages 5 to 15, in grades kindergarten through 8. Residence and water histories were obtained through self-reporting and verification by the school principal.
CONTROL POPULATION:	None.
EXPOSURE PERIOD:	Children were continuous residents of the community so their exposure period was from birth to the age at which study examination took place (5-15 years old). The date(s) the study was conducted were not provided.
EXPOSURE GROUPS:	The school used well water with a natural fluoride concentration of 4.5 ppm (5.6 times the recommended water fluoride level of 0.8 ppm for community fluoridation in that area). The final study population was divided into four groups based on the fluoride concentration of the home water supplies: Group 1, 0.00-0.24 ppm (average 0.18 ppm); Group 2, 0.25-1.99 ppm (average 0.87 ppm); Group 3, 2.00-3.99 ppm (average 3.13 ppm); and Group 4, 4.00-6.50 ppm (average 4.82 ppm).
EXPOSURE ASSESSMENT	Samples of home water supplies were collected from 292 of the students.
ANALYTICAL METHODS:	The fluoride concentration of the water samples was determined by the electrode method (Harwood, 1969).
STUDY DESIGN	The objective of the study was to determine if continuous, lifetime use of home drinking water naturally fluoridated to optimum levels combined with the use of school water having 4.5 ppm natural fluoride, beginning at school age, causes objectionable levels of dental fluorosis in school-age children in rural southeastern North Carolina. The study population of children, ages 5 to 15, in grades kindergarten through 8 was examined for the presence or absence of dental fluorosis according to the definitions and examination criteria of Dean (see NRC 2006, pages 88-89). All examinations were performed in a designated room in the school; portable dental chairs and lights, a No. 23 explorer, and a plane surface mirror were used. Color transparencies were made at the time of the examination. A sample of these representing the spectrum of fluorosis severity were later reviewed and scored by an independent investigator. Residence histories and water supplies were obtained through self-reporting and verification by the school principal. Only data from children who were continuous residents of the community and who returned a water sample were included in the study analyses (221 of 295). The study population was divided into four groups based fluoride concentration in their home water supplies. For each group, a qualitative and quantitative Community Index of Dental Fluorosis (Fci) was calculated according to methods suggested by Dean (1935). To measure the effects of home and school fluoride exposure, only students with at least one erupted premolar or second molar were included in the analysis, resulting in a final sample of 120 students.
PARAMETERS MONITORED:	Dental fluorosis was evaluated using a modified Dean's Index in which two scores were determined on each student, one representing fluorosis prevalence in early erupting permanent teeth and one in late erupting permanent teeth. Each score was based on the most severely affected tooth in each group of teeth. At least one tooth of the group had to be present for a score to be assigned.

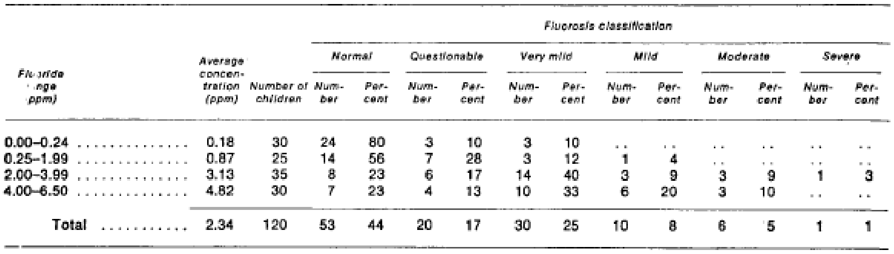
	A quantitative and qualitative Community Index of Dental Fluorosis (Fci) was calculated for each of the exposure groups. To determine the quantitative index, a weight was assigned to each of six classifications of fluorosis given at the time of the examination, and the weighted scores for all individuals within each group were averaged. For the qualitative index, seven descriptive terms – negative, borderline, slight, medium, rather marked, marked, and very marked – were derived from the percentage distribution of the six classifications of fluorosis.
STATISTICAL METHODS:	None were described in the study report.
RESULTS:	The study results are provided in Tables 1-3 taken directly from Rozier, 1981.

Table 1. Comparison of photographs and clinical examinations for the presence or absence of dental fluorosis for 63 teeth scores of 41 school children



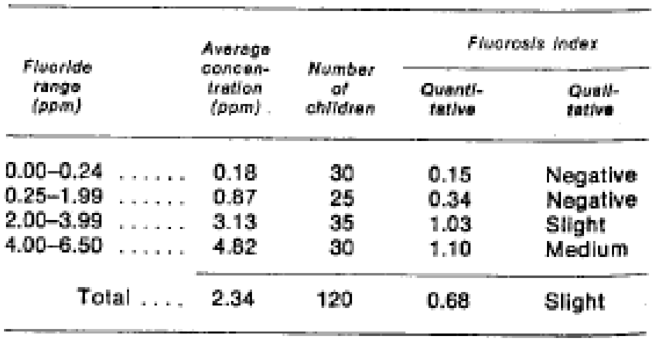
Photograph	Clinical examination		Total
	Normal	Fluorosis	
Normal	11	1	12
Fluorosis	3	48	51
Total	14	49	63

Table 2. Frequency distribution of fluorosis classifications for school children with at least 1 late erupting tooth, grouped by fluoride content of their home water supplies



Fluoride range (ppm)	Average concentration (ppm)	Number of children	Fluorosis classification											
			Normal		Questionable		Very mild		Mild		Moderate		Severe	
			Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
0.00–0.24	0.18	30	24	80	3	10	3	10	..	..	..	..	..	..
0.25–1.99	0.87	25	14	56	7	28	3	12	1	4	..	..	..	..
2.00–3.99	3.13	35	8	23	6	17	14	40	3	9	3	9	1	3
4.00–6.50	4.82	30	7	23	4	13	10	33	6	20	3	10	..	..
Total	2.34	120	53	44	20	17	30	25	10	8	6	5	1	1

Table 3. Fluorosis index for children with at least 1 late erupting tooth, grouped by fluoride content of their home water supplies



Fluoride range (ppm)	Average concentration (ppm)	Number of children	Fluorosis index	
			Quantitative	Qualitative
0.00–0.24	0.18	30	0.15	Negative
0.25–1.99	0.87	25	0.34	Negative
2.00–3.99	3.13	35	1.03	Slight
4.00–6.50	4.82	30	1.10	Medium
Total	2.34	120	0.68	Slight

STUDY AUTHORS' CONCLUSIONS:	The study authors concluded that the study results suggest that children consuming water at home containing the optimal fluoride concentration and drinking water at school containing 4.5 ppm F (5.6 times the recommended water fluoride level of 0.8 ppm for community fluoridation in that area) are not at risk to dental fluorosis that

		impairs appearance.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Harwood, J.E. 1969. The use of an ion-selective electrode for routine fluoride analyses on water samples. Water Res 3:273-280. Dean, H.T. 1942. The investigation of physiological effects by the epidemiological method. *In* Fluoride and dental health, edited by F.R. Moulton. American Association for the Advancement of Science, Washington, D.C., No. 19, pp. 23-31.
PROFILER'S REMARKS	***Initials/Date*** VAD/03-13-07	In general, there was a good dose-response relationship between increased frequency and severity of fluorosis and increasing concentrations of fluoride in the water supplies (Table 2). However, study flaws were noted. The demographics of the study population were not described; therefore, no determination can be made about whether it was representative of the general U.S. population. Exposure to other sources of fluoride, in addition to drinking water, was not considered. The number of each gender of the study population was not provided. Four examiners evaluated the children for fluorosis, but no measure of inter- or intra-examiner consistency was provided. The LOAEL for severe fluorosis occurred at or above 2.0 ppm F in home drinking water (only 1 of 65 children); however, the overall exposure was greater because the fluoride level in the school drinking water was 4.5 ppm. Further, the data were not analyzed statistically to determine if the occurrence of severe fluorosis was significant. The fact that severe fluorosis was not seen at 4.0-6.5 ppm F in their home drinking water raises questions about the methodology used. If the children were examined after all permanent teeth had erupted, the overall incidence rate is likely to have been different.
PROFILER's ESTIM. NOAEL		The study design did not identify a no-fluorosis intake dose.
PROFILER'S ESTIM. LOAEL		The LOAEL for fluorosis in children aged 5-15 years was 0.00-0.24 ppm. Children at the lowest range of fluoride concentration in their home water supplies had mild fluorosis.
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable,(_); Poor (X); Medium (_); Strong (_)
CRITICAL EFFECTS:		Dental fluorosis (permanent teeth)

Ruan, J.P., Z.Q. Yang, Z.L. Wang, A., Astrøm, A., Bårdsen, A., and Bjorvatn, K.. 2005a. Dental fluorosis and dental caries in permanent teeth: rural schoolchildren in high-fluoride areas in the Shaanxi province, China. Acta Odont. Scand. 63: 258-265.

ENDPOINT STUDIED:

Dental fluorosis and dental caries (DMFS = decayed, missing, filled tooth surfaces) in permanent teeth

TYPE OF STUDY:

Case control, retrospective

POPULATION STUDIED:

China/ Shaanxi Province: 477 schoolchildren from two rural areas (Bao Ji County and Jing Bian County). The province is in northwestern China between 31-39°N and 105-110°E. The children were age 12-13, approximately half male and half female, and attended 13 village primary schools in communities with comparable socioeconomic standards. The drinking water source was groundwater obtained from 28 deep (20-30 m) wells, and was unchanged over the last ≥13 years.

CONTROL POPULATION:

For most of the comparisons made there was no control population *per se*, rather, children were subdivided into five fluoride exposure groups that were compared to one another. For evaluation of the relationship between the prevalence of dental fluorosis (TF score of ≥3) and the associated fluorosis risk factor, the following groups were used as the reference groups for the analyses: those that did not use (local) clay pots in which to store drinking water compared to those that did, fluoride group A (0.3-0.5 mg F/L) compared to other concentrations, males compared to females, and 12-year olds compared to 13 year olds (see Table V of Ruan et al., 2005a).

EXPOSURE PERIOD:

Lifetime (to ages 12-13).

EXPOSURE GROUPS:

Schoolchildren aged 12-13 from two rural areas in Shaanxi Province, China, who obtained their lifetime water supply from one of 28 wells. The children were subdivided into five fluoride exposure groups (A, B, C, D, E) based on their well water fluoride concentration, as shown in Table I. The distribution of the children in the five groups by gender and age is shown in Table II.

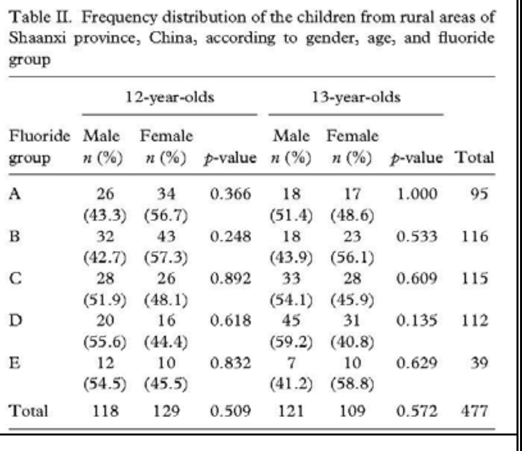


Table II. Frequency distribution of the children from rural areas of Shaanxi province, China, according to gender, age, and fluoride group

	12-year-olds			13-year-olds			
Fluoride group	Male n (%)	Female n (%)	p-value	Male n (%)	Female n (%)	p-value	Total
A	26 (43.3)	34 (56.7)	0.366	18 (51.4)	17 (48.6)	1.000	95
B	32 (42.7)	43 (57.3)	0.248	18 (43.9)	23 (56.1)	0.533	116
C	28 (51.9)	26 (48.1)	0.892	33 (54.1)	28 (45.9)	0.609	115
D	20 (55.6)	16 (44.4)	0.618	45 (59.2)	31 (40.8)	0.135	112
E	12 (54.5)	10 (45.5)	0.832	7 (41.2)	10 (58.8)	0.629	39
Total	118	129	0.509	121	109	0.572	477

EXPOSURE ASSESSMENT:

Drinking water fluoride concentrations were measured in 500 mL samples taken from the 28 wells (1-2 per village) that were the primary source of drinking water. Samples were collected in pre-cleaned polyethylene bottles and analyzed for fluoride in 2002. The water fluoride concentrations ranged from 0.3-7.6 ppm, as shown in Table I.

Quantitative exposure data from other sources were not provided. The communities had no dental fluoride supply or supplement program. According to local custom, eating fluoride-rich seafood or beverages was rare during childhood, and (fluoride-containing) tea was rarely drunk before the age of 5. Calcium deficiency, which can promote fluoride uptake, is common in

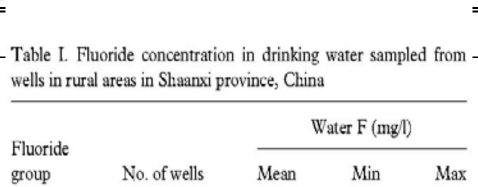


Table I. Fluoride concentration in drinking water sampled from wells in rural areas in Shaanxi province, China

		Water F (mg/l)		
Fluoride group	No. of wells	Mean	Min	Max

	Chinese populations. Infants are generally breast-fed <4 months, and are given water sweetened with sugar as early as one month after birth (for weaning or supplementary food).
ANALYTICAL METHODS:	The well water samples were analyzed for fluoride with a fluoride selective electrode (Model PF-1, Electric and Optic Accessory Factory, Shanghai, China) by the Shaanxi Institute of Endemic Disease Control. Data were not provided for any other water quality parameters.
STUDY DESIGN	Well water fluoride concentrations were determined in 2002. Children from 13 schools were selected who were 12-13 years old and lifelong residents of villages where the same water source had been used for the last 13 years. For data analysis, the children were subdivided into five fluoride exposure groups (A, B, C, D, E) based on their water fluoride concentration, which ranged from 0.3-7.6 mg/L (Table I). The children's teeth were examined in 2002. The exams were conducted outside of their schools, after the teeth were cleaned and dried with cotton balls, using regular chairs, indirect natural light, and dental mirrors and explorers, per World Health Organization (WHO) guidelines. One dentist assessed the buccal surface of each permanent tooth in the mouth and scored dental fluorosis using a modified Thylstrup-Fejerskov (TF) Index (Fejerskov et al., 1988). Teeth were excluded from analysis if the buccal surface was covered with calculus or if <50% of the crown had erupted (all 2^{nd} molars were excluded). The median of all scored teeth for an individual was used as that individual's TF score, and was used to evaluate the prevalence of dental fluorosis (TF >0) and the mean TF score of each fluorosis exposure group. Dental caries were scored using the DMFS index per WHO guidelines. Missing teeth were considered to be due to caries if the child had a history of pain. A re-examination after one month of the four upper incisors of 24 children for fluorosis and of the first molars for dental caries determined that intra-examiner reliability was good (Cohen's Kappa value of 0.703 and 0.91 for fluorosis and dental caries, respectively). To determine whether storage of the drinking water in clay pots (which may either take up or leach fluoride) affected the prevalence of fluorosis or dental caries, the children were asked to fill out questionnaires regarding their means of water storage. Of the 477 children, 362 participated from groups A-D; the children in group E were not allowed to participate by their school teacher.
PARAMETERS MONITORED:	Dental fluorosis was assessed using a modified Thylstrup-Fejerskov (TF) index, and dental caries were evaluated using the DMFS index (see Section 2 for description of indices).
STATISTICAL METHODS:	The SPSS (Statistical Package for Social Sciences software, version 11.5) PC program was used for statistical analysis. The gender and age distribution of the subjects were evaluated by the binomial test. The Chi-square test was used to evaluate the prevalence of dental fluorosis and dental caries in the five exposure groups. The mean TF score and DMFT were compared with the univariate general linear model one-way analysis of variance (GLM-ANOVA) and the post-hoc Bonferroni test. Binary logistic regression analyses were used to estimate the risk of dental fluorosis (TF score >0) and severe dental fluorosis (TF score ≥3), with the individual median TF score as the dependent variable. Significance was defined as $P < 0.05$.
RESULTS:	
Dental fluorosis	There was a direct correlation between drinking water fluoride levels and the prevalence of dental fluorosis (Figures 1 and 2; Table III). The percent of children with dental fluorosis (TF score >0) increased from 14% in group A to ~98% in group E, the percent with a median TF score ≥3 increased from ~2% in group A to ~95% in group E, and the percent with a TF score >4 increased from 0% in group A to ~60% in group E. Analogously, the mean (of the individual median) TF scores increased from 0.30 for group A to 4.78 for group E, and were statistically different between all groups except between groups C and D. Gender had no effect on the TF scores, whereas the mean TF scores were greater in children of age 13 than 12, the difference being statistically significant ($p<0.01$) for groups B and D (Figure 3).

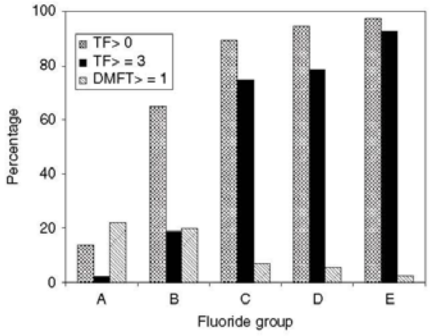


Figure 1. Prevalence of dental fluorosis at TF score > 0, TF score ≥ 3 and dental caries (DMF-T ≥ 1) in permanent teeth of the children from rural areas of Shaanxi province, China, by fluoride group.

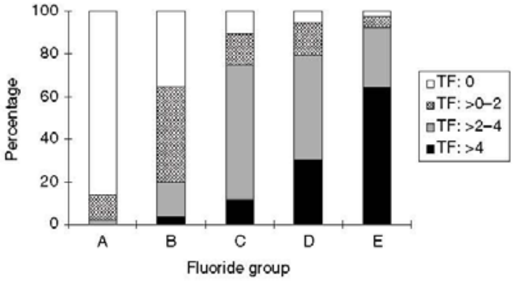


Figure 2. Percentage distribution of TF score in permanent teeth of the children from rural areas of Shaanxi province, China, according to fluoride group.

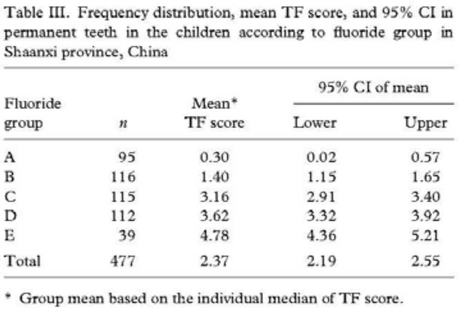


Table III. Frequency distribution, mean TF score, and 95% CI in permanent teeth in the children according to fluoride group in Shaanxi province, China

Fluoride group	n	Mean* TF score	95% CI of mean Lower	95% CI of mean Upper
A	95	0.30	0.02	0.57
B	116	1.40	1.15	1.65
C	115	3.16	2.91	3.40
D	112	3.62	3.32	3.92
E	39	4.78	4.36	5.21
Total	477	2.37	2.19	2.55

* Group mean based on the individual median of TF score.

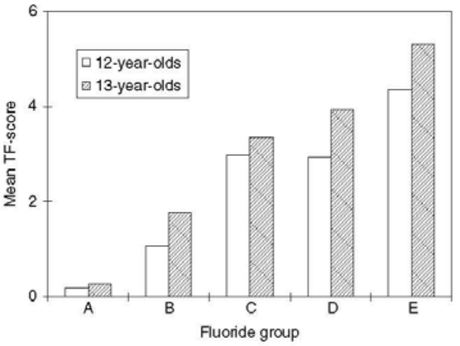


Figure 3. Mean TF score in permanent teeth of the children from rural areas of Shaanxi province, China, according to age and fluoride group.

Dental caries (DMFT)

The water fluoride concentration was inversely related to the fraction of children with dental caries (DMFT ≥ 1), which ranged from 22.1% in group A to 2.6% in group E (Table IV and Figure 1). The mean group DMFT values were also inversely related to the water fluoride concentration, and differed statistically from one another. In fact, children exposed to the highest fluoride concentration (group E), who had the highest mean TF score (4.78), had the lowest prevalence of caries among all the groups. The majority (>80%) of the children had only 1 or 2 caries, and 73 of the 83 decayed teeth were first molars.

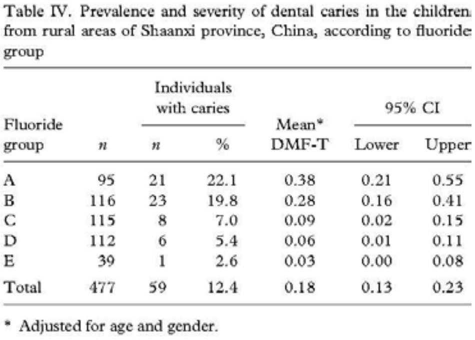


Table IV. Prevalence and severity of dental caries in the children from rural areas of Shaanxi province, China, according to fluoride group

Fluoride group	n	Individuals with caries n	Individuals with caries %	Mean* DMF-T	95% CI Lower	95% CI Upper
A	95	21	22.1	0.38	0.21	0.55
B	116	23	19.8	0.28	0.16	0.41
C	115	8	7.0	0.09	0.02	0.15
D	112	6	5.4	0.06	0.01	0.11
E	39	1	2.6	0.03	0.00	0.08
Total	477	59	12.4	0.18	0.13	0.23

* Adjusted for age and gender.

Effect of clay pot water storage on dental fluorosis

More than half of the 362 children (from groups A-D) who participated in the survey revealed that their drinking water was stored in clay pots prior to use. Statistical analysis found no relationship between the type of container used to store water and the prevalence of dental fluorosis, although the severity of fluorosis was greater if the water was stored in clay pots (Tables V and VI). Children from families that drank water stored in clay pots had lower mean DMFT scores than those who did not, but the difference was not statistically significant.

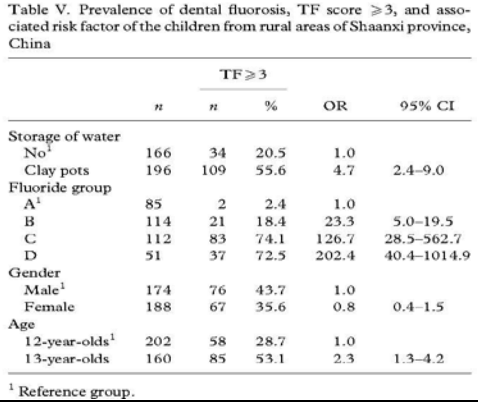


Table V. Prevalence of dental fluorosis, TF score ⩾3, and associated risk factor of the children from rural areas of Shaanxi province, China

		TF⩾3			
	n	*n*	%	OR	95% CI
Storage of water					
No[1]	166	34	20.5	1.0	
Clay pots	196	109	55.6	4.7	2.4–9.0
Fluoride group					
A[1]	85	2	2.4	1.0	
B	114	21	18.4	23.3	5.0–19.5
C	112	83	74.1	126.7	28.5–562.7
D	51	37	72.5	202.4	40.4–1014.9
Gender					
Male[1]	174	76	43.7	1.0	
Female	188	67	35.6	0.8	0.4–1.5
Age					
12-year-olds[1]	202	58	28.7	1.0	
13-year-olds	160	85	53.1	2.3	1.3–4.2

[1] Reference group.

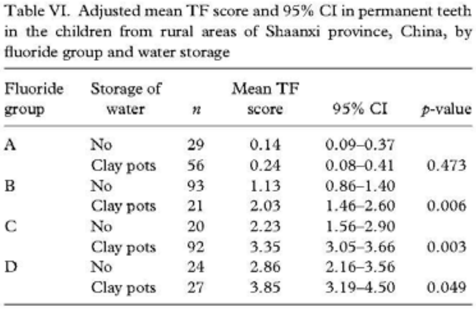


Table VI. Adjusted mean TF score and 95% CI in permanent teeth in the children from rural areas of Shaanxi province, China, by fluoride group and water storage

Fluoride group	Storage of water	*n*	Mean TF score	95% CI	*p*-value
A	No	29	0.14	0.09–0.37	
	Clay pots	56	0.24	0.08–0.41	0.473
B	No	93	1.13	0.86–1.40	
	Clay pots	21	2.03	1.46–2.60	0.006
C	No	20	2.23	1.56–2.90	
	Clay pots	92	3.35	3.05–3.66	0.003
D	No	24	2.86	2.16–3.56	
	Clay pots	27	3.85	3.19–4.50	0.049

STUDY AUTHORS' CONCLUSIONS:

Ruan et al. (2005a) concluded that there was a direct correlation between drinking water fluoride concentration and the prevalence and severity of dental fluorosis in permanent teeth. Fluorosis was low grade and uncommon at water fluoride concentrations <0.5 mg/L, whereas >60% of children drinking water with 0.8-1.4 mg F/L had fluorosis. The authors speculated that the greater degree of fluorosis in China than in Japan and Western countries at a given water fluoride concentrations could be in part due to calcium deficiency in the Chinese population. It was also noted that the DMFT of the Chinese 12-year olds was much lower than that of Western countries. Gender had no effect on fluorosis. Mean TF scores were greater in children age 13 than 12, although the difference was statistically significant for only two of the five groups (B and D).

An increase in water fluoride concentration was associated with a statistically significant reduction in caries. However, the study authors concluded that the harmful effects of fluoride (not specified; presumably fluorosis) outweigh the benefits of fluoride in their particular circumstances.

The increase of severity of dental fluorosis for children who drank water stored in clay pots was of uncertain significance. There are differences in composition of various clays, how clay pots are made, and in their ability to absorb fluoride from the water (some may leach fluoride into the water). During the present study, clay pots used for domestic water storage were not specifically examined for their fluoride interaction characteristics.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

Ruan, J.P., Z.L. Wang, Z.Q. Yang et al. 2005b. Dental fluorosis in primary teeth: a study in rural schoolchildren in Shaanxi Province, China. Int. J. Ped. Dent. 15: 412-419.

Fejerskov, O., F. Manjii, A. Baelum and I.J. Moler. 1988. Dental fluorosis; a handbook for health workers. Copenhagen: Munksgaard (Denmark).

PROFILER'S REMARKS ***SM/ 1-16- 2007***

This was a well-conducted study that clearly showed that the prevalence and severity of fluorosis increased with the drinking water fluoride concentration. The study also showed that the prevalence of caries decreased as water fluoride concentration increased. The study authors downplay the data indicating that the prevalence of caries was lower at the highest fluoride concentration (group E), which had the highest mean TF score (4.78), than in all other groups. Gender had no effect on fluorosis, but the effect of age was equivocal, as the differences between 12 and 13-year olds the age groups was small. The study authors conclude that the presence of fluorosis was the children's primary health problem, and that the fluorosis outweighed the benefits of caries reduction, but do not really explain why they consider this to be the case.

The same authors concurrently studied fluorosis in primary teeth of 7-8 year-olds in the same area (Ruan et al. 2005b; see profile). This study also found that fluorosis severity and prevalence increased with water fluoride concentration, but the severity was slightly greater in 7-year olds than in 8-year olds, irrespective of gender.

The major study drawback is the lack of quantitation of fluoride intake from drinking water and

		other possible sources. The study authors noted possible differences in susceptibility to fluorosis in the Chinese population due to dietary factors such as calcium deficiency. Other drawbacks include the use of natural light to examine the children, and lack of data regarding how many teeth/child were examined, and lack of quantitation of fluorosis and dental caries on a per tooth basis, and by tooth type. It would have been helpful for subsequent analysis if these data had all been presented as numeric values instead of bar graphs.
PROFILER'S ESTIM. NOEL/NOAEL for fluorosis		The NOAEL for fluorosis was 0.3-0.6 mg/L (mean=0.4 mg/L) in the drinking water (exposure group A), which caused no fluorosis in 86% of the children and only mild fluorosis (TF ≤4, no pitting) in the remaining 14%. A concentration at which no fluorosis occurred (NOEL) was not identified.
PROFILER'S ESTIM. LOEL/ LOAEL for fluorosis		The LOAEL for fluorosis was 0.8-1.4 mg/L (mean=1.0 mg/L), corresponding to exposure group B, for which 40% had TF=0; ~58% had TF=1-4, and ~2% had TF>4. This group was chosen as the LOAEL because some subjects had severe dental fluorosis (pitting occurred).
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable ( ), Poor (), Medium (x), Strong () The study shows a direct correlation between water fluoride concentration and the incidence of fluorosis or dental caries. The major study drawback is the lack of quantitation of fluoride intake from drinking water and other possible sources, but estimates can be made of the children's fluoride intake based on age and expected water consumption and dietary profile. The data are also amenable to analysis of the dose-response relationship between water fluoride concentration and the prevalence of dental caries.
CRITICAL EFFECT(S):		Dental fluorosis; dental caries

Ruan, J.P., Z.L. Wang, Z.Q. Yang, Bårdsen, A., Åstrøm, A., and Bjorvatn, K. 2005b. Dental fluorosis in primary teeth: a study in rural schoolchildren in Shaanxi Province, China. Int. J. Ped. Dent. 15: 412-419.

ENDPOINT STUDIED: Dental fluorosis in primary teeth

TYPE OF STUDY: Case control, retrospective

POPULATION STUDIED: China/ Shaanxi Province: 472 schoolchildren from two rural areas (Baoji County and Jingbian County). The province is in northwestern China between 31-39°N and 105-110°E. The children were age 7-8, approximately half male and half female, and attended 13 village primary schools. The communities had comparable socioeconomic standards. The drinking water source was mainly groundwater obtained from 20-30 m deep wells. The source of village water was unchanged over the last 9 years. No other source of fluoride was known in these communities. Shaanxi Province is known for the presence of endemic dental and skeletal fluorosis (Liu et al 1999).

CONTROL POPULATION: There was no control population *per se*, rather, children were subdivided into four fluoride exposure groups, which were all compared to one another.

EXPOSURE PERIOD: Lifetime, from prior to birth through the study exam at ages 7-8.

EXPOSURE GROUPS: Schoolchildren aged 7-8 from two rural areas in Shaanxi Province, China, who obtained their lifetime water supply from one of 27 wells. The children were subdivided into four fluoride exposure groups (A, B, C, D) based on their well water fluoride concentration, as shown in Table 1. The distribution of the children in the four groups by sex and age is shown in Table 2.

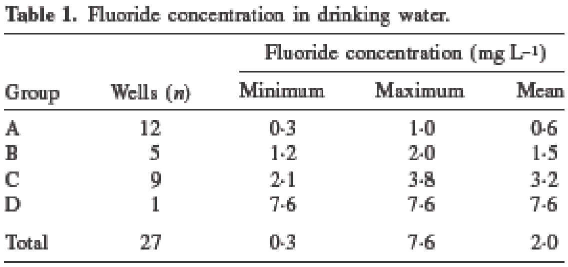


Table 1. Fluoride concentration in drinking water.

		Fluoride concentration (mg L⁻¹)		
Group	Wells (*n*)	Minimum	Maximum	Mean
A	12	0·3	1·0	0·6
B	5	1·2	2·0	1·5
C	9	2·1	3·8	3·2
D	1	7·6	7·6	7·6
Total	27	0·3	7·6	2·0

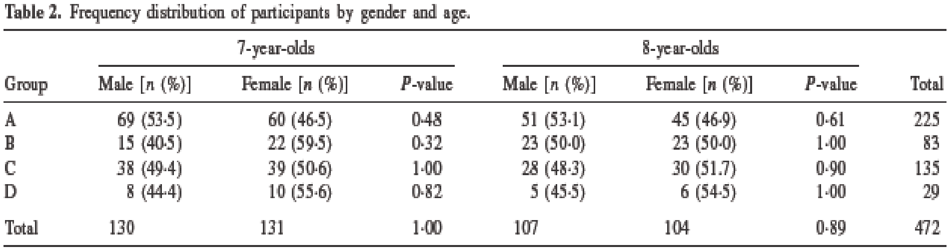


Table 2. Frequency distribution of participants by gender and age.

	7-year-olds			8-year-olds			
Group	Male [*n* (%)]	Female [*n* (%)]	*P*-value	Male [*n* (%)]	Female [*n* (%)]	*P*-value	Total
A	69 (53·5)	60 (46·5)	0·48	51 (53·1)	45 (46·9)	0·61	225
B	15 (40·5)	22 (59·5)	0·32	23 (50·0)	23 (50·0)	1·00	83
C	38 (49·4)	39 (50·6)	1·00	28 (48·3)	30 (51.7)	0·90	135
D	8 (44·4)	10 (55·6)	0·82	5 (45·5)	6 (54·5)	1·00	29
Total	130	131	1·00	107	104	0·89	472

EXPOSURE ASSESSMENT: Drinking water fluoride concentrations were obtained for 500 mL samples taken from the 27 wells (1-2 per village) that were the primary source of drinking water for the 472 children. Samples were collected and analyzed for fluoride during the summer and fall of 2002. The water fluoride concentrations ranged from 0.3-7.6 ppm.

One of the criteria for selection of the village school for study was that "apart from the drinking water, no fluoride source should be available." No further information was provided regarding other possible sources of fluoride exposure.

ANALYTICAL METHODS:

The well water samples were analyzed for fluoride with a fluoride selective electrode (Model PF-1, Electric and Optic Accessory Factory, Shanghai, China) by the Shaanxi Institute of Endemic Disease Control. Data were not provided for any other water quality parameters.

STUDY DESIGN

Well water fluoride concentrations were determined in the summer and fall of 2002, and used as a basis for selecting the participating schools. Children were selected from the schools who were 7-8 years old and lifelong residents of villages where the same water source had been used for the last 9 years. For data analysis, the children were subdivided into four fluoride exposure groups (A, B, C, D) based on their water fluoride concentration, which ranged from 0.3-7.6 mg/L (Table 1).

The children's teeth were examined in 2002. The exams were conducted outside of their schools, after the teeth were cleaned and dried with cotton balls, using regular chairs, indirect natural light, and dental mirrors and explorers, per World Health Organization guidelines. One dentist assessed the buccal surface of each primary tooth in the mouth and scored dental fluorosis using a modified Thylstrup-Fejerskov Index (TFI). Intra-examiner reliability was moderate (Cohen's kappa of 0.58), as determined by a repeat examination of 29 children after one month.

The TFI score of the upper right second molar was used as an individual's overall TFI score. The mandible and maxilla TFI scores were those of the right upper and lower second molars. The dentition distribution of the TFI scores was based on the scores for all of the teeth of a given individual.

PARAMETERS MONITORED:

Dental fluorosis was assessed using a modified Thylstrup-Fejerskov Index (TFI) (see Section 2 for description).

STATISTICAL METHODS:

The SPSS (Statistical Package for Social Sciences software version 11.5) computer program was used for statistical analysis. The gender distribution of the subjects was evaluated by the Binomial test. The Chi-square test was used to evaluate the prevalence of dental fluorosis (TFI score ≥1) in the four exposure groups. The KruskałWallis *H*-test and the Mann-Whitney U-test were used to evaluate the median of the TFI scores in the four groups by gender and age. The percentage of dental fluorosis of the maxillary and mandibular dentitions was compared by the Wilcoxon signed-rank test. Significance was defined as $P < 0.05$.

RESULTS:

Dental fluorosis

As shown in Table 3, there was a direct correlation between dental fluorosis and the fluoride level in the drinking water. The percent of children with dental fluorosis (TFI score ≥1) increased from 6.2% in group A (0.3-1.0 mg/L fluoride) to 96.6% in group D (7.6 mg/L fluoride). Similarly, the median and 25th and 75th percentile TFI scores increased from zero for group A to 4 for group D. The median TFI scores were statistically different between all groups except between groups B and C.

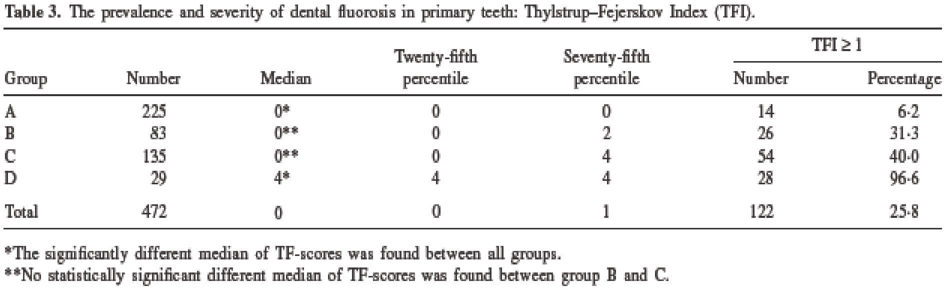


Table 3. The prevalence and severity of dental fluorosis in primary teeth: Thylstrup–Fejerskov Index (TFI).

					TFI ≥ 1	
Group	Number	Median	Twenty-fifth percentile	Seventy-fifth percentile	Number	Percentage
A	225	0*	0	0	14	6·2
B	83	0**	0	2	26	31·3
C	135	0**	0	4	54	40·0
D	29	4*	4	4	28	96·6
Total	472	0	0	1	122	25·8

*The significantly different median of TF-scores was found between all groups.
**No statistically significant different median of TF-scores was found between group B and C.

There were no statistically significant effects of gender on the median and 25th and 75th percentile TFI scores of the four groups (Table 4). Age had a significant effect on the

TFI score only for fluoride group C (2.1-3.8 mg/L), as the 7-year olds had higher 75th percentile scores than the 8-year olds.

Table 4. Median of Thylstrup–Fejerskov Index (TFI) scores by age and gender for the four fluoride groups.

	Group A			Group B			Group C			Group D		
Variable	*n*	Median	Percentile (25, 75)	*n*	Median	Percentile (25, 75)	*n*	Median	Percentile (25, 75)	*n*	Median	Percentile (25, 75)
Gender:												
male	120	0	0, 0	38	0	0, 3	66	0	0, 4	13	4	4, 4
female	105	0	0, 0	45	0	0, 3	69	0	0, 4	16	4	4, 4
Age (years):												
7	129	0	0, 0	37	0	0, 3	77	0*	0, 4	18	4	4, 4·25
8	96	0	0, 0	46	0	0, 1	58	0	0, 2·25	11	4	4, 5

*$P < 0·05$.

The distribution of subjects in the four fluoride exposure groups according to their TFI score is shown in Table 5. The severity of fluorosis clearly increased with the water fluoride concentration, the percent of fluorosis-free children (TFI score = 0) decreasing from 93.8% of group A to 3.4% of group D.

Table 5. Percentage distribution of individuals according to Thylstrup–Fejerskov Index (TFI) score and group.

	TFI score				
Group	0	1–2	3–4	5–6	> 7
A	93·8	4·0	2·2	0·0	0·0
B	68·7	8·4	21·7	0·0	1·2
C	60·0	6·7	28·1	4·4	0·7
D	3·4	0·0	72·4	20·7	3·4

The percentage of dental fluorosis was slightly greater in the upper jaw (maxillary teeth) than in the lower jaw (mandibular teeth) for all four fluoride exposure groups, although the difference was statistically significant for only group A. Fluorosis was distributed symmetrically in both the mandible and the maxilla in all groups. The second primary molar was the most fluorosed tooth, then the first molar, then the canines, the central incisors, and lastly the lateral incisors. The results are depicted in Figures 1 and 2.

PROFILER'S COMMENT: The tooth numbering system utilized in Figs 1 and 2 is that of the Fédération Dentaire Internationale (FDI) World Dental Federation ISO-3950, where 1s are central incisors, 2s are laterals, etc. The FDI "baby teeth" notation employs 51-55 for upper R, 61-65 for upper L, 81-85 for lower R and 71-75 for lower L.

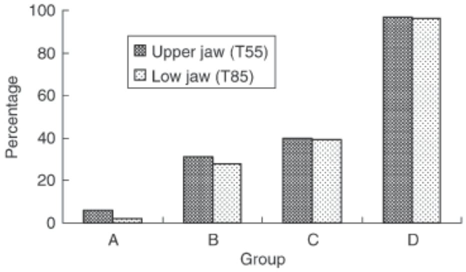
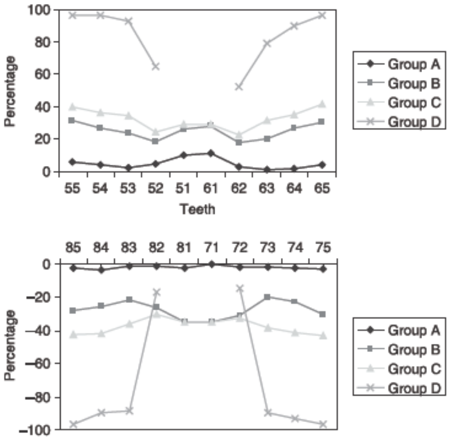


Fig. 1. Comparison of the percentage of dental fluorosis in the upper and lower jaw by fluoride group.

	 **Fig. 2.** Percentage of dental fluorosis according to tooth type and group.
STUDY AUTHORS’ CONCLUSIONS:	Ruan et al. (2005b) concluded that there was a positive relationship between the prevalence and severity of dental fluorosis in primary teeth and drinking water fluoride concentration. Fluorosis was distributed symmetrically throughout the mouth, with the second molar being the most affected, and the lateral incisors being the least affected. Gender had no effect on fluorosis, and age had a small equivocal effect. Because most of the TFI scores were 3-4, the authors speculated that there may be a dental fluorosis cut-off point above which the ameloblasts lose their ability to produce adequate enamel. Ruan et al. (2005b) asserted that fluorosis in primary teeth is an early warning of excessive fluoride exposure, and provides a basis for intervention to prevent fluorosis of the permanent teeth. The authors encourage feeding infants breast milk because it is low in fluoride, irrespective of the mother’s fluoride intake.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Ruan, J.P., Z.Q. Yang, Z.L. Wang, et al. 2005a. Dental fluorosis and dental caries in permanent teeth: rural schoolchildren in high-fluoride areas in the Shaanxi province, China. Acta Odont. Scand. 63: 258-265. Liu, X.L. 1999. A brief introduction to local disease control in Shaanxi Province. Endemic Diseases Bulletin 14: 72-73.
PROFILER’S REMARKS ***Initials/date SM/ 1-12-2007***	This was a well-conducted study that clearly showed that the prevalence and severity of fluorosis increased with the drinking water fluoride concentration. The lack of a statistically significant difference in the TFI scores of groups B and C may be due to the fact that these groups were exposed to very similar water fluoride concentrations. The study also showed that the distribution of fluorosis was symmetric in the mouth, that the second molars were the most susceptible to fluorosis, and that gender had no effect on fluorosis. A conclusion regarding the effect of age could not be made, not surprisingly, since the children were close in age. The same authors concurrently studied fluorosis in permanent teeth of 12-13 year-olds in the same area (Ruan et al. 2005a; see profile). This study also found that fluorosis severity and prevalence increased with water fluoride concentration, but the severity was slightly greater in 13-year olds than in 12-year olds, irrespective of gender. Drawbacks of the study include (1) the less-than-optimal intra-examiner reliability (Cohen’s kappa of 0.58), as determined by a repeat examination of 29 children after one month, (2) the use of natural light to examine the children, and (3) the lack of quantitation of the children’s fluoride intake, including that from other sources besides drinking water.
PROFILER’S ESTIM. NOEL/NOAEL for fluorosis	The NOAEL for fluorosis was 0.3 to ≤1.0 mg/L in the drinking water, corresponding to exposure group A (0.3-1.0 mg/L, mean=0.6 mg/L). At ≤1.0 ppm, fluorosis severity was

	limited to mild or moderate (score 1-4), and 93.6% of the subjects had a TFI score of 0. A concentration at which no fluorosis occurred (NOEL) was not identified.
PROFILER'S ESTIM. LOEL/ LOAEL for fluorosis	The LOAEL for fluorosis was 1.2-2.0 mg/L (mean=1.5 mg/L), corresponding to exposure group B, for which TFI=0 of 68.7%, TFI=1-4 of 30.1%, and TFI >7 of 1.2% of the subjects. This group was chosen as the LOAEL because some subjects had severe dental fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable ( ), Poor (), Medium (x), Strong () The study shows a clear dose-response for water fluoride concentration vs. dental fluorosis, despite some drawbacks. These include moderate intra-examiner reliability, the use of natural light for examination, and lack of quantitation of fluoride intake from drinking water and other possible sources. Estimates can be made of the children's fluoride intake based on age and expected water consumption and dietary profile.
CRITICAL EFFECT(S):	Dental fluorosis in primary teeth

Rwenyonyi, C.M, K. Bjorvatn, J.M. Birkeland and O. Haugejorden. 1999. Altitude as a risk indicator of dental fluorosis in children residing in areas with 0.5 and 2.5 mg fluoride per litre in drinking water. Caries Res 33:267-274.

<table>
<tr><td></td><td></td></tr>
<tr><td>ENDPOINT STUDIED:</td><td>Dental fluorosis (permanent teeth)</td></tr>
<tr><td></td><td></td></tr>
<tr><td>TYPE OF STUDY:</td><td>Cross sectional survey</td></tr>
<tr><td></td><td></td></tr>
<tr><td>POPULATION STUDIED:</td><td>Uganda/Rift Valley region: Children aged 10-14 years (mean 12.2 years) from three rural schools of Kisoro district and two schools in Kasese district, both mountainous areas of Uganda. Within the Kisoro district, the Mutolere/Kagera (n=163) and Kabindi (n=155) areas were at altitudes of 1,750 and 2,800 m, respectively. Within the Kasese district, the Mpondwe (n=81) and Kyabayenze (n=82) areas were at altitudes of 900 and 2,200 m, respectively.

Children had to satisfy the following criteria to participate in the study: 1) be born between 1982 and 1987 (aged 10-14 years) and raised in the village where they presently lived; 2) should have not been absent from the village for more than one month in any calendar year and should have used drinking water from the same source during the first six years of life.</td></tr>
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<tr><td>CONTROL POPULATION:</td><td>None.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE PERIOD:</td><td>Birth to 10-14 years. Study was conducted in 1996 and 1997.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE GROUPS:</td><td>Within the Kisoro district, the water fluoride content was 2.5 mg/L (range 2.41-2.60; n=17).
Within the Kasese district, the water fluoride content was 0.5 mg/L (range 0.47-0.51; n=6).</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE ASSESSMENT</td><td>The three areas in the Kisoro district were supplied with piped water from the same spring. The two areas in Kasese district obtained water from the same river either directly or through a piped system. Samples of drinking water in the Kisoro and Kasese areas were analyzed for fluoride. Questionnaires were used to determine fluoride from other sources, including the following: boiling of drinking water, clay pots (for water storage), trona (calcium carbonate used as food additive), tea, infant formula, vegetarian diet, milk and fluoride toothpaste. The fluoride exposure from liquid (FEL) for each child was calculated from the reported number of cups of liquid consumed per day and the fluoride levels in the drinking water.

Table 1 was copied directly from Rwenyonyi et al. (1999).

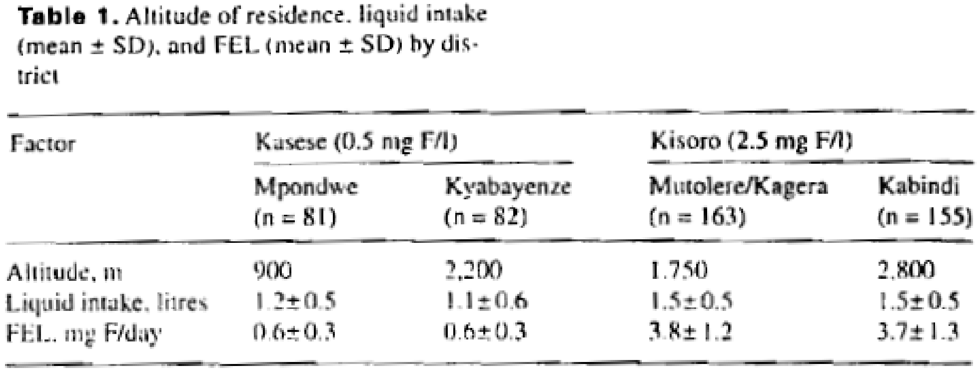
Table 1. Altitude of residence. liquid intake (mean ± SD), and FEL (mean ± SD) by district
<table>
<tr><th>Factor</th><th colspan="2">Kasese (0.5 mg F/l)</th><th colspan="2">Kisoro (2.5 mg F/l)</th></tr>
<tr><th></th><th>Mpondwe (n = 81)</th><th>Kyabayenze (n = 82)</th><th>Mutolere/Kagera (n = 163)</th><th>Kabindi (n = 155)</th></tr>
<tr><td>Altitude, m</td><td>900</td><td>2,200</td><td>1.750</td><td>2.800</td></tr>
<tr><td>Liquid intake, litres</td><td>1.2±0.5</td><td>1.1±0.6</td><td>1.5±0.5</td><td>1.5±0.5</td></tr>
<tr><td>FEL, mg F/day</td><td>0.6±0.3</td><td>0.6±0.3</td><td>3.8±1.2</td><td>3.7±1.3</td></tr>
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<tr><td></td><td></td></tr>
<tr><td>ANALYTICAL METHODS:</td><td>Analyses of the drinking water were conducted using a fluoride ion combination electrode.</td></tr>
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STUDY DESIGN	The objective of the study was to assess the association between altitude and dental fluorosis among Ugandan children in two fluoride districts while controlling for other factors related to fluorosis. All children who satisfied the criteria were lined up in the school yard, with two lines according to gender. Every third child was selected for the study, totalling 491 children. Ten children were excluded, 9 because of non-continuous residence in the villages and 1 who could not be traced for an interview. All the children were ethnic Bantu Africans and their socio-economic backgrounds appeared to be the same. There was no significant difference in the distribution of children according to gender. Written consent to participate in the study was given by the children's parents. A random sample of 481 children aged 10-14 years was examined for fluorosis using the Thylstrup and Fejerskov index (TF; see NRC, 2006, pages 88-89). A few days after the clinical examination, the child and his/her mother were interviewed according to a structured questionnaire to determine other sources of fluoride, including use of the following: boiling of drinking water, clay pots (for water storage), trona (calcium carbonate used as food additive), tea, infant formula, vegetarian diet, milk and fluoride toothpaste.
PARAMETERS MONITORED:	The prevalence of dental fluorosis was determined by clinical examination. One trained dentist examined the children under field conditions. The child was seated outside the school building and only sunlight was used for illumination. The surfaces of the permanent teeth were cleaned and dried with cotton balls prior to the examination. For all permanent teeth with at least 50% of the crown erupted, the severity of the fluorosis was assessed on the buccal/labial surfaces using the modified TF index. About 10% of the children (n=46) had their upper right central incisor re-examined a day later for a reliability test. There was no evidence of a systematic error. A few days after the clinical examination, the child and his/her mother were interviewed according to a structured questionnaire to determine other sources of fluoride, including boiling water, clay pots (for water storage), trona (calcium carbonate used as food additive), tea, infant formula, vegetarian diet, milk and fluoride toothpaste.
STATISTICAL METHODS:	Chi-square statistics were used when comparing frequency distribution of children on the basis of the prevalence and severity of dental fluorosis, age, gender and other variables (see Table 2). Student's t test for paired observations was used to check for systematic errors in TF scores. Spearman's rank correlation coefficient (r) was used to study the bivariate association between variables. Student's t test for independent samples was used to test whether r was significantly different from zero and to test differences between means of quantitative variables. Stepwise multiple linear regression analyses were used to control for confounding and to identify factors explaining variation in the percentage of teeth affected by fluorosis. Multiple logistic regression analyses were used to estimate the magnitude of risk of developing dental fluorosis.
RESULTS:	The distribution of children according to independent variables is presented in Table 2 taken directly from Rwenyonyi, 1999.

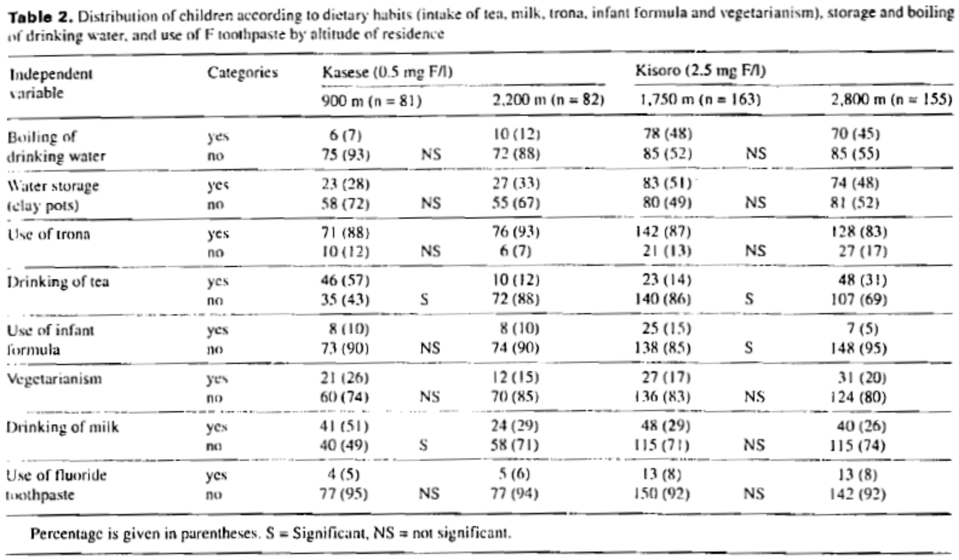

Table 2. Distribution of children according to dietary habits (intake of tea, milk, trona, infant formula and vegetarianism), storage and boiling of drinking water, and use of F toothpaste by altitude of residence

Independent variable	Categories	Kasese (0.5 mg F/l)			Kisoro (2.5 mg F/l)		
		900 m (n = 81)		2,200 m (n = 82)	1,750 m (n = 163)		2,800 m (n = 155)
Boiling of drinking water	yes	6 (7)		10 (12)	78 (48)		70 (45)
	no	75 (93)	NS	72 (88)	85 (52)	NS	85 (55)
Water storage (clay pots)	yes	23 (28)		27 (33)	83 (51)		74 (48)
	no	58 (72)	NS	55 (67)	80 (49)	NS	81 (52)
Use of trona	yes	71 (88)		76 (93)	142 (87)		128 (83)
	no	10 (12)	NS	6 (7)	21 (13)	NS	27 (17)
Drinking of tea	yes	46 (57)		10 (12)	23 (14)		48 (31)
	no	35 (43)	S	72 (88)	140 (86)	S	107 (69)
Use of infant formula	yes	8 (10)		8 (10)	25 (15)		7 (5)
	no	73 (90)	NS	74 (90)	138 (85)	S	148 (95)
Vegetarianism	yes	21 (26)		12 (15)	27 (17)		31 (20)
	no	60 (74)	NS	70 (85)	136 (83)	NS	124 (80)
Drinking of milk	yes	41 (51)		24 (29)	48 (29)		40 (26)
	no	40 (49)	S	58 (71)	115 (71)	NS	115 (74)
Use of fluoride toothpaste	yes	4 (5)		5 (6)	13 (8)		13 (8)
	no	77 (95)	NS	77 (94)	150 (92)	NS	142 (92)

Percentage is given in parentheses. S = Significant, NS = not significant.

Study results in Tables 3 through 7 and Figures 1-3 are shown directly from Rwenyonyi, 1999.

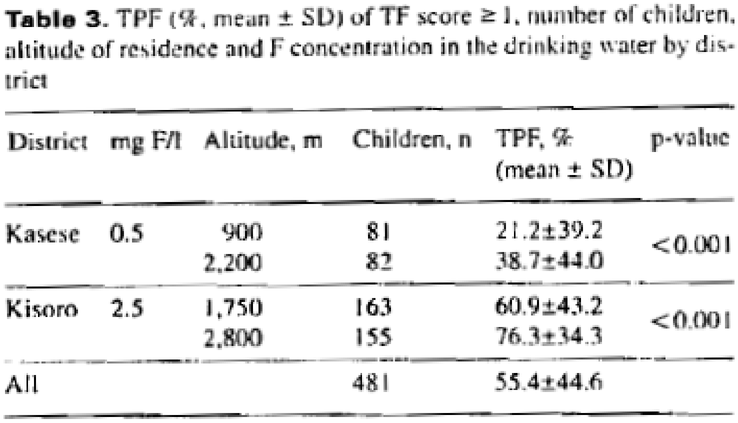

Table 3. TPF (%, mean ± SD) of TF score ≥ 1, number of children, altitude of residence and F concentration in the drinking water by district

District	mg F/l	Altitude, m	Children, n	TPF, % (mean ± SD)	p-value
Kasese	0.5	900	81	21.2±39.2	<0.001
		2,200	82	38.7±44.0	
Kisoro	2.5	1,750	163	60.9±43.2	<0.001
		2,800	155	76.3±34.3	
All			481	55.4±44.6	

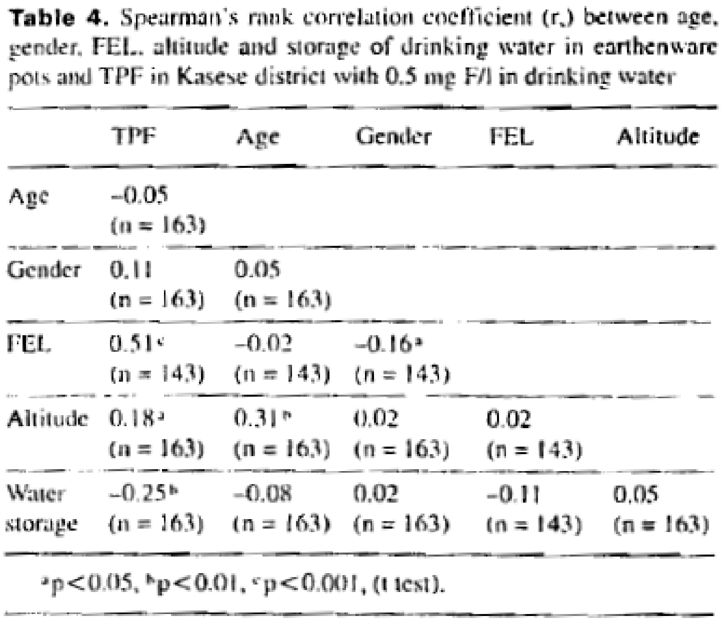

Table 4. Spearman's rank correlation coefficient (r_s) between age, gender, FEL, altitude and storage of drinking water in earthenware pots and TPF in Kasese district with 0.5 mg F/l in drinking water

	TPF	Age	Gender	FEL	Altitude
Age	−0.05 (n = 163)				
Gender	0.11 (n = 163)	0.05 (n = 163)			
FEL	0.51^{c} (n = 143)	−0.02 (n = 143)	-0.16^{a} (n = 143)		
Altitude	0.18^{a} (n = 163)	0.31^{b} (n = 163)	0.02 (n = 163)	0.02 (n = 143)	
Water storage	-0.25^{b} (n = 163)	−0.08 (n = 163)	0.02 (n = 163)	−0.11 (n = 143)	0.05 (n = 163)

$^{a}p<0.05$, $^{b}p<0.01$, $^{c}p<0.001$, (t test).

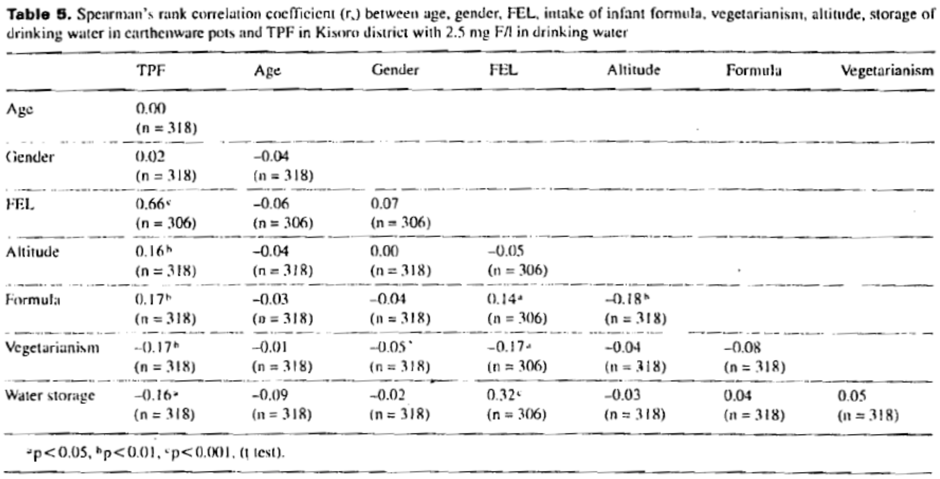

Table 5. Spearman's rank correlation coefficient (r_s) between age, gender, FEL, intake of infant formula, vegetarianism, altitude, storage of drinking water in earthenware pots and TPF in Kisoro district with 2.5 mg F/l in drinking water

	TPF	Age	Gender	FEL	Altitude	Formula	Vegetarianism
Age	0.00 (n = 318)						
Gender	0.02 (n = 318)	−0.04 (n = 318)					
FEL	0.66^{c} (n = 306)	−0.06 (n = 306)	0.07 (n = 306)				
Altitude	0.16^{b} (n = 318)	−0.04 (n = 318)	0.00 (n = 318)	−0.05 (n = 306)			
Formula	0.17^{b} (n = 318)	−0.03 (n = 318)	−0.04 (n = 318)	0.14^{a} (n = 306)	-0.18^{b} (n = 318)		
Vegetarianism	-0.17^{b} (n = 318)	−0.01 (n = 318)	−0.05 (n = 318)	-0.17^{a} (n = 306)	−0.04 (n = 318)	−0.08 (n = 318)	
Water storage	-0.16^{a} (n = 318)	−0.09 (n = 318)	−0.02 (n = 318)	0.32^{c} (n = 306)	−0.03 (n = 318)	0.04 (n = 318)	0.05 (n = 318)

$^{a}p<0.05$, $^{b}p<0.01$, $^{c}p<0.001$, (t test).

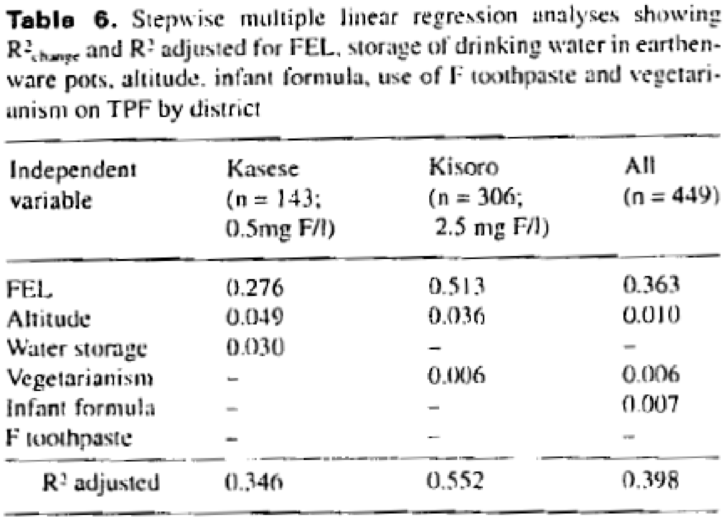

Table 6. Stepwise multiple linear regression analyses showing R^2_{change} and R^2 adjusted for FEL, storage of drinking water in earthenware pots, altitude, infant formula, use of F toothpaste and vegetarianism on TPF by district

Independent variable	Kasese (n = 143; 0.5mg F/l)	Kisoro (n = 306; 2.5 mg F/l)	All (n = 449)
FEL	0.276	0.513	0.363
Altitude	0.049	0.036	0.010
Water storage	0.030	–	–
Vegetarianism	–	0.006	0.006
Infant formula	–	–	0.007
F toothpaste	–	–	–
R^2 adjusted	0.346	0.552	0.398

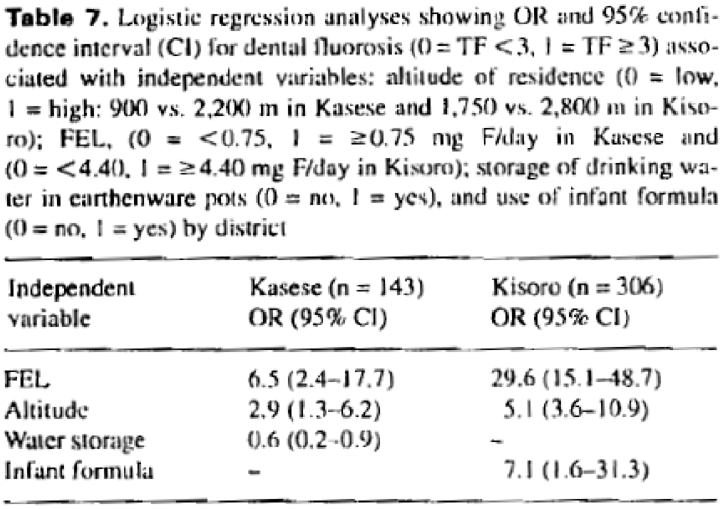

Table 7. Logistic regression analyses showing OR and 95% confidence interval (CI) for dental fluorosis (0 = TF <3, 1 = TF ≥ 3) associated with independent variables: altitude of residence (0 = low, 1 = high: 900 vs. 2,200 m in Kasese and 1,750 vs. 2,800 m in Kisoro); FEL, (0 = <0.75, 1 = ≥0.75 mg F/day in Kasese and (0 = <4.40, 1 = ≥4.40 mg F/day in Kisoro); storage of drinking water in earthenware pots (0 = no, 1 = yes), and use of infant formula (0 = no, 1 = yes) by district

Independent variable	Kasese (n = 143) OR (95% CI)	Kisoro (n = 306) OR (95% CI)
FEL	6.5 (2.4–17.7)	29.6 (15.1–48.7)
Altitude	2.9 (1.3–6.2)	5.1 (3.6–10.9)
Water storage	0.6 (0.2–0.9)	–
Infant formula	–	7.1 (1.6–31.3)

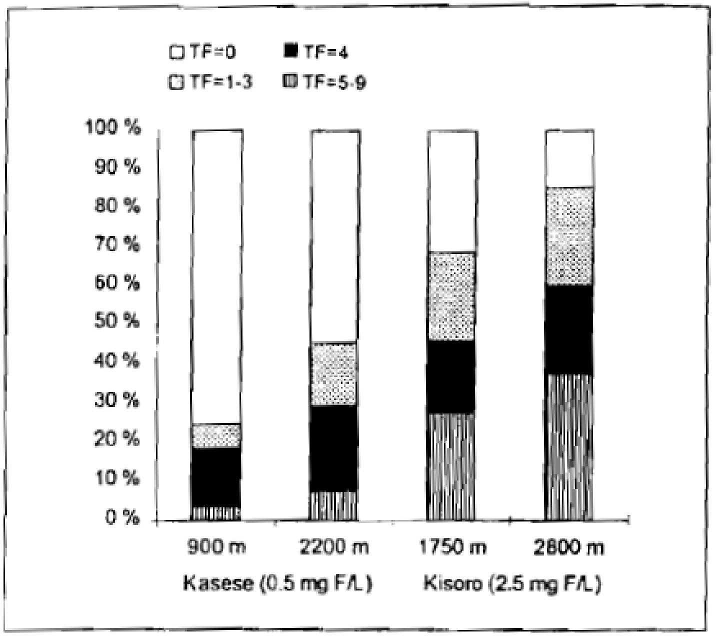

Fig. 1. Distribution of children according to the highest TF scores recorded, F concentration of the drinking water and altitude of residence by district.

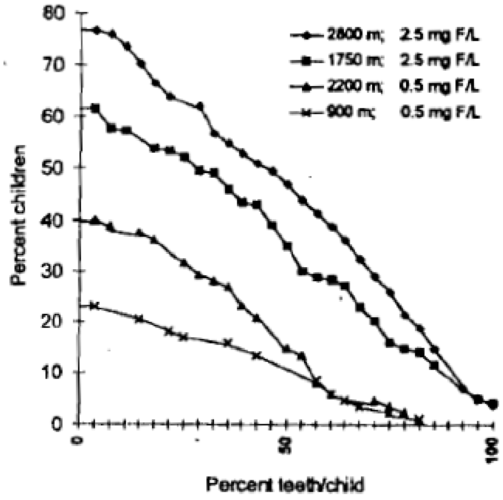

Fig. 2. Cumulative frequency distribution of children according to the proportion of teeth per child exhibiting dental fluorosis of TF scores ≥3, at different altitudes of residence and F concentrations of the drinking water.

<table>
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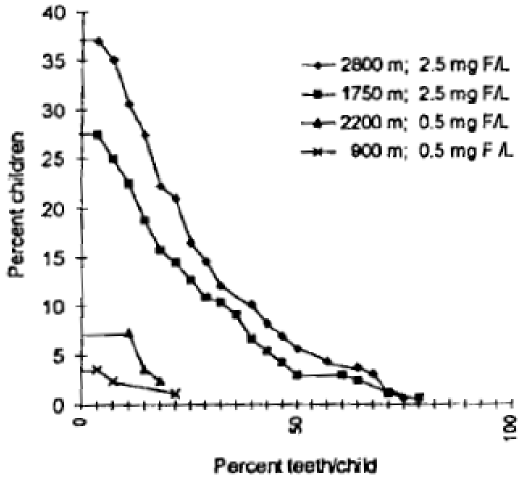


Fig. 3. Cumulative frequency distribution of children according to the proportion of teeth per child exhibiting dental fluorosis of TF scores ≥5, at different altitudes of residence and F concentrations of the drinking water.

</td>
</tr>
<tr>
<td colspan="2">STUDY AUTHORS' CONCLUSIONS:</td>
<td>The study authors concluded that most of the variance in the prevalence and severity of dental fluorosis was explained by the fluoride intake from liquid, but altitude remained a significant risk indicator after controlling for the effect of other potential confounding factors by multiple and logistic regression analyses.</td>
</tr>
<tr>
<td colspan="2">DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)</td>
<td>None</td>
</tr>
<tr>
<td>PROFILER'S REMARKS</td>
<td><i>Initials/Date</i>
VAD/03-07-07</td>
<td>The study results are not representative of the U.S. population since the study was conducted in Uganda. The number of participating children in the Kisoro district was almost twice the number in the Kasese district which could have biased the study. No reliability tests of the interviews were conducted because of the field conditions and therefore, the possibility of a recall bias cannot be ruled out. The examiner was not blinded to the children's district and hence fluoride exposure level. The study report does not indicate when the drinking water analyses were done; seasonal variations are known to occur.

The technical reviewer agrees with the profiler's estimated LOAEL but the applicability to the U.S. population is limited due to some outside sources of fluoride not observed in the U.S. (i.e. use of trona, storing water in clay pots) and the high altitude of the areas profiled.</td>
</tr>
<tr>
<td colspan="2">PROFILER's ESTIM. NOAEL</td>
<td>The study design did not identify a no-fluorosis intake dose.</td>
</tr>
<tr>
<td colspan="2">PROFILER'S ESTIM. LOAEL</td>
<td>In this study, the LOAEL was 0.5 mg/L. In the district with 0.5 mg/L fluoride in the drinking water, 25% of children at 900 m had dental fluorosis (TF score ≥1 on at least one tooth), whereas 45% of children living at 2,200 m were affected.</td>
</tr>
<tr>
<td colspan="2">SUITABILITY FOR DOSE RESPONSE MODELING</td>
<td>Not suitable,(_); Poor (_); Medium (X); Strong (_)</td>
</tr>
</table>

	Although the study does provide dose response data, it is presented in graphical form and therefore, not suitable for modeling.
CRITICAL EFFECTS:	Dental fluorosis (permanent teeth)

Selwitz, R.H., R.E. Nowjack-Raymer, A. Kingman, and W.S. Driscoll. 1998. Dental caries and dental fluorosis among school children who were lifelong residents of communities having either low or optimal levels of fluoride in drinking water. J. Public Health Dent. 58(1):28-35.

ENDPOINT STUDIED:	Dental fluorosis; dental caries
TYPE OF STUDY:	Cross-sectional survey of dental caries and dental fluorosis; follow-up of similar studies conducted in 1980; 1985 and 1990 (Horowitz et al 1984; Driscoll et al 1983, 1986; Heifetz et al 1988; Selwitz et al 1995).
POPULATION STUDIED:	US/Illinois; children in two age groups, 8-10 yr (86 males and 81 females) and 13-16 yr (45 males and 49 females) residing in Kewanee.
CONTROL POPULATION:	US/Nebraska: children in two age groups, 8-10 yr and 13-16 yr, residing in Holdrege, and Broken Bow, NE. Like the Illinois communities, the two Nebraska communities were small, rural Midwestern towns. Each had a per capita income of approximately $15,000, an agricultural economy, the same number of local dental practitioners, and similar percentages of high school graduates entering college.
EXPOSURE PERIOD:	Lifetime (8-10 yr; 13-16 yr), up until the dental examinations which were conducted in the Spring (NE) or Fall (Kewanee, IL) of 1990.
EXPOSURE GROUPS:	Drinking water fluoride concentration was 1 ppm in Kewanee, IL, and <0.3 ppm in Holdrege and Broken Bow, NE.
EXPOSURE ASSESSMENT:	Information was obtained from parents by questionnaire concerning the use of fluoride toothpaste, prescription fluoride drops or tablets, and professional fluoride dental treatments.
ANALYTICAL METHODS:	Based on information provided in an earlier report (Selwitz et al 1995), mean fluoride water concentrations were determined by averaging all available readings. The optimal water fluoride level for Kewanee, IL was reported to be 1 ppm. In Nebraska, 76 of the children received their drinking water from private wells; random water samples were analyzed with a fluoride-sensitive electrode (Orion Research, Inc.) for 62% of the wells to verify that the fluoride levels were negligible.
PARAMETERS MONITORED:	Dental caries was assessed using the DMFS scoring system; dental fluorosis was evaluated with TSIF scoring system (see Section 2 for descriptions of scoring systems).
STATISTICAL METHODS:	Differences in mean DMFS scores of participants by community were tested for statistical significance using the least square means option under the SAS (Statistical Analysis System) general linear models procedure (SAS 1990). The chi-square test of homogeneity was used to compare differences in the prevalence of dental sealants among the communities and differences in responses to questions regarding the participants' fluoride histories (SAS 1990). For dental fluorosis, the primary subject-based summary measure used in the statistical analyses consisted of the percentage of fluorosed surfaces per subject. Mean scores for this variable (MPFS) were computed for subjects in the three communities. Fixed effects ANOVA models were used to make comparisons among the subgroups. The LSMEANS procedure in SAS, which adjusts the group means for confounders present in the model, was used to compare adjusted means for statistical significance (SAS 1990). For individual comparisons, an $\alpha = 0.02$ value was used to control the overall experiment-wise Type I error rate as a compromise between the more stringent Bonferroni α/k value and the unadjusted $\alpha = 0.05$ value. This procedure adjusts for multiple comparisons, but retains the property of better power for conducting individual comparisons (Kleinbaum et al 1988). All

levels of significance reported are calculated P-values.

RESULTS:

Caries

The mean DMFS score adjusted for age, sealant presence, and fluoride use was significantly lower in Kewanee (1.8) than was the adjusted mean caries score in either Holdrege (2.9) or Broken Bow (3.6) (see Table 2, copied directly from Selwitz et al 1998).

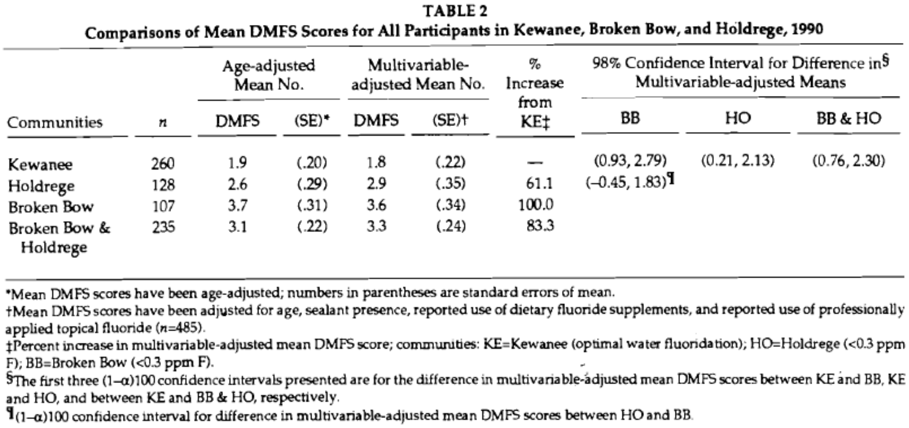


TABLE 2
Comparisons of Mean DMFS Scores for All Participants in Kewanee, Broken Bow, and Holdrege, 1990

		Age-adjusted Mean No.		Multivariable-adjusted Mean No.		% Increase from	98% Confidence Interval for Difference in§ Multivariable-adjusted Means		
Communities	n	DMFS	(SE)*	DMFS	(SE)†	KE‡	BB	HO	BB & HO
Kewanee	260	1.9	(.20)	1.8	(.22)	—	(0.93, 2.79)	(0.21, 2.13)	(0.76, 2.30)
Holdrege	128	2.6	(.29)	2.9	(.35)	61.1	(–0.45, 1.83)¶		
Broken Bow	107	3.7	(.31)	3.6	(.34)	100.0			
Broken Bow & Holdrege	235	3.1	(.22)	3.3	(.24)	83.3			

*Mean DMFS scores have been age-adjusted; numbers in parentheses are standard errors of mean.

†Mean DMFS scores have been adjusted for age, sealant presence, reported use of dietary fluoride supplements, and reported use of professionally applied topical fluoride (n=485).

‡Percent increase in multivariable-adjusted mean DMFS score; communities: KE=Kewanee (optimal water fluoridation); HO=Holdrege (<0.3 ppm F); BB=Broken Bow (<0.3 ppm F).

§The first three (1–α)100 confidence intervals presented are for the difference in multivariable-adjusted mean DMFS scores between KE and BB, KE and HO, and between KE and BB & HO, respectively.

¶(1–α)100 confidence interval for difference in multivariable-adjusted mean DMFS scores between HO and BB.

Dental fluorosis

The mean percent of fluorosed tooth surfaces per person, adjusted for age and use of dietary fluoride supplements, was similar in the three communities (approximately 15%); more than 80% of tooth surfaces in all participants were fluorosis-free.

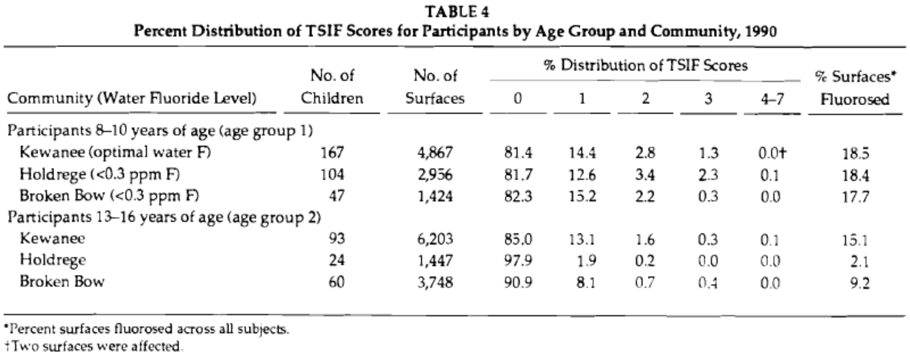


TABLE 4
Percent Distribution of TSIF Scores for Participants by Age Group and Community, 1990

	No. of	No. of	% Distribution of TSIF Scores					% Surfaces*
Community (Water Fluoride Level)	Children	Surfaces	0	1	2	3	4–7	Fluorosed
Participants 8–10 years of age (age group 1)								
Kewanee (optimal water F)	167	4,867	81.4	14.4	2.8	1.3	0.0†	18.5
Holdrege (<0.3 ppm F)	104	2,956	81.7	12.6	3.4	2.3	0.1	18.4
Broken Bow (<0.3 ppm F)	47	1,424	82.3	15.2	2.2	0.3	0.0	17.7
Participants 13–16 years of age (age group 2)								
Kewanee	93	6,203	85.0	13.1	1.6	0.3	0.1	15.1
Holdrege	24	1,447	97.9	1.9	0.2	0.0	0.0	2.1
Broken Bow	60	3,748	90.9	8.1	0.7	0.4	0.0	9.2

*Percent surfaces fluorosed across all subjects.

†Two surfaces were affected.

STUDY AUTHORS' CONCLUSIONS:

Findings from the present study suggest that water fluoridation still is beneficial and that dental sealants can play a significant role in preventing dental caries. In addition, findings from this survey appear to support the premise that the difference in dental fluorosis prevalence between fluoridated and nonfluoridated communities has narrowed considerably in recent years.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

SAS Institute Inc. 1990. SAS/STAT user's guide. Version 6.4th ed. Vol2. Cary, NC: SAS Institute, 1990:891-6.

SAS Institute Inc. 1990. SAS procedures guide. Version 6. 3rd ed. Cary, NC: SAS Institute, 1990:325-36.

Kleinbaum DG, Kupper LL, Muller KE. Applied regression analysis and other multivariable methods. 2nd ed. Boston: PWS-Kent Publishing Co.

PROFILER'S REMARKS ***Initials/date DMO/1/12/07***

Although severe fluorosis was documented in a small percentage of the study populations, insufficient data were provided to correlate severe fluorosis with a

		significant increase in caries. The range in fluoride concentrations in drinking water was insufficient to correlate fluoride concentrations in drinking water with fluorosis
PROFILER'S ESTIM. NOEL/NOAEL		Insufficient data
PROFILER'S ESTIM. LOEL/ LOAEL		Insufficient data
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( )
CRITICAL EFFECT(S):		Dental fluorosis and caries.

Selwitz, R.H., R.E. Nowjack-Raymer, A. Kingman, and W.S. Driscoll. 1995. Prevalence of dental caries and dental fluorosis in areas with optimal and above-optimal water fluoride concentrations: A 10-year follow-up survey. J. Public Health Dent. 55(2):85-93.

ENDPOINT STUDIED: Dental fluorosis; dental caries

TYPE OF STUDY: Cross-sectional survey of dental caries and dental fluorosis in children residing in Illinois in 1990; follow-up of similar studies conducted in 1980 and 1985 (Horowitz et al 1984; Driscoll et al 1983, 1986; Heifetz et al 1988).

POPULATION STUDIED: US/Illinois; children in two age groups, 8-10 yr (369 children) and 14-16 yr (188 children). All of the 14-16 yr olds examined in 1990 had been participants in the 1985 study as 8-10 yr olds.

CONTROL POPULATION: None

EXPOSURE PERIOD: 8-10 yrs and 14-16 yrs (examinations conducted in October, 1990).

EXPOSURE GROUPS: Seven study sites were grouped into four categories of exposure:

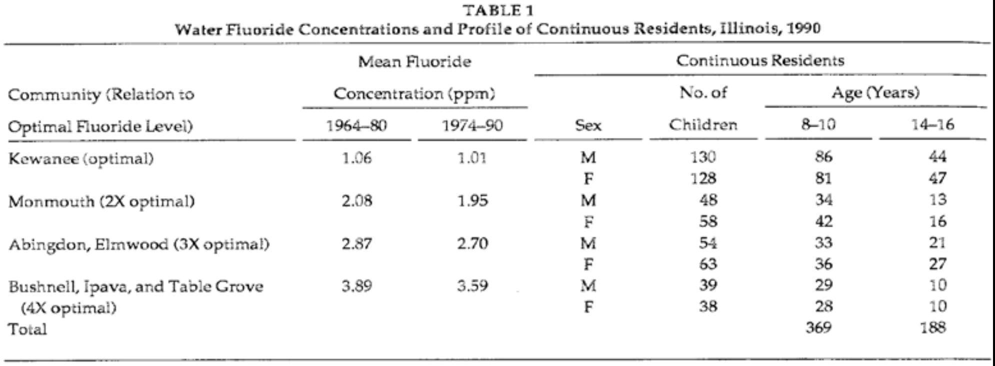


TABLE 1
Water Fluoride Concentrations and Profile of Continuous Residents, Illinois, 1990

Community (Relation to Optimal Fluoride Level)	Mean Fluoride Concentration (ppm) 1964–80	Mean Fluoride Concentration (ppm) 1974–90	Sex	Continuous Residents No. of Children	Age (Years) 8–10	Age (Years) 14–16
Kewanee (optimal)	1.06	1.01	M	130	86	44
			F	128	81	47
Monmouth (2X optimal)	2.08	1.95	M	48	34	13
			F	58	42	16
Abingdon, Elmwood (3X optimal)	2.87	2.70	M	54	33	21
			F	63	36	27
Bushnell, Ipava, and Table Grove (4X optimal)	3.89	3.59	M	39	29	10
			F	38	28	10
Total					369	188

The study participants had lived continuously in their communities since birth, and had always used the community water supply as their primary drinking water source.

PROFILER'S NOTE: Water supply of Bushnell (in 4X category) underwent alteration in 1982 with addition of lime softening process, which resulted in change to fluoride content of distributed supply (from 3.8 ppm to average of 2.5 ppm observed at time of 1990 examinations). Thus, children ingesting water from the Bushnell system had not been exposed to 4X water since 1982 (approx. 8 years at the time of the 1990 exam).

Children in the 8-10 year group were exposed to water with a concentration of 2.5 mg/L for either all of their lives or 8 out of ten years.

The children in the 14-16 year group had been exposed to water with 3.89 mg/L from birth to 6 years or birth to 8 years. If enamel formation is complete by 8 or 9 years, then they should be considered to be exposed to 3.89 ppm for the dose response analysis while the younger group should be considered to be exposed to 2.5 ppm for the most recent analysis.

EXPOSURE ASSESSMENT Dental exams took place in local schools with use of portable dental chairs, artificial lights and plane surface mouth mirrors. TSIF was determined by the same dentists who had performed these assessments in earlier surveys; to determine level of inter-examiner agreement, a 12% random sample received duplicate exams. Dental caries criteria were those of the ADA.

No attempt made to quantify alternate sources of fluoride such as mouth rinses, dentifrices,

	topical applications, and food supply; authors agree that these sources play a major role in an individual's composite fluoride intake.
ANALYTICAL METHODS:	Mean fluoride water concentrations were determined by averaging all available readings for each community obtained from state and local water officials. The optimal water fluoride level for that geographic area was reported to be 1 ppm.
STUDY DESIGN	Dental fluorosis and caries incidence were evaluated in 369 children 8-10 yrs old and 188 children 14-16 yrs old from seven communities in Illinois having different levels of fluoride in drinking water (mean values ranging from 1.06 ppm to 3.89 ppm in 1964-1980 and from 1.01 ppm to 3.59 ppm in 1974-1990). Comparisons were made using acceptable methods of diagnosis (TSIF index for fluorosis, and DMFS index for caries) and statistical analysis (two way ANOVA). Comparisons were made with data from the same populations obtained in 1980 and 1985.
PARAMETERS MONITORED:	Tooth surface index of fluorosis (TSIF) was utilized in the examinations (see Section 2 description). Caries incidence was determined by the decayed, missing and filled surface index (DMFS index). Radiographs were not taken.
STATISTICAL METHODS:	Differences in mean DMFS were tested using analysis of covariance, adjusting for age. The significance level for interpretation of calculated P-values was adjusted for multiple comparisons using the Bonferroni procedure (Bohannan et al 1984). Mean score for dental fluorosis (percent of fluorosed surfaces per subject) were computed for subpopulations and fluoride level using fixed effects ANOVA models. The LSMeans procedure in SAS was used to compare adjusted means for statistical significance. Bonferroni corrections were used to limit the over all experimental type I error rate at between 5% and 10%. Statistical significance was set at p=0.002. Inter-examiner agreements for TSIF were 79.4 % and 87.5 %; corresponding to kappa values of 0.54 (moderate agreement) and 0.64 (substantial agreement).
RESULTS:	
Dental Fluorosis	TSIF scores for the 8-10 yr old children examined in 1990 are shown in Table 3 (copied directly from Selwitz et al., 1995), with comparisons to the children examined in 1980 and 1985.

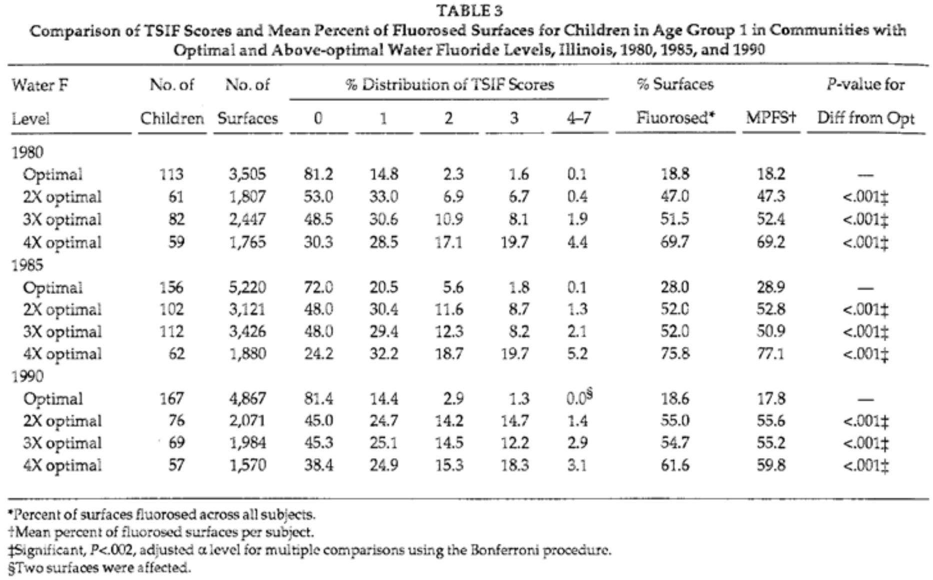


TABLE 3

Comparison of TSIF Scores and Mean Percent of Fluorosed Surfaces for Children in Age Group 1 in Communities with Optimal and Above-optimal Water Fluoride Levels, Illinois, 1980, 1985, and 1990

Water F Level	No. of Children	No. of Surfaces	% Distribution of TSIF Scores					% Surfaces Fluorosed*	MPFS†	*P*-value for Diff from Opt
			0	1	2	3	4–7			
1980										
Optimal	113	3,505	81.2	14.8	2.3	1.6	0.1	18.8	18.2	—
2X optimal	61	1,807	53.0	33.0	6.9	6.7	0.4	47.0	47.3	<.001‡
3X optimal	82	2,447	48.5	30.6	10.9	8.1	1.9	51.5	52.4	<.001‡
4X optimal	59	1,765	30.3	28.5	17.1	19.7	4.4	69.7	69.2	<.001‡
1985										
Optimal	156	5,220	72.0	20.5	5.6	1.8	0.1	28.0	28.9	—
2X optimal	102	3,121	48.0	30.4	11.6	8.7	1.3	52.0	52.8	<.001‡
3X optimal	112	3,426	48.0	29.4	12.3	8.2	2.1	52.0	50.9	<.001‡
4X optimal	62	1,880	24.2	32.2	18.7	19.7	5.2	75.8	77.1	<.001‡
1990										
Optimal	167	4,867	81.4	14.4	2.9	1.3	0.0§	18.6	17.8	—
2X optimal	76	2,071	45.0	24.7	14.2	14.7	1.4	55.0	55.6	<.001‡
3X optimal	69	1,984	45.3	25.1	14.5	12.2	2.9	54.7	55.2	<.001‡
4X optimal	57	1,570	38.4	24.9	15.3	18.3	3.1	61.6	59.8	<.001‡

*Percent of surfaces fluorosed across all subjects.
†Mean percent of fluorosed surfaces per subject.
‡Significant, *P*<.002, adjusted α level for multiple comparisons using the Bonferroni procedure.
§Two surfaces were affected.

TSIF scores for the 14-16 yr old children examined in 1990 are shown in Table 4 (copied directly from Selwitz et al., 1995), with comparisons to the children examined in 1980 and 1985.

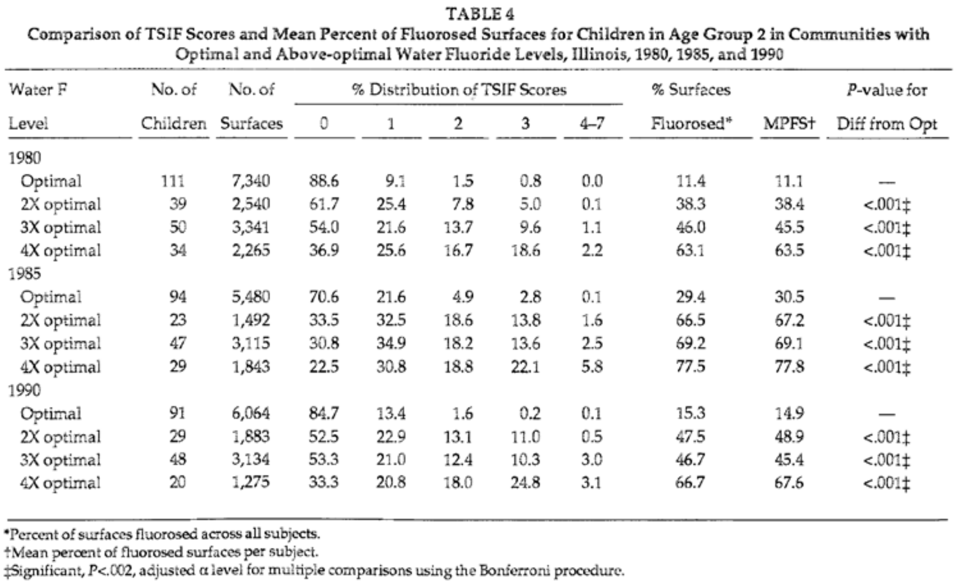


TABLE 4
Comparison of TSIF Scores and Mean Percent of Fluorosed Surfaces for Children in Age Group 2 in Communities with Optimal and Above-optimal Water Fluoride Levels, Illinois, 1980, 1985, and 1990

Water F Level	No. of Children	No. of Surfaces	% Distribution of TSIF Scores 0	1	2	3	4–7	% Surfaces Fluorosed*	MPFS†	*P*-value for Diff from Opt
1980										
Optimal	111	7,340	88.6	9.1	1.5	0.8	0.0	11.4	11.1	—
2X optimal	39	2,540	61.7	25.4	7.8	5.0	0.1	38.3	38.4	<.001‡
3X optimal	50	3,341	54.0	21.6	13.7	9.6	1.1	46.0	45.5	<.001‡
4X optimal	34	2,265	36.9	25.6	16.7	18.6	2.2	63.1	63.5	<.001‡
1985										
Optimal	94	5,480	70.6	21.6	4.9	2.8	0.1	29.4	30.5	—
2X optimal	23	1,492	33.5	32.5	18.6	13.8	1.6	66.5	67.2	<.001‡
3X optimal	47	3,115	30.8	34.9	18.2	13.6	2.5	69.2	69.1	<.001‡
4X optimal	29	1,843	22.5	30.8	18.8	22.1	5.8	77.5	77.8	<.001‡
1990										
Optimal	91	6,064	84.7	13.4	1.6	0.2	0.1	15.3	14.9	—
2X optimal	29	1,883	52.5	22.9	13.1	11.0	0.5	47.5	48.9	<.001‡
3X optimal	48	3,134	53.3	21.0	12.4	10.3	3.0	46.7	45.4	<.001‡
4X optimal	20	1,275	33.3	20.8	18.0	24.8	3.1	66.7	67.6	<.001‡

*Percent of surfaces fluorosed across all subjects.
†Mean percent of fluorosed surfaces per subject.
‡Significant, *P*<.002, adjusted α level for multiple comparisons using the Bonferroni procedure.

Other Effects

DMFS scores for children in areas with above optimal water fluoridation did not change significantly from 1980 to1990. In areas with optimal water fluoride levels, the mean DMFS score of 1.9 in 1990 was significantly lower than that in 1980, and the proportion of fluorosed tooth surfaces increased significantly from 1980 to 1985 but then declined by 1990 to the level observed in 1980.

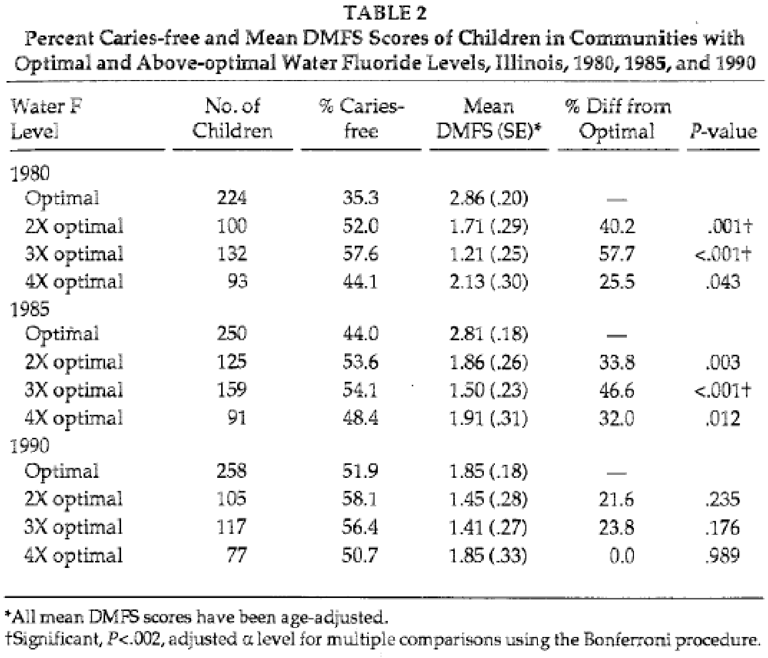


TABLE 2
Percent Caries-free and Mean DMFS Scores of Children in Communities with Optimal and Above-optimal Water Fluoride Levels, Illinois, 1980, 1985, and 1990

Water F Level	No. of Children	% Caries-free	Mean DMFS (SE)*	% Diff from Optimal	*P*-value
1980					
Optimal	224	35.3	2.86 (.20)	—	
2X optimal	100	52.0	1.71 (.29)	40.2	.001†
3X optimal	132	57.6	1.21 (.25)	57.7	<.001†
4X optimal	93	44.1	2.13 (.30)	25.5	.043
1985					
Optimal	250	44.0	2.81 (.18)	—	
2X optimal	125	53.6	1.86 (.26)	33.8	.003
3X optimal	159	54.1	1.50 (.23)	46.6	<.001†
4X optimal	91	48.4	1.91 (.31)	32.0	.012
1990					
Optimal	258	51.9	1.85 (.18)	—	
2X optimal	105	58.1	1.45 (.28)	21.6	.235
3X optimal	117	56.4	1.41 (.27)	23.8	.176
4X optimal	77	50.7	1.85 (.33)	0.0	.989

*All mean DMFS scores have been age-adjusted.
†Significant, *P*<.002, adjusted α level for multiple comparisons using the Bonferroni procedure.

The high level of cavities at optimal limit the usefulness of this data on the cavities.

Tables 3 and 4 of Selwitz et al (follow) illustrate the percent distribution of TSIF scores on permanent tooth surfaces across all subjects, and the mean percent of fluorosed surfaces per subject (MPFS) among optimal and above-optimal communities.

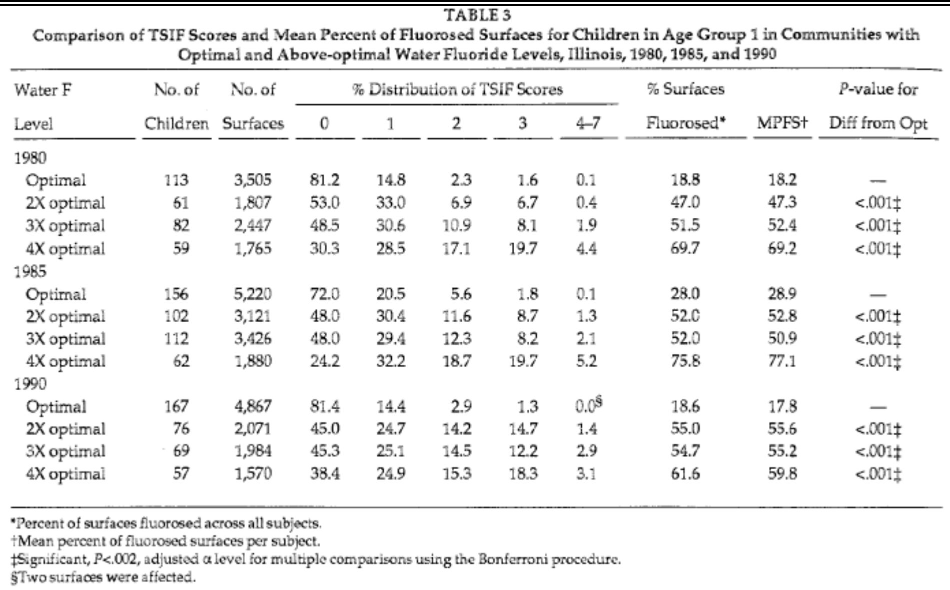


TABLE 3
Comparison of TSIF Scores and Mean Percent of Fluorosed Surfaces for Children in Age Group 1 in Communities with Optimal and Above-optimal Water Fluoride Levels, Illinois, 1980, 1985, and 1990

Water F Level	No. of Children	No. of Surfaces	% Distribution of TSIF Scores 0	1	2	3	4–7	% Surfaces Fluorosed*	MPFS†	P-value for Diff from Opt
1980										
Optimal	113	3,505	81.2	14.8	2.3	1.6	0.1	18.8	18.2	—
2X optimal	61	1,807	53.0	33.0	6.9	6.7	0.4	47.0	47.3	<.001‡
3X optimal	82	2,447	48.5	30.6	10.9	8.1	1.9	51.5	52.4	<.001‡
4X optimal	59	1,765	30.3	28.5	17.1	19.7	4.4	69.7	69.2	<.001‡
1985										
Optimal	156	5,220	72.0	20.5	5.6	1.8	0.1	28.0	28.9	—
2X optimal	102	3,121	48.0	30.4	11.6	8.7	1.3	52.0	52.8	<.001‡
3X optimal	112	3,426	48.0	29.4	12.3	8.2	2.1	52.0	50.9	<.001‡
4X optimal	62	1,880	24.2	32.2	18.7	19.7	5.2	75.8	77.1	<.001‡
1990										
Optimal	167	4,867	81.4	14.4	2.9	1.3	0.0§	18.6	17.8	—
2X optimal	76	2,071	45.0	24.7	14.2	14.7	1.4	55.0	55.6	<.001‡
3X optimal	69	1,984	45.3	25.1	14.5	12.2	2.9	54.7	55.2	<.001‡
4X optimal	57	1,570	38.4	24.9	15.3	18.3	3.1	61.6	59.8	<.001‡

*Percent of surfaces fluorosed across all subjects.
†Mean percent of fluorosed surfaces per subject.
‡Significant, P<.002, adjusted α level for multiple comparisons using the Bonferroni procedure.
§Two surfaces were affected.

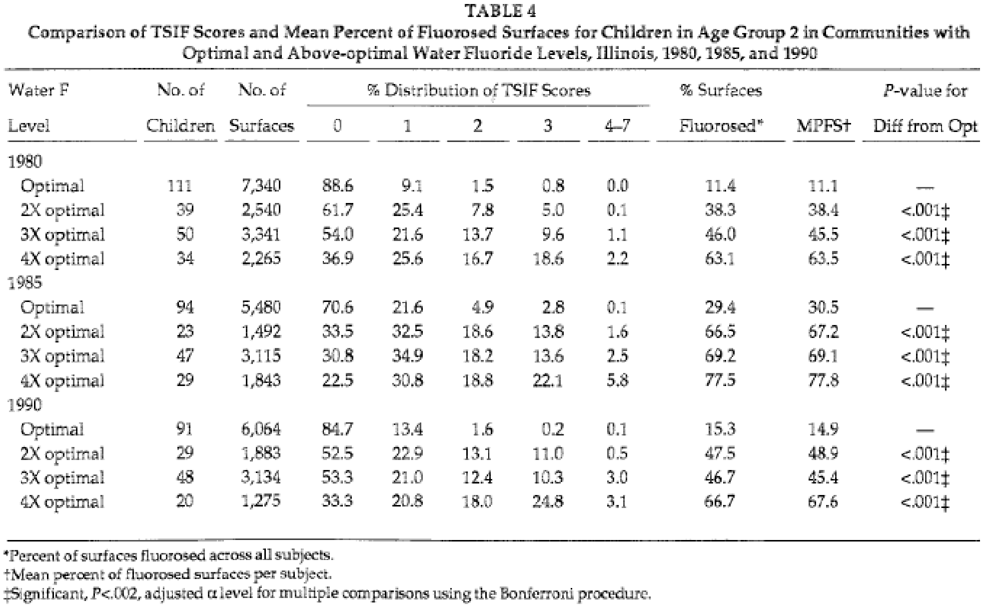


TABLE 4
Comparison of TSIF Scores and Mean Percent of Fluorosed Surfaces for Children in Age Group 2 in Communities with Optimal and Above-optimal Water Fluoride Levels, Illinois, 1980, 1985, and 1990

Water F Level	No. of Children	No. of Surfaces	% Distribution of TSIF Scores 0	1	2	3	4–7	% Surfaces Fluorosed*	MPFS†	P-value for Diff from Opt
1980										
Optimal	111	7,340	88.6	9.1	1.5	0.8	0.0	11.4	11.1	—
2X optimal	39	2,540	61.7	25.4	7.8	5.0	0.1	38.3	38.4	<.001‡
3X optimal	50	3,341	54.0	21.6	13.7	9.6	1.1	46.0	45.5	<.001‡
4X optimal	34	2,265	36.9	25.6	16.7	18.6	2.2	63.1	63.5	<.001‡
1985										
Optimal	94	5,480	70.6	21.6	4.9	2.8	0.1	29.4	30.5	—
2X optimal	23	1,492	33.5	32.5	18.6	13.8	1.6	66.5	67.2	<.001‡
3X optimal	47	3,115	30.8	34.9	18.2	13.6	2.5	69.2	69.1	<.001‡
4X optimal	29	1,843	22.5	30.8	18.8	22.1	5.8	77.5	77.8	<.001‡
1990										
Optimal	91	6,064	84.7	13.4	1.6	0.2	0.1	15.3	14.9	—
2X optimal	29	1,883	52.5	22.9	13.1	11.0	0.5	47.5	48.9	<.001‡
3X optimal	48	3,134	53.3	21.0	12.4	10.3	3.0	46.7	45.4	<.001‡
4X optimal	20	1,275	33.3	20.8	18.0	24.8	3.1	66.7	67.6	<.001‡

*Percent of surfaces fluorosed across all subjects.
†Mean percent of fluorosed surfaces per subject.
‡Significant, P<.002, adjusted α level for multiple comparisons using the Bonferroni procedure.

STUDY AUTHORS' CONCLUSIONS:

Dental fluorosis seen in children in areas with optimal water fluoride levels appeared to increase from 1980 to 1985, but did not continue to increase from 1985 to 1990. Dental fluorosis seen in children in areas with 4X above optimal water fluoride levels remained stable or showed no sustained increase from 1980 to 1990. Apparent increase in prevalence of fluorosis observed for all permanent tooth surfaces (younger children in optimal community and older children in optimal + 2X and 3X communities) declined by 1990 to levels observed 10 years before; explanations for this shift can not be determined with certainty.

A clear majority of tooth surfaces affected by dental fluorosis at the optimal level received a TSIF score of 1. At above-optimal water fluoride concentrations, dental fluorosis either remained stable or demonstrated no sustained increase over the decade-long study.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT

For definitions and descriptions of scales and indices, please see Section 2 and List of Acronyms.

Driscoll, WS et al 1983. Prevalence of dental caries and dental fluorosis in areas with optimal

FOUND IN NRC (2006)		and above-optimal water fluoride concentrations. J. Am. Dent. Assoc. 107: 42-47.
PROFILER'S REMARKS	***Initials/date*** ***DMO*** ***11/30/2006*** ***and*** ***12/15/2006***	Concerns regarding confounding of 4X community category (fluoride concentration of Bushnell community water supply altered dramatically in 1982), thus affecting interpretation of 4X community findings. As in many epidemiological studies, fluoride ingestion from alternative sources is not characterized.
PROFILER'S ESTIM. NOEL/NOAEL		Dental fluorosis observed at all fluoride concentrations examined; thus, estimating a NOAEL is not possible from these data.
PROFILER'S ESTIM. LOEL/ LOAEL		The lowest fluoride concentration at which opacities were observed is 1 ppm.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor (_), Medium (X), Strong (_) Data collected for combined "4X" communities for 1990 (and possibly 1985) is compromised by significant downward concentration of fluoride in the community of Bushnell due to 1982 installation of water softening treatment unit to community water supply. Uncompromised dose response may be possible with optimal, 2X and 3X communities while acknowledging that alternate sources of fluoride have not been controlled; to be determined.
CRITICAL EFFECTS		Dental fluorosis and caries

Stephen, K.W., L.M.D. Macpherson, W.H. Gilmour, R.A.M. Stuart and M.C.W. Merrett. 2002. A blind caries and fluorosis prevalence study of school-children in naturally fluoridated and nonfluoridated townships of Morayshire, Scotland. Community Dent Oral Epidemiol 30:70-9.

ENDPOINT STUDIED:

Dental caries and fluorosis

TYPE OF STUDY:

Blind prevalence study of dental caries and fluorosis.

POPULATION STUDIED:

Scotland/ Morayshire; Burghead, Findhorn, Kinlos, Buckie and Portessie. Children from school grade 1 (aged 5-6 years) and grade 4-7 (aged 8-12 years). 70 lifetime and 31 school-lifetime (permanently present therein since commencing full-time schooling at age 4.5/5 years) out of an eligible total of 125 children exposed to 1 ppm F in drinking water (F subjects); and 179 lifetime and 37 school-lifetime children out of 281 eligible subjects exposed to drinking water with 0.03 ppm F (N-F subjects).

The socioeconomic status (SES) analysis showed that 17% of F subjects were in “high” SES groups I or II, 75% in “nonmanual” group III and 8% in “manual groups” IV or V. For the N-F children, the corresponding percentages were 23%, 60% and 17%, thus revealing a higher percentage of N-F subjects at either end of the SES scale.

The study population is presented in Table 1 taken directly from Stephen, 2002.

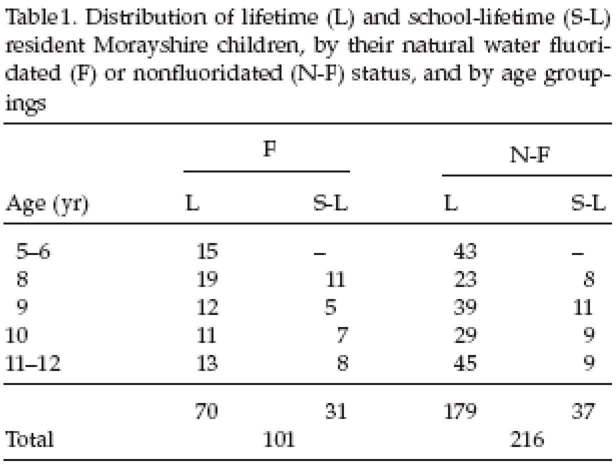


Table1. Distribution of lifetime (L) and school-lifetime (S-L) resident Morayshire children, by their natural water fluoridated (F) or nonfluoridated (N-F) status, and by age groupings

	F		N-F	
Age (yr)	L	S-L	L	S-L
5–6	15	–	43	–
8	19	11	23	8
9	12	5	39	11
10	11	7	29	9
11–12	13	8	45	9
	70	31	179	37
Total	101		216	

A total of 15 F and 43 N-F 5/6 year-old children were examined for caries. For the 8-12 year-olds, 55 life-time and 31 school-lifetime F children and 136 lifetime and 37 school-lifetime N-F children were examined for caries; only the lifetime children in the F and N-F groups were examined for fluorosis.

CONTROL POPULATION:

Children from non-fluoridated water communities (N-F subjects) served as controls.

EXPOSURE PERIOD:

Exposure from birth to age 5-6 years to fluoridated (F) water (n = 15) or nonfluoridated (N-F) water (n = 43). Exposure from birth to age 8-12 (n = 55 for F and n = 136 for N-F) or only during school-lifetime beginning at age 4.5-5 yr (31 F; 37 N-F).

EXPOSURE GROUPS:

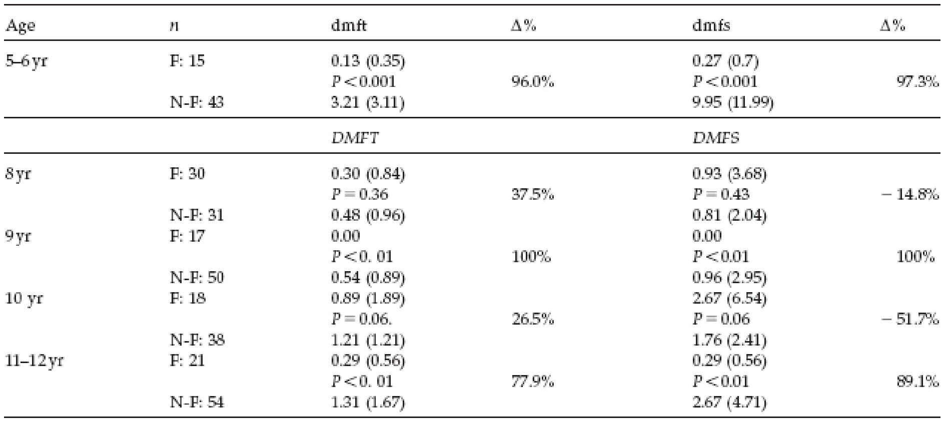
The drinking water in Burghead, Findhorn, and Kinlos was naturally fluoridated at a level of 1 ppm. The drinking water in Buckie and Portessie was non-fluoridated (N-F) with a fluoride concentration of 0.03 ppm.

EXPOSURE ASSESSMENT

A simple parental questionnaire assessment was circulated along with the participation permission slip to determine if and when any regular fluoride supplement and dentifrice

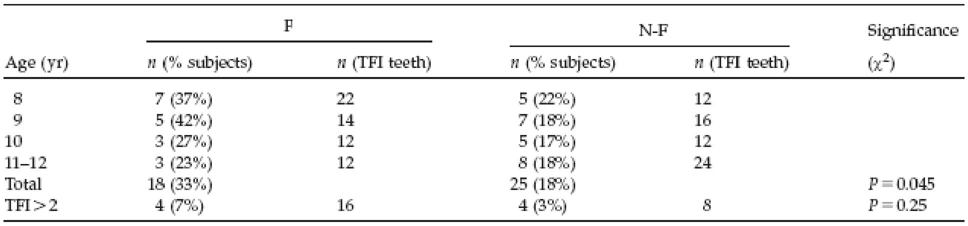
	usage had occurred from 0-6, 7-11 and 12-23 months of age and from 2-3 years or >3 years of age; and also to attempt to determine the brand(s) of fluoride/nonfluoride dentifrice currently and previously used by each subject.
ANALYTICAL METHODS:	None provided.
STUDY DESIGN	The objective of the study was to determine the prevalence of dental caries and fluorosis in Grade 1 (aged 5/6 year) and Grade 4-7 (aged 8-12 years) children from three naturally water-fluoridated (1ppm) communities and two nearby nonfluoridated communities (0.03 ppm F) in rural Morayshire, Scotland. A blind clinical caries study of 5-6 year-old lifetime and 8-12 year-old lifetime/schooltime residents was conducted. In addition, 8-12 year-old lifetime residents of the fluoridated or nonfluoridated communities were examined for dental fluorosis of the permanent teeth. To ensure subject anonymity, children were requested to attend the examination without any obvious school-identifying and hence community-identifying apparel. Each child was asked about their own perception of the aesthetics of their maxillary front teeth. Fluorosis was assessed clinically using the Thylstrup-Fejerskov Index (TFI, see NRC, 2006, pages 88-89), as well as photographically. The photographic slides were later blindly scored by four dental and two lay jurors, alongside the UK benchmark mildly mottled (TFI=2) fluorosis comparator slide, judged in previous studies to be aesthetically lay-acceptable. Information on their child's fluoride supplement and dentifrice usage histories was obtained through parental questionnaires. A head-of-household occupation information was requested to enable socioeconomic status comparisons to be made as per Registrar General for Scotland classification criteria (Anonymous, 1992).
PARAMETERS MONITORED:	DMFT/s and DMFT/S assessments (with random 10% re-examination) were carried out by the lead study author. Subjects were examined supine as per the 1994-modified Scottish Health Boards' Dental Epidemiological Programme (SHBDEP), at the "Dentinal 2V" level of caries detection (i.e., "…definite dentinal caries evidence by visual inspection, even in the absence of clinical cavitation"), supplemented by the use of a ball-ended, disposable CPITN periodontal probe. As per SHBDEP acceptable practice, no sharp explorer or air-drying was used, but gauze was available for tooth-surface cleansing where required. For fluorosis scoring, a lay assistant asked each 8-12 year-old lifetime subject, the standard SHBDEP question: "Are you aware of any marks on you upper front teeth which will not brush off?". Clinically, the labial surface of teeth 13-23 were assessed, without drying, for diffuse, homologous tooth mottling as per the TFI criteria (see NRC, 2006, pages 88-89) with 10% re-examination. Color positive transparency photographs were obtained of these teeth using a Yashica "Dental Eye" camera. The slides were viewed "blind" and scored randomly under standardized projection conditions by two study authors, by two other dental and two lay staff "jury" members with a 10% random re-viewing for inter- and intra-observer agreement calculations. The slides were projected on a screen. Simultaneously, on a separate, identical screen, a single "Fluorosis Impact Factor" color slide (TFI=2) was projected. This level of diffuse, symmetrical mottling has been established as the most "aesthetically acceptable" to 85% of 534 English teenagers shown a series of colored photographs of non-mottled and symmetrically diffuse mottled (TFI=0-4) maxillary front teeth (Hawley, 1996; see NRC, 2006, page 98). Panelists were given a brief "slide tutorial" to remind them of the photographically visible mottling criteria appropriate to award a diagnosis of fluorosis from TFI=1 and upwards.
STATISTICAL METHODS:	Caries data were compared between groups by the Mann-Whitney U-test, with the Chi-Square test applied to compare percentages between groups. Cohen's Kappa was used to measure intra-and inter-observer agreements for categorical variables, while Dahlberg's Direct Error Variance Method was employed to assess the intra-observer agreement (reliability coefficient) for clinically scored caries and diffuse, symmetrical, dental fluorosis data.
RESULTS:	Study results in Tables 3 and 4 are shown directly from Stephen, 2002.

Table3. Mean (SD) dental caries data for water-fluoridated (F) and nonfluoridated (N-F) Morayshire pupils (Mann–Whitney U)



Age	n	dmft	Δ%	dmfs	Δ%
5–6 yr	F: 15	0.13 (0.35)		0.27 (0.7)	
		$P < 0.001$	96.0%	$P < 0.001$	97.3%
	N-F: 43	3.21 (3.11)		9.95 (11.99)	
		DMFT		*DMFS*	
8 yr	F: 30	0.30 (0.84)		0.93 (3.68)	
		$P = 0.36$	37.5%	$P = 0.43$	− 14.8%
	N-F: 31	0.48 (0.96)		0.81 (2.04)	
9 yr	F: 17	0.00		0.00	
		$P < 0.\ 01$	100%	$P < 0.01$	100%
	N-F: 50	0.54 (0.89)		0.96 (2.95)	
10 yr	F: 18	0.89 (1.89)		2.67 (6.54)	
		$P = 0.06.$	26.5%	$P = 0.06$	− 51.7%
	N-F: 38	1.21 (1.21)		1.76 (2.41)	
11–12 yr	F: 21	0.29 (0.56)		0.29 (0.56)	
		$P < 0.\ 01$	77.9%	$P < 0.01$	89.1%
	N-F: 54	1.31 (1.67)		2.67 (4.71)	

Table4. Number of teeth scored clinically as TFI positive, in the number (and percentage) of lifetime fluoridated (F) and nonfluoridated (N-F) pupils listed per age-group examined. Also shown are similar data for all TFI > 2 scores



	F		N-F		Significance
Age (yr)	n (% subjects)	n (TFI teeth)	n (% subjects)	n (TFI teeth)	(χ^2)
8	7 (37%)	22	5 (22%)	12	
9	5 (42%)	14	7 (18%)	16	
10	3 (27%)	12	5 (17%)	12	
11–12	3 (23%)	12	8 (18%)	24	
Total	18 (33%)		25 (18%)		$P = 0.045$
TFI > 2	4 (7%)	16	4 (3%)	8	$P = 0.25$

STUDY AUTHORS' CONCLUSIONS:

The study authors concluded that considerable caries benefit has accrued to those Morayshire rural children who have received naturally fluoridated water (at 1 ppm) throughout their lives, as compared to their socioeconomically similar, nonfluoridated rural counterparts. Only borderline mild fluorosis disadvantages were noted clinically and none by the subjects' own aesthetic perceptions. No evidence was found to suggest any delay in permanent tooth eruption patterns of subjects in the fluoridated water group.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

Anonymous. 1992. Definitions of social class and socio-economic groups. Edinburgh:General Register Office (Scotland).

PROFILER'S REMARKS

Initials/Date
VAD/01-05-07

The children in the study were from a rural area and were most likely all white (not stated in the study report), and therefore, the population was not representative of the U.S. general population. The number of subjects in some categories was small and there were unequal numbers for some comparisons of fluoridated and nonfluoridated communities. For example, there were 15 children from fluoridated communities and 43 from nonfluoridated communities in the 5-6 year-old group. Only 4 children in the fluoridated and 4 children in the nonfluoridated water groups had TFI scores of greater than 2 on a scale of 1-8 (see NRC, 2006, page 89); therefore, results are applicable only to the mild fluorosis category.

Data not useful for evaluating the occurrence of severe fluorosis. Some information is provided that might be used in the analysis of relative source contributions.

PROFILER's ESTIM. NOAEL

The study design did not estimate a NOAEL.

PROFILER’S ESTIM. LOAEL	The study design did not estimate a LOAEL.
SUITABILITY FOR DOSE RESPONSE MODELING	Not suitable,(_); Poor (X_); Medium (); Strong (_) Only two exposure levels were evaluated and only mild levels of fluorosis were recorded.
CRITICAL EFFECTS:	Dental caries (deciduous and permanent teeth) and fluorosis (permanent teeth 13-23)

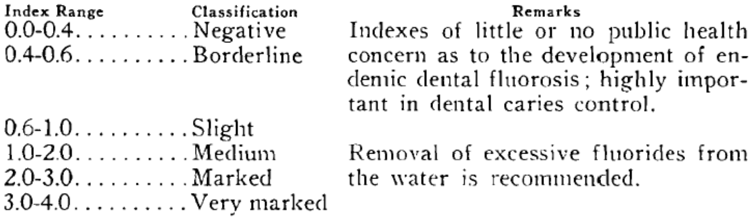
Striffler, DF. 1955. Fluoridation in New Mexico: It's Present Status. NM State Dent J 5(2):3-11.

ENDPOINT STUDIED:	Dental caries, fluorosis, gingivitis.
TYPE OF STUDY:	Cohort
POPULATION STUDIED:	263 junior-high school age children residing in Lordsburg, New Mexico (NM) where the drinking water was 3.25 ppm fluoride.
POPULATION STUDIED:	573 junior-high school age children residing in Belen, NM where the drinking water was 0.9 ppm fluoride.
POPULATION STUDIED:	485 junior-high school age children residing in Lovington, NM where the drinking water was **0.8 ppm fluoride**.
CONTROL POPULATION:	888 junior-high school age children residing in Santa Fe, NM where the drinking water had only **traces** of fluoride.
EXPOSURE PERIOD:	Water history was assessed for children from birth until 8 years of age.
EXPOSURE GROUPS:	2290 New Mexico junior-high-age children were surveyed. The subjects were grouped based on residence in four communities with various levels of fluoride in the drinking water as follows: 263 subjects in Lordsburg (3.25 ppm F in the drinking water), 573 in Belen (0.9 ppm F), 485 in Lovington (0.8 ppm F), and 888 in Santa Fe (traces of F).
EXPOSURE ASSESSMENT:	In each community, the students were surveyed for drinking water history and their parents were surveyed to verify the information. Subjects were inspected for caries experience, for gingivitis, and for chronic endemic dental fluorosis.
ANALYTICAL METHODS:	All fluoride determinations were made by the NM Department of Public Health Laboratory, Chemistry Section. In each case, a minimum of 12 samples were analyzed. No significant changes had been made in the water supplies since before the subjects studied had been born.
STUDY DESIGN	2290 NM junior-high-age children were surveyed by the Division of Dental Health of the NM Department of Public Health during 1954. The subjects were grouped based on residence in one of four communities with various drinking water fluoride levels: Lordsburg (3.25 ppm F), Belen (0.9 ppm F), Lovington (0.8 ppm F), or Santa Fe (traces of F). This age group was selected because it is the earliest that the effects of fluoride could be noted in all of the permanent teeth (excluding third molars). In each community, the students were checked for drinking water history in four ways. 1) Each student filled out a survey which asked questions regarding place of birth, continuous residence in the community in which they currently resided, and whether they had been away from that place for ≥90 days at any one time from birth through 8 years of age. 2) Parents completed an identical survey. 3) Each subject was questioned about water history at the time of examination. 4) Any discrepancies were resolved by a home visit by the school nurse. All children who had not had city water for any period longer than 90 days between their birth and 8 years of age or whose water histories could not be resolved were ruled out and not classed as continuous residents. Careful checks were made into possible histories of drinking bottled water, ditch water, or private well water. Confounding factors were considered: socio-economic level; food habits; amount of dental care; national origin; different examiners/ examining conditions. Subjects were inspected for caries experience as measured by the DMF rate, for gingivitis as measured by the PMA index, and for chronic endemic dental fluorosis according to Dean's modified classification. Dean's Index of Dental Fluorosis was utilized to evaluate the significance of fluorosis in a community. The subjects were examined with new sharp No. 5 explorers, new mouth mirrors, and Burton EENT spotlights. Compressed air was available. Bite-wing x-rays were not used.

PROFILER’S NOTE: Bite-wing x-rays were not used; however, the authors state that as long as the clinical inspection is done is the same manner by the same examiner, as they were in this survey, then the findings are reliably comparable.

PARAMETERS MONITORED:

Subjects were inspected for caries experience as measured by the DMF rate (decayed, filled, missing), for gingivitis as measured by the PMA index (papillary, marginal, attached), and for chronic endemic dental fluorosis according to Dean’s modified classification (normal, questionable, very mild, moderate, and severe). Dean’s Index of Dental Fluorosis was utilized to evaluate the significance of fluorosis in a community. The significance of the community fluorosis index is as follows:



Index Range	Classification	Remarks
0.0-0.4	Negative	Indexes of little or no public health concern as to the development of endemic dental fluorosis; highly important in dental caries control.
0.4-0.6	Borderline	
0.6-1.0	Slight	
1.0-2.0	Medium	Removal of excessive fluorides from the water is recommended.
2.0-3.0	Marked	
3.0-4.0	Very marked	

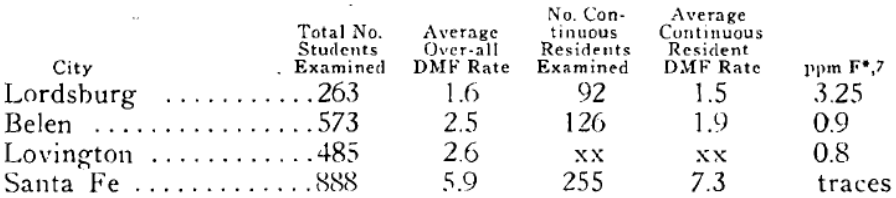
STATISTICAL METHODS:

Statistical methods were not reported.

RESULTS:

Caries

The following table was copied directly from Striffler (1955) and shows DMF rates for each community, broken down by total average and continuous resident average (xx indicates insufficient number of continuous residents to warrant inclusion). Santa Fe (traces of F) continuous residents had almost four times as much tooth decay as Belen (0.9 ppm F) continuous residents. Within Santa Fe, continuous residents had a DMF rate of 7.3, all Santa Fe subjects had a DMF rate of 5.9 regardless of water history, and all subjects who had been off Santa Fe water for ≥90 days had a DMF rate of 5.3. Thus, dentally speaking, it was a handicap to have been born and reared on Santa Fe’s F-deficient water and an advantage to have been away from Santa Fe, even for as little as 90 days of more.



City	Total No. Students Examined	Average Over-all DMF Rate	No. Continuous Residents Examined	Average Continuous Resident DMF Rate	ppm F*,7
Lordsburg	263	1.6	92	1.5	3.25
Belen	573	2.5	126	1.9	0.9
Lovington	485	2.6	xx	xx	0.8
Santa Fe	888	5.9	255	7.3	traces

Figure 2 was copied directly from Striffler (1955) shows the average number of decayed, missing, and filled teeth per continuous resident by age in the four communities.

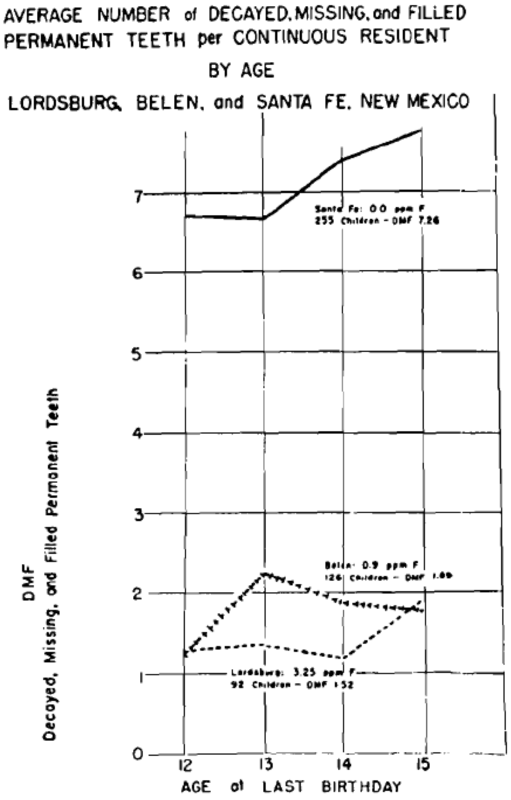
<table>
<tr><td></td><td>

Fig. 2</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Fluorosis</td><td>DMF rates were related to fluorosis classification to determine if there is point at which tooth decay increases with the degree of fluorosis. DMF rates dropped sharply as slight evidence of fluorosis were detected, but as the fluorosis became moderate and severe the DMF rates started to climb back up, but never to the peak achieved where no fluorosis was present.

No continuous residents of Belen (0.9 ppm F) were found with cosmetically objectionable fluorosis. Of 159 continuous residents, 56 had very mild fluorosis, 32 were questionable and 71 normal. The community index of dental fluorosis was 0.62. The public health significance of this index is considered borderline to slight (see “Parameters Monitored” section for significance of index). The following summary was copied directly from Striffler (1955).
<table>
<tr><th>Classification</th><th>Weight (w)</th><th>Frequency (f)</th><th>fxw</th></tr>
<tr><td>Normal</td><td>0.0</td><td>71</td><td>0</td></tr>
<tr><td>Questionable</td><td>0.5</td><td>32</td><td>16</td></tr>
<tr><td>Very Mild</td><td>1.0</td><td>30</td><td>30</td></tr>
<tr><td>Mild</td><td>2.0</td><td>26</td><td>52</td></tr>
<tr><td>Moderate</td><td>3.0</td><td>0</td><td>0</td></tr>
<tr><td>Severe</td><td>4.0</td><td>0</td><td>0</td></tr>
<tr><td></td><td></td><td>N=159</td><td>≤ (fw) =98</td></tr>
</table>
$$\text{Index} = \frac{\leq (fw)}{N} = \frac{98}{159} = 0.62$$</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Gingivitis</td><td>No association could be made between prevalence of gingivitis and fluoride content of the water supply. Subjects in Lordsburg with 3.25 ppm F in the drinking water had no more gingivitis than those in Santa Fe with only traces of F in the drinking water.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>Confounding factors</td><td>No significant differences in socio-ecomonic level were found between any of the communities, based on percentage of families earning over $2,000 per year. An analysis of a food habits survey conducted jointly by the NM Department of Public Health and NM A&M College showed no appreciable differences in the consumption of milk, vegetables, proteins, or other essential nutrients. In only one respect was there a major difference. Santa Fe children consumed significantly less sweets than children in the other communities. In terms of dental care, Santa Fe residents had received</td></tr>
</table>

		the most dental attention (F of the DMF rate) and had access to more dentists and public dental clinics. No significant differences were founding national origin or racial types. All inspections were done with same type of mouth mirror, explorer, lights, and portable chairs and were done under similar conditions and the same examiner (with the exception of Lordsburg where two additional dentists helped examine, but with calibration beforehand). Based on these circumstances, fluoride content of the drinking water remains the one significant variable responsible for the extreme differences in amounts of tooth decay.
STUDY AUTHORS' CONCLUSIONS:		The usual amount of fluoride recommended in most parts of the United Sates, 1.0 ppm, is too much for the climate of most of NM; hence, 0.7 ppm is recommended as the optimum level for NM (New Mexico department of Public Health). The communities surveyed having adequate amounts of fluoride had as much as 70% less permanent tooth decay amongst their continuous residents sampled than did Santa Fe with only traces of fluoride. Other factors than fluoride such as socio-economic status, food habits, amount of dental care, availability of dental clinics, incomparability of inspections, and racial origins were ruled out as possible variables which might have influenced the extreme differences in decay experience amounts in the 2,290 children examined. No association could be made between fluoride in the drinking water and prevalence of gingivitis. The DMF index was related to fluorosis classification increasing from a low level with mild fluorosis to a higher level with severe fluorosis.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		None.
PROFILER'S REMARKS	***Initials/date SJG/ 10/18/07***	The study was well-conducted and had adequate study design. However, the study was very poorly designed for development of a dose response to fluoride as limited data was presented and no statistical analyses were conducted. Junior-high school age children residing in four communities with different fluoride levels in the drinking water were inspected for dental caries, fluorosis, and gingivitis. This age was adequate to assess effects on permanent teeth, particularly when considering drinking water history from birth until age 8 years old. Several variables were considered to support the role of fluoride on the differences in DMF rates and fluorosis. The only differences in variables found were in Santa Fe where children ate fewer sweets and had more access to dental care, factors that would be expected to decrease the risk of caries. Overall DMF rate decreased as community water fluoride level increased, from 5.9, 2.6, 2.5 and 1.6 in communities with traces of fluoride, 0.8, 0.9, and 3.25 ppm F, respectively. The same trend was seen in continuous residents where rates ranged from 7.3 to 1.5 in Santa Fe (traces) and Lordsburg (3.25 ppm F), indicating that children are protected from dental caries as fluoride levels increase. No association could be made between fluorides in the drinking water and prevalence of gingivitis. Although DMF rates were related to fluorosis classification, with the authors claiming decreased DMF rates as slight evidence of fluorosis was detected and increased DMF rates as fluorosis became more severe, no data was presented to support this finding. The only data presented for fluorosis was the community index from one community (Belen, 0.9 ppm F, annual mean temperature 56.6°F), 0.62, indicating that 0.9 ppm F may be borderline too excessive for optimal dental health (i.e., preventing caries while not contributing to fluorosis. This is in line with the recommendation by the New Mexico Department of Health that 0.7 ppm F be considered optimal for most of the NM climate.
PROFILER'S ESTIM. NOEL/NOAEL		Study design was not suitable for development of a NOAEL.
PROFILER'S ESTIM. LOEL/ LOAEL		Study design was suitable for development of a LOAEL for dental caries and fluorosis. Exposure to **≥0.8 ppm F** in the drinking water appeared to offer protective benefits with respect to **dental caries** while **0.9 ppm F** resulted in a community fluorosis index of 0.62, slightly above the index range

	where removal of excessive fluorides from the water is recommended due to **questionable to very mild fluorosis**.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:	Not suitable (), Poor (X), Medium (), Strong () While the study was well-conducted, the study design was poorly conducive to provide data for a dose-response. The study indicated protective effects of fluoride in the drinking water above trace levels (**≥0.8 ppm F**) with respect to dental caries and questionable to very mild fluorosis at **0.9 ppm F** in only one community (no data for the other communities). Similar fluorosis data for the other communities with various water fluoride levels were not presented, so it is unclear whether a lower effect level or a dose-response effect would be found.
CRITICAL EFFECT(S):	Caries, fluorosis

Susheela, A.K. and M. Bhatnagar. 2002. Reversal of fluoride induced cell injury through elimination of fluoride and consumption of diet rich in essential nutrients and antioxidants. Molec. Cell Biochem. 234/235: 335-340.

ENDPOINT STUDIED:	Dental and skeletal fluorosis; fluoride in serum, urine, and drinking water, and health symptoms of people with fluorosis.
TYPE OF STUDY:	Prospective cohort
POPULATION STUDIED:	India/New Delhi and neighboring states: 10 people (6 males, 4 females, aged 8-60) with clinical manifestations of fluorosis, who lived in rural areas.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	Unknown
EXPOSURE GROUPS:	10 people who were exposed to excessively high levels of fluoride in their drinking water and/or in their food, which resulted in their clinical diagnosis of fluorosis.
EXPOSURE ASSESSMENT:	Fluoride levels in the blood, urine, and drinking water were measured using an ion selective electrode. Exposure prior to the study initiation was not quantified, but was confirmed by establishing that the subjects' drinking water had high fluoride levels, and by evaluating tooth discoloration in children of the family, joint stiffness, and finding a family history of gastrointestinal (GI) complaints that would disappear 10-15 days after switching to safe low-fluoride water. During the one-year intervention program, the subject's clinical symptoms and the fluoride levels in the drinking water, blood, and urine were monitored and reported at 1-3 unspecified time points (impact assessments). The only information provided regarding other possible sources of fluoride exposure was that three of the patients (who had relatively low fluoride in their drinking water) ingested food contaminated with fluoride.
ANALYTICAL METHODS:	Fluoride levels in the serum, urine, and drinking water were measured using ion selective electrode technology.
STUDY DESIGN:	Ten subjects with clinical manifestations of fluorosis were referred to the study investigators by clinicians from hospitals in New Delhi, India, and from neighboring states. The clinical diagnosis of fluorosis was made in hospitals on the basis of the people's case histories, clinical complaints, forearm X-rays, and by testing fluoride levels in their blood, urine, and drinking water. In rural areas without diagnostic facilities, fluorosis was diagnosed after first determining that the drinking water had high fluoride levels. Then the following were evaluated: tooth discoloration of children in the family, joint stiffness by three physical tests in the subject (ability to bend over and touch the toes without bending the knees; to touch the chest with the chin; and to touch the back of the head with the hands), and a family history of GI complaints, which would disappear 10-15 days after switching to safe water. Once fluorosis was confirmed, the subjects participated in an intervention protocol, which consisted of drinking safe defluoridated water from village sources or home filtration with activated alumina, and nutritional counseling to avoid high-fluoride foods and to consume adequate vitamins C, E, and other antioxidants. Subjects were monitored for up to a year afterwards at three unspecified intervals (i.e., impact assessments), at which time their serum, urine, and health status were assessed. Evaluated health manifestations included GI complaints, muscular weakness, polyurea, polydypsea, and pain and rigidity in the joints). A single value was provided for the water fluoride concentration during

intervention, with no description of how/when the value was obtained.

PARAMETERS MONITORED:

Subjects were monitored for levels of fluoride in serum, urine, and drinking water, and health symptoms on 1-3 occasions for up to a year after the beginning of fluoride intervention.

STATISTICAL METHODS:

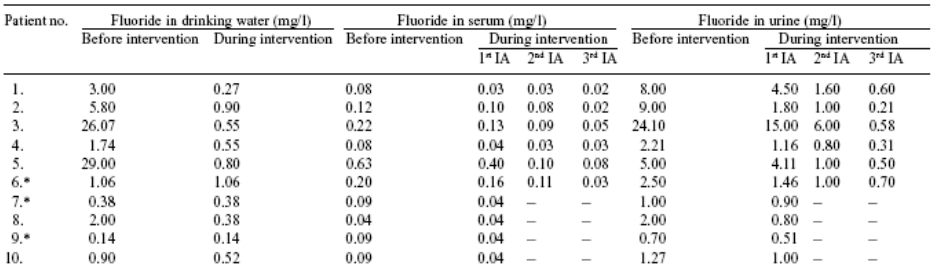
No statistical analysis was conducted.

RESULTS:

Fluoride levels in the drinking water, serum, and urine of fluorosis patients

In all subjects, serum and urine fluoride levels progressively decreased over the course of the one-year intervention period, as shown in Table 1. For 2/10 of the subjects (1 and 2), serum fluoride was reduced to levels considered normal (0.02 mg/L). Urinary fluoride levels were still above those considered normal (0.1 mg/L) for all subjects by the third (last) impact assessment. Water fluoride concentration during the intervention period was significantly lower than prior to intervention for 7 of the 10 subjects, and was unchanged for the remaining three subjects, who ate food contaminated with fluoride.

Table 1. Fluoride level in patients with Fluorosis before and during intervention



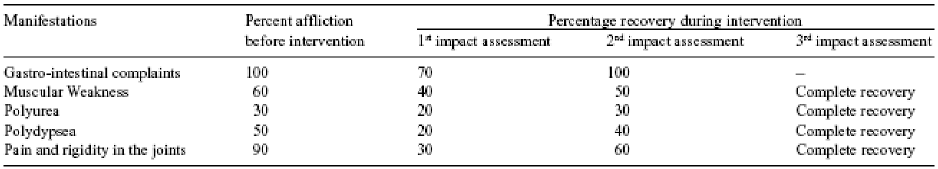
Patient no.	Fluoride in drinking water (mg/l)		Fluoride in serum (mg/l)				Fluoride in urine (mg/l)			
	Before intervention	During intervention	Before intervention	During intervention			Before intervention	During intervention		
				1st IA	2nd IA	3rd IA		1st IA	2nd IA	3rd IA
1.	3.00	0.27	0.08	0.03	0.03	0.02	8.00	4.50	1.60	0.60
2.	5.80	0.90	0.12	0.10	0.08	0.02	9.00	1.80	1.00	0.21
3.	26.07	0.55	0.22	0.13	0.09	0.05	24.10	15.00	6.00	0.58
4.	1.74	0.55	0.08	0.04	0.03	0.03	2.21	1.16	0.80	0.31
5.	29.00	0.80	0.63	0.40	0.10	0.08	5.00	4.11	1.00	0.50
6.*	1.06	1.06	0.20	0.16	0.11	0.03	2.50	1.46	1.00	0.70
7.*	0.38	0.38	0.09	0.04	–	–	1.00	0.90	–	–
8.	2.00	0.38	0.04	0.04	–	–	2.00	0.80	–	–
9.*	0.14	0.14	0.09	0.04	–	–	0.70	0.51	–	–
10.	0.90	0.52	0.09	0.04	–	–	1.27	1.00	–	–

Permissible limit of fluoride in drinking water: 1.0 mg / L or less. Normal upper limit of fluoride in serum: 0.02mg/L [53]. Normal upper limit of fluoride in urine: 0.1 mg/L [53]. IA – Impact assessment. *Food contaminated with fluoride.

Health symptoms of fluorosis patients

All 10 patients had complete recovery of their health symptoms by the end of the third impact assessment, as shown in Table 2. Recovery was the quickest for GI complaints, with 70% of the participants reporting a recovery at the first impact assessment. Symptoms were ameliorated more quickly in subjects who drank low-fluoride water and had nutritional supplements, as compared to those who only drank the low-fluoride water.

Table 2. Health improvements: expressed by the patients (n = 10)



Manifestations	Percent affliction before intervention	Percentage recovery during intervention		
		1st impact assessment	2nd impact assessment	3rd impact assessment
Gastro-intestinal complaints	100	70	100	–
Muscular Weakness	60	40	50	Complete recovery
Polyurea	30	20	30	Complete recovery
Polydypsea	50	20	40	Complete recovery
Pain and rigidity in the joints	90	30	60	Complete recovery

STUDY AUTHORS' CONCLUSIONS:

Susheela and Bhatnagar (2002) concluded that fluorosis can be reversed. Removing fluoride sources and a diet containing essential nutrients and antioxidants can significantly improve health (i.e. reduce fluoride toxicity) and reduce fluoride in the urine and serum of fluorosis patients. This was shown in 10 patients who had complete recovery of a variety of clinical symptoms and lower urine and serum fluorine after reducing their intake of fluoride in the drinking water.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

PROFILER'S REMARKS	***Initials/date SM/1/10/07***	The study unambiguously showed that reducing water fluoride intake led to decreased fluoride levels in the serum and urine of fluorosis patients, as well as recovery from a number of health symptoms that appeared to be fluorosis-induced.

		The data may be useful for estimating the levels of serum fluoride associated with adverse health effects. Insufficient data were provided, however, for a quantitative dose-response assessment of water fluoride levels and fluorosis in the subjects, or of the decrease of urinary and serum fluoride with time. For example, there were no quantitative estimates of the cumulative fluoride intake of the 10 subjects, and the time at which the serum and urine were collected were not provided. Also, the study had no reference control group.
PROFILER'S ESTIM. NOEL/NOAEL		Cannot be determined from this study.
PROFILER'S ESTIM. LOEL/ LOAEL		Cannot be determined from this study.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (x), Poor ( ), Medium ( ), Strong ( ) Data were insufficient for a quantitative dose-response assessment of water fluoride levels and fluorosis, or for the decrease of urinary and serum fluoride with time. No reference control group was provided.
CRITICAL EFFECT(S):		Increased serum and urinary fluoride levels, associated with adverse health symptoms (GI complaints, muscular weakness, polyurea, polydypsea, and pain and rigidity in the joints).

Szpunar, S.M. and B.A. Burt. 1988. Dental caries, fluorosis, and fluoride exposure in Michigan schoolchildren. J Dent Res 67(5):802-806.

ENDPOINT STUDIED: Dental caries and fluorosis (permanent teeth)

TYPE OF STUDY: Case sectional survey

POPULATION STUDIED: U.S./Michigan: Study participation was sought from children aged 6-12 years who were continuous residents of four Michigan communities with varying levels of fluoride in the drinking water. Of the 1103 children who returned a questionnaire, 556 were continuous residents of the following communities and qualified for study participation: Cadillac (n=131), Hudson (n=133), Redford (249) and Richmond (n=43). Table 1 is included below as copied directly from Szpunar and Burt, 1988.

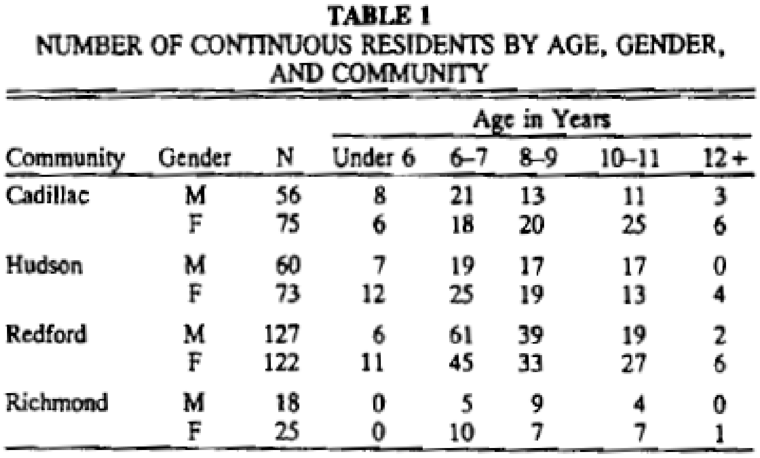


TABLE 1
NUMBER OF CONTINUOUS RESIDENTS BY AGE, GENDER, AND COMMUNITY

			Age in Years				
Community	Gender	N	Under 6	6–7	8–9	10–11	12+
Cadillac	M	56	8	21	13	11	3
	F	75	6	18	20	25	6
Hudson	M	60	7	19	17	17	0
	F	73	12	25	19	13	4
Redford	M	127	6	61	39	19	2
	F	122	11	45	33	27	6
Richmond	M	18	0	5	9	4	0
	F	25	0	10	7	7	1

CONTROL POPULATION: None.

EXPOSURE PERIOD: Children were lifelong residents of the communities so their exposure period was birth to 6-12 years old. The date when the study took place was not provided.

EXPOSURE GROUPS: Children aged 6-12 years were exposed to drinking water with one of four fluoride levels: Cadillac (0.0 ppm), Hudson (0.8 ppm), Redford (1.0 ppm) or Richmond (1.2 ppm).

EXPOSURE ASSESSMENT Only fluoride concentration in water was evaluated. Average water fluoride concentrations were obtained from the Michigan Department of Public Health's listings of the fluoridation status of communities served by public water supplies for the past 20 years. The levels for the Cadillac, Hudson, Redford and Richmond communities were 0.0, 0.8, 1.0 and 1.2 ppm, respectively.

ANALYTICAL METHODS: Not provided.

STUDY DESIGN The objective of the study was to investigate the prevalence of dental caries and fluorosis in the permanent teeth of Michigan schoolchildren, residing in four different communities, to the various concentrations of fluoride in the water supplies. Questionnaires on demographic information, residence history, details of fluoride exposure and use of dental services and infant nutrition were completed by parents. A total of 556 children who were continuous residents were examined for dental caries by means of the DMFS (decayed, missing or filled surfaces) index applied with the criteria of the National Institute of Dental Research (NIDR). Following the caries examination, the Tooth Surface Index of Fluorosis (TSIF; see

NRC, 2006, page 90) was used to measure the prevalence and severity of dental fluorosis. Russell's criteria for differential diagnosis of fluorosis were also employed. (Russell, 1961).

Equipment used in the screening included a portable dental chair, Rolux fiber-optic light, mouth mirrors and no. 23 explorers. One examiner conducted all the examinations. A reproducibility test was conducted on 24 randomly selected subjects to test for intra-examiner reliability.

PARAMETERS MONITORED:

The permanent teeth of children were examined for dental caries by means of the DMFS index applied with the criteria of the NIDR. Following the caries examination, the TSIF was used to measure the prevalence and severity of dental fluorosis. Russell's criteria for differential diagnosis of fluorosis were also employed.

PROFILER'S NOTE: The TSIF values are described in Section 2.

STATISTICAL METHODS:

All statistical analyses were carried out by means of the Michigan Interactive Data Analysis System. The analysis of variance (ANOVA) was used to test differences in mean DMFS values among different age groups, by area of residence, and by use of fluoride sources and dental services. Multiple pair-wise comparisons were performed when indicated by ANOVA results. Categorical methods were used to determine a list of variables that were consistently associated with caries or fluorosis. Then, these variables, along with the age and education variables, were used as the independent predictors in logistic regression analysis. The intra-examiner reliability was tested on 24 randomly-selected children. The percentage agreement between DMFS scores from the first and second examinations was calculated and Pearson product-moment correlations were computed for the first and second examination results for both caries and fluorosis. The kappa statistic was used to quantify agreement in scoring the presence or absence of fluorosis between the two examinations. The agreement between the two examinations for DMFS scores was 96%. The Pearson product-moment correlation between DMFS scores from the first and second examinations was 0.92 ($p<0.01$). The agreement between first and second examinations for fluorosis (presence/absence) was 92%. For these data, the kappa value was 0.85, suggesting a high degree of consistency. The Pearson product-moment correlation for the sum of permanent surfaces scored as free from fluorosis was 0.94 (<0.01).

RESULTS:

Study results in Tables 2-5 are shown directly from Szpunar and Burt, 1988.

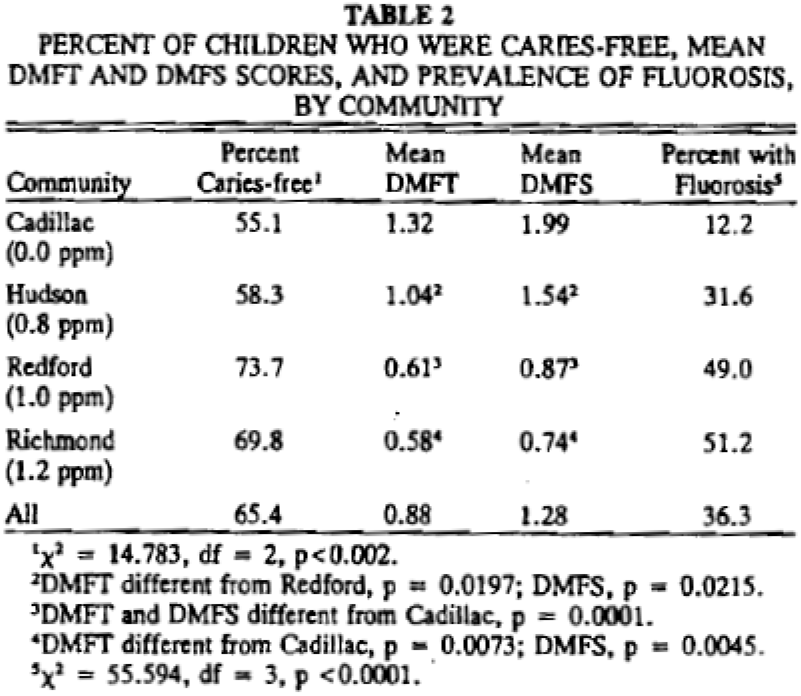


TABLE 2

PERCENT OF CHILDREN WHO WERE CARIES-FREE, MEAN DMFT AND DMFS SCORES, AND PREVALENCE OF FLUOROSIS, BY COMMUNITY

Community	Percent Caries-free[1]	Mean DMFT	Mean DMFS	Percent with Fluorosis[5]
Cadillac (0.0 ppm)	55.1	1.32	1.99	12.2
Hudson (0.8 ppm)	58.3	1.04[2]	1.54[2]	31.6
Redford (1.0 ppm)	73.7	0.61[3]	0.87[3]	49.0
Richmond (1.2 ppm)	69.8	0.58[4]	0.74[4]	51.2
All	65.4	0.88	1.28	36.3

[1] $\chi^2 = 14.783$, df = 2, $p<0.002$.

[2] DMFT different from Redford, p = 0.0197; DMFS, p = 0.0215.

[3] DMFT and DMFS different from Cadillac, p = 0.0001.

[4] DMFT different from Cadillac, p = 0.0073; DMFS, p = 0.0045.

[5] $\chi^2 = 55.594$, df = 3, $p < 0.0001$.

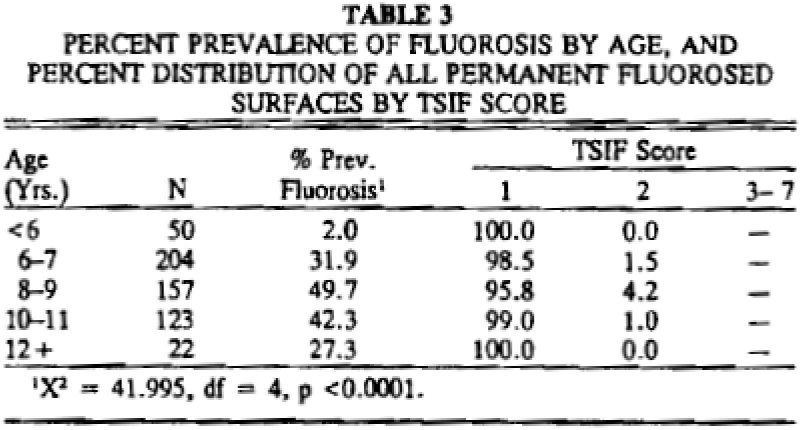


TABLE 3
PERCENT PREVALENCE OF FLUOROSIS BY AGE, AND PERCENT DISTRIBUTION OF ALL PERMANENT FLUOROSED SURFACES BY TSIF SCORE

Age (Yrs.)	N	% Prev. Fluorosis[1]	TSIF Score 1	2	3–7
<6	50	2.0	100.0	0.0	–
6–7	204	31.9	98.5	1.5	–
8–9	157	49.7	95.8	4.2	–
10–11	123	42.3	99.0	1.0	–
12+	22	27.3	100.0	0.0	–

[1] $X^2 = 41.995$, df = 4, p <0.0001.

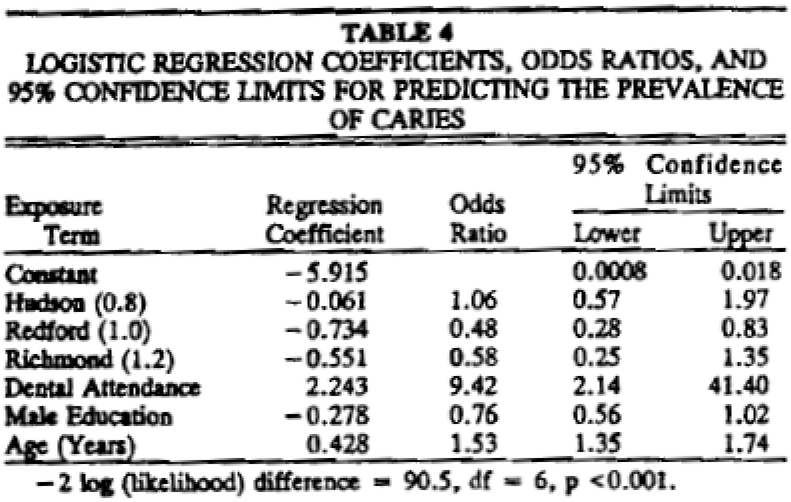


TABLE 4
LOGISTIC REGRESSION COEFFICIENTS, ODDS RATIOS, AND 95% CONFIDENCE LIMITS FOR PREDICTING THE PREVALENCE OF CARIES

Exposure Term	Regression Coefficient	Odds Ratio	95% Confidence Limits Lower	Upper
Constant	−5.915		0.0008	0.018
Hudson (0.8)	−0.061	1.06	0.57	1.97
Redford (1.0)	−0.734	0.48	0.28	0.83
Richmond (1.2)	−0.551	0.58	0.25	1.35
Dental Attendance	2.243	9.42	2.14	41.40
Male Education	−0.278	0.76	0.56	1.02
Age (Years)	0.428	1.53	1.35	1.74

−2 log (likelihood) difference = 90.5, df = 6, p <0.001.

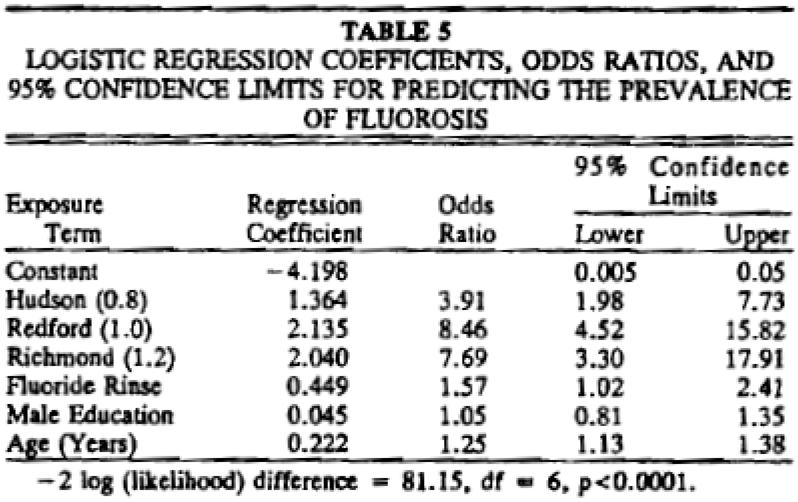


TABLE 5
LOGISTIC REGRESSION COEFFICIENTS, ODDS RATIOS, AND 95% CONFIDENCE LIMITS FOR PREDICTING THE PREVALENCE OF FLUOROSIS

Exposure Term	Regression Coefficient	Odds Ratio	95% Confidence Limits Lower	Upper
Constant	−4.198		0.005	0.05
Hudson (0.8)	1.364	3.91	1.98	7.73
Redford (1.0)	2.135	8.46	4.52	15.82
Richmond (1.2)	2.040	7.69	3.30	17.91
Fluoride Rinse	0.449	1.57	1.02	2.41
Male Education	0.045	1.05	0.81	1.35
Age (Years)	0.222	1.25	1.13	1.38

−2 log (likelihood) difference = 81.15, df = 6, p<0.0001.

STUDY AUTHORS' CONCLUSIONS:	The study authors concluded that the prevalence of both caries and fluorosis was significantly associated with the fluoride concentration in the community water supply.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT	Russell, A.I. 1961. The differential diagnosis of fluoride and non-fluoride enamel opacities. J Public Health Dent 21:143-146.

FOUND IN NRC (2006)		
PROFILER'S REMARKS	***Initials/Date*** VAD/03-10-07	Although demographic information was collected, it was not provided in the study report. Therefore, no determination can be made about whether the study population was representative of the U.S. general population. Comparison of the questionnaire responses from children who were examined and children who were not examined (but returned questionnaires) showed significant differences in some characteristics of dental attendance and oral hygiene practices, suggesting that non-participants received more frequent dental care and practiced better oral hygiene. Various sections of the study report indicate that study participants were 6-12 years of age. However, in Table 1, which included the number of continuous residents by age, gender and community of residence, there were categories for "under 6" and "12+" years. In addition, the number of participants in each group and number in each age range of exposure level varied widely. The fluoride concentration in the drinking water for Redford was given as "1.0 ppm adjusted" under the Material and Methods section but no explanation on the type of adjustment was provided. Only mild fluorosis was reported so results are restricted to this level of the effect. The technical reviewer agrees that the study is a poor model for dose response modelling because all of the groups (even exposed to water with 0.0 ppm fluoride) experienced fluorosis, but it does demonstrate the trend of decreasing incidence of caries and increasing incidence of fluorosis as the fluoride levels increase. The study also suggests other sources of fluoride must be used in this group of children.
PROFILER's ESTIM. NOAEL		The study design did not identify a no-flurosis intake dose. Mild fluorosis of the permanent teeth was observed in 12.2% of children in the Cadillac community where the fluoride level in the drinking water was reported as 0.0 ppm.
PROFILER'S ESTIM. LOAEL		The study design did not identify a LOAEL.
SUITABILITY FOR DOSE RESPONSE MODELING		Not suitable,(_); Poor (X_); Medium (); Strong (_)
CRITICAL EFFECTS:		Dental fluorosis and caries (permanent teeth)

Thaper et al. 1989. Prevalence and Severity of Dental Fluorosis in Primary and Permanent Teeth at Varying Fluoride Levels. J. Indian Soc. Prev. Dent. pp.38-42

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Cross-sectional study of fluorosis in primary and permanent teeth and fluoride levels in drinking water
POPULATION STUDIED:	India/State of Rajasthan, 792 children (sex not specified), 6, 8, or 10 yrs old from 16 rural areas. The dental hygiene habits of the children and the socio-economic status of the parents were not evaluated. The average annual maximum temperature of the area was not reported.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	From birth to 6, 8 or 10 yr old. It was not stated when the individual examinations were conducted.
EXPOSURE GROUPS:	Exposure groups were 1.04 ppm fluoride (mean value for 4 rural areas), 2.4 ppm (mean value for 5 areas), 3.91 ppm (mean value for 4 areas), and 6.0 ppm (mean value for two areas). The sources of the drinking water were open or tube wells.
EXPOSURE ASSESSMENT:	Drinking water was the only exposure route evaluated
ANALYTICAL METHODS:	Orion ion-specific electrode was used to analyze for the fluoride content in the drinking water
STUDY DESIGN	The prevalence and severity of dental fluorosis in both primary and permanent teeth was studied in Indian children, ages 6, 8, and 10 years old. The children were examined for dental fluorosis using Dean's Index of Fluorosis (see Section 2). 10% of the children examined each day were re-examined. The prevalence of dental fluorosis in the primary and permanent teeth were calculated and correlated with the levels of fluoride in the drinking water (four exposure groups were used).
PARAMETERS MONITORED:	Dean's Index was used to evaluate the grade of dental fluorosis.
STATISTICAL METHODS:	Not stated
RESULTS:	
Dental fluorosis	See Table 2 for the prevalence of dental fluorosis in primary and permanent teeth at varying fluoride levels, Table 3 for the severity of dental fluorosis in primary teeth at varying fluoride levels, and Table 4 for the severity of dental fluorosis in permanent teeth at varying fluoride levels.

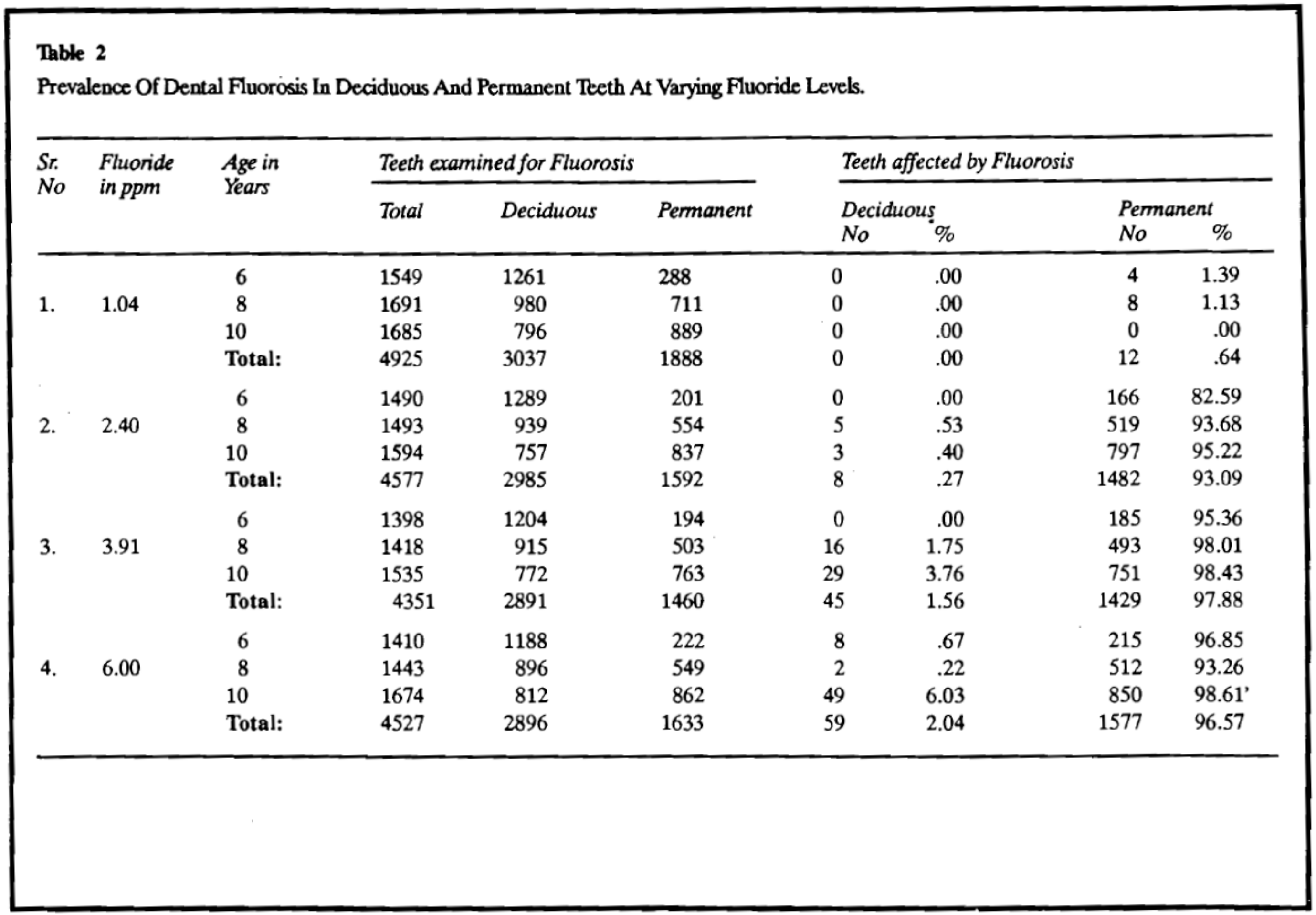


Table 2

Prevalence Of Dental Fluorosis In Deciduous And Permanent Teeth At Varying Fluoride Levels.

Sr. No	*Fluoride in ppm*	*Age in Years*	*Teeth examined for Fluorosis*			*Teeth affected by Fluorosis*			
			Total	*Deciduous*	*Permanent*	*Deciduous*		*Permanent*	
						No	*%*	*No*	*%*
1.	1.04	6	1549	1261	288	0	.00	4	1.39
		8	1691	980	711	0	.00	8	1.13
		10	1685	796	889	0	.00	0	.00
		Total:	4925	3037	1888	0	.00	12	.64
2.	2.40	6	1490	1289	201	0	.00	166	82.59
		8	1493	939	554	5	.53	519	93.68
		10	1594	757	837	3	.40	797	95.22
		Total:	4577	2985	1592	8	.27	1482	93.09
3.	3.91	6	1398	1204	194	0	.00	185	95.36
		8	1418	915	503	16	1.75	493	98.01
		10	1535	772	763	29	3.76	751	98.43
		Total:	4351	2891	1460	45	1.56	1429	97.88
4.	6.00	6	1410	1188	222	8	.67	215	96.85
		8	1443	896	549	2	.22	512	93.26
		10	1674	812	862	49	6.03	850	98.61’
		Total:	4527	2896	1633	59	2.04	1577	96.57

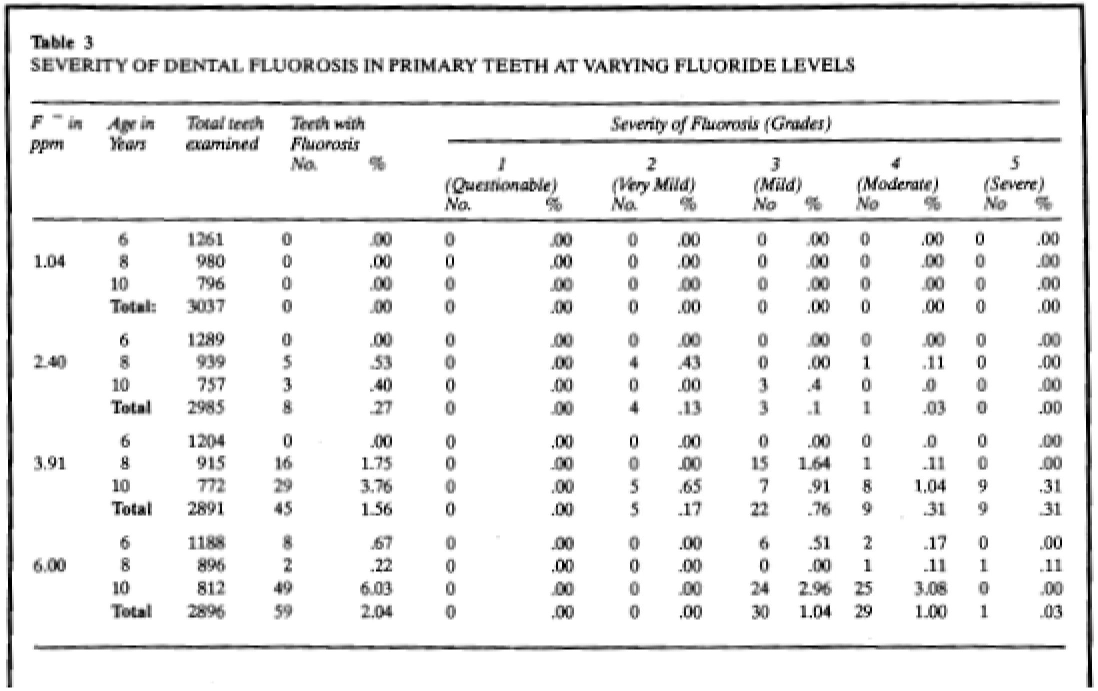


Table 3

SEVERITY OF DENTAL FLUOROSIS IN PRIMARY TEETH AT VARYING FLUORIDE LEVELS

F⁻ in ppm	*Age in Years*	*Total teeth examined*	*Teeth with Fluorosis*		*Severity of Fluorosis (Grades)*									
					1 (Questionable)		*2 (Very Mild)*		*3 (Mild)*		*4 (Moderate)*		*5 (Severe)*	
			No.	*%*	*No.*	*%*	*No.*	*%*	*No*	*%*	*No*	*%*	*No*	*%*
1.04	6	1261	0	.00	0	.00	0	.00	0	.00	0	.00	0	.00
	8	980	0	.00	0	.00	0	.00	0	.00	0	.00	0	.00
	10	796	0	.00	0	.00	0	.00	0	.00	0	.00	0	.00
	Total:	3037	0	.00	0	.00	0	.00	0	.00	0	.00	0	.00
2.40	6	1289	0	.00	0	.00	0	.00	0	.00	0	.00	0	.00
	8	939	5	.53	0	.00	4	.43	0	.00	1	.11	0	.00
	10	757	3	.40	0	.00	0	.00	3	.4	0	.0	0	.00
	Total	2985	8	.27	0	.00	4	.13	3	.1	1	.03	0	.00
3.91	6	1204	0	.00	0	.00	0	.00	0	.00	0	.0	0	.00
	8	915	16	1.75	0	.00	0	.00	15	1.64	1	.11	0	.00
	10	772	29	3.76	0	.00	5	.65	7	.91	8	1,04	9	.31
	Total	2891	45	1.56	0	.00	5	.17	22	.76	9	.31	9	.31
6.00	6	1188	8	.67	0	.00	0	.00	6	.51	2	.17	0	.00
	8	896	2	.22	0	.00	0	.00	0	.00	1	.11	1	.11
	10	812	49	6.03	0	.00	0	.00	24	2.96	25	3.08	0	.00
	Total	2896	59	2.04	0	.00	0	.00	30	1.04	29	1.00	1	.03

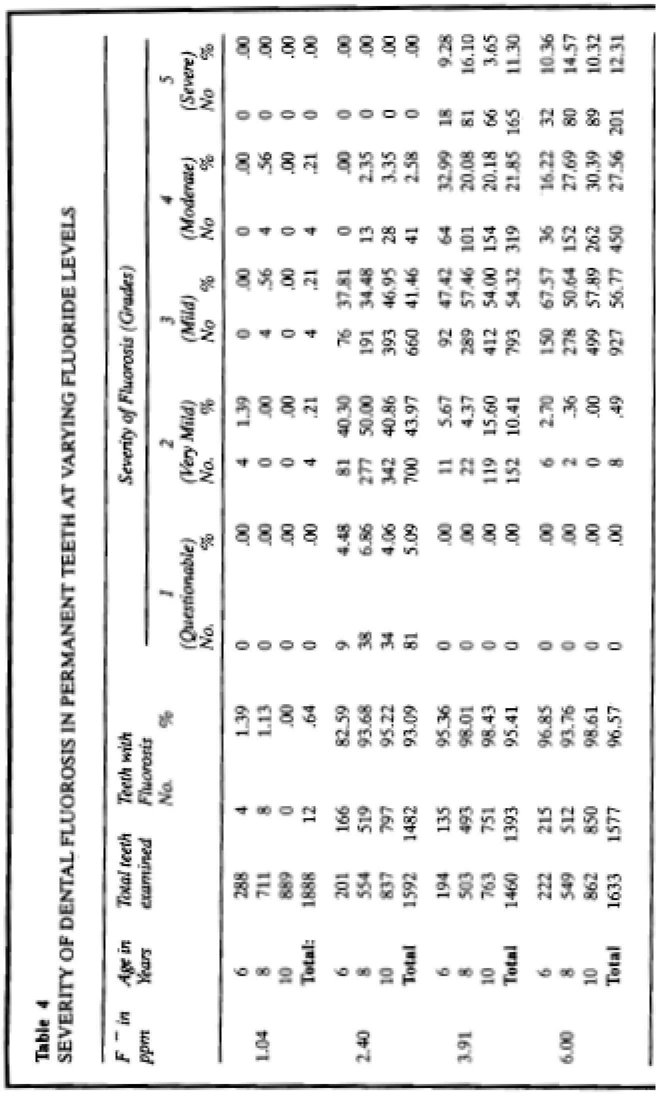


Table 4

SEVERITY OF DENTAL FLUOROSIS IN PERMANENT TEETH AT VARYING FLUORIDE LEVELS

F^- in ppm	Age in Years	Total teeth examined	Teeth with Fluorosis		Severity of Fluorosis (Grades)									
					1 (Questionable)		2 (Very Mild)		3 (Mild)		4 (Moderate)		5 (Severe)	
			No.	%	No.	%	No.	%	No	%	No	%	No	%
1.04	6	288	4	1.39	0	.00	4	1.39	0	.00	0	.00	0	.00
	8	711	8	1.13	0	.00	0	.00	4	.56	4	.56	0	.00
	10	889	0	.00	0	.00	0	.00	0	.00	0	.00	0	.00
	Total:	1888	12	.64	0	.00	4	.21	4	.21	4	.21	0	.00
2.40	6	201	166	82.59	9	4.48	81	40.30	76	37.81	0	.00	0	.00
	8	554	519	93.68	38	6.86	277	50.00	191	34.48	13	2.35	0	.00
	10	837	797	95.22	34	4.06	342	40.86	393	46.95	28	3.35	0	.00
	Total	1592	1482	93.09	81	5.09	700	43.97	660	41.46	41	2.58	0	.00
3.91	6	194	135	95.36	0	.00	11	5.67	92	47.42	64	32.99	18	9.28
	8	503	493	98.01	0	.00	22	4.37	289	57.46	101	20.08	81	16.10
	10	763	751	98.43	0	.00	119	15.60	412	54.00	154	20.18	66	3.65
	Total	1460	1393	95.41	0	.00	152	10.41	793	54.32	319	21.85	165	11.30
6.00	6	222	215	96.85	0	.00	6	2.70	150	67.57	36	16.22	32	10.36
	8	549	512	93.76	0	.00	2	.36	278	50.64	152	27.69	80	14.57
	10	862	850	98.61	0	.00	0	.00	499	57.89	262	30.39	89	10.32
	Total	1633	1577	96.57	0	.00	8	.49	927	56.77	450	27.56	201	12.31

STUDY AUTHORS' CONCLUSIONS:		The prevalence of dental fluorosis in primary teeth was lower as compared to permanent teeth at all ages and at all fluoride levels. The prevalence of dental fluorosis in both primary and permanent teeth increased with every increase of fluoride level in drinking water. At 2.4 ppm, the percentage of permanent teeth having objectionable fluorosis was very low compared to at 3.91 and 6.0 ppm.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		None
PROFILER'S REMARKS	***Initials/date SBG 3/27/07***	This study was in India, so it would not be representative of the U.S. population. The two major deficiencies of the study were the lack of information on fluoride exposure

		from non-drinking water sources, and the lack of statistical analysis of the data. The higher occurrence of severe fluorosis in 8-yr-olds exposed to 3.91 ppm fluoride than in 6, 8 or 10-yr-olds exposed to 6.00 ppm, may reflect difference in exposure to non-drinking water fluoride. The percentage occurrence of fluorosis was based on the number of teeth showing the effect rather than the number of individuals; therefore the data may not be directly comparable with other studies.
PROFILER'S ESTIM. NOEL/NOAEL		Based on the data presented in Table 4, the NOAEL for severe dental fluorosis (in permanent teeth) (Dean's Index of 4) is 2.4 ppm
PROFILER'S ESTIM. LOEL/ LOAEL		Based on the data presented in Table 4, the LOAEL for severe dental fluorosis (in permanent teeth) (Dean's Index of 4) is 3.91 ppm.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor (_), Medium (X), Strong (_) Although a NOAEL and a LOAEL were identified, no statistical analyses were applied to the data, so this limits the study's suitability for dose-response modeling.
CRITICAL EFFECT(S):		Dental fluorosis

Villa, A.E., Guerrero, S., Icaza, G., Villalobos, J., Anabalón, M. 1998. Dental fluorosis in Chilean children: evaluation of risk factors. Community Dent Oral Epidemiol. 26: 310-315.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Case control study
POPULATION STUDIED:	Chile/San Felipe: Public and private school children, residing in San Felipe, Chile were categorized in two groups according to their age when artificial water fluoridation was introduced in 1986: Group I: born after1986 (n=68) and Group II: 16-24 months old in 1986 (n=38).
CONTROL POPULATION:	Public and private school children, residing in San Felipe, Chile: Group III: >24 months old in 1986 (n=30).
EXPOSURE PERIOD:	Clinical examinations were performed in July-August 1996, ten years after the addition of fluoride to the water supply (January 1986).
EXPOSURE GROUPS:	Children who volunteered for the study and attended one of the five schools selected at random were categorized into groups according to their age at the initiation of water fluoridation (1986). The mean fluoride water concentration for San Felipe was 0.93 mg/L (range 0.65 to 1.42 mg/L). The range of fluctuation around the mean value was ±12% in 87% of the samples.
EXPOSURE ASSESSMENT:	All children were clinically examined for dental fluorosis in all fully erupted permanent teeth. No radiographs were taken during the surveys.
ANALYTICAL METHODS:	The reported values come from daily samples of the waterworks facility serving San Felipe. Data on how fluoride concentrations in the water supply were measured were not reported. Other water quality parameter data were not included in the study report.
STUDY DESIGN	In the study, 136 permanent residents of the optimally fluoridated community of San Felipe, Chile were categorized into one of three groups according to their age when water fluoridation was introduced in 1986. Group I was born after 1986 (n=68); Group II was 16-24 months old in 1986 (n= 38); and Group III was >24 months old in 1986. The study population included children from two private and three public basic schools. Selection of the schools was made at random from all private schools whose pupils are considered to have high socio-economic status and from all public schools whose pupils are of low socio-economic status. Eligible subjects were permanent residents of San Felipe, answered the questionnaire, had no orthodontic attachments on central maxillary incisors, (CMI) restorations or un-erupted teeth, and were not diagnosed as 'questionable' (fluorosis score=0.5). The subjects were clinically examined for dental fluorosis in July-August 1996. Examinations: Enamel fluorosis was evaluated in all fully erupted permanent teeth according to Dean's index and Russell's criteria (Russell 1961) for differentiating fluoride and non-fluoride opacities. Teeth were not dried before inspection and were examined under tangential natural light. Each tooth was assigned an individual score to compare prevalence and severity of fluorosis in each group of teeth according to a slightly modified WHO form. Examinations were performed by one examiner; approximately 12% of children were re-examined 4 weeks later in a single-blind fashion to monitor diagnostic standards (kappa value= 0.87). Pre-tested questionnaires were developed for this study to collect information from parents concerning children's nursery school attendance, residence histories, and the frequency, extent, and duration of breast-feeding and tooth brushing practices. The interviewer and parents were blind to the child's fluorosis status. Subjects were defined

as ‘cases’ (score ≥1) or ‘non-cases’ (control; score=0) based on their fluorosis score in the central maxillary incisors (CMI).

PARAMETERS MONITORED:

Dental fluorosis was assessed and recorded according to Dean’s index. Russell’s (1961) criteria were used to differentiate fluoride and non-fluoride opacities. No radiographs were taken during the surveys.

STATISTICAL METHODS:

Data were analyzed using the SAS statistical package. Logistic regression analyses were used to develop a model of exposures associated with very mild to moderate enamel fluorosis. Odds ratios from the regression coefficient were used to estimate the relative risk for each factor, adjusting for confounding variables. Ninety-five percent confidence intervals were generated for all adjusted odds ratios. The independent variables were breastfeeding duration and age at the onset of community water fluoridation; other independent variables included sex, socio-economic status, nursery school attendance, age when tooth brushing started, and tea ingestion.

RESULTS:

Dental fluorosis

Table 1 was copied directly from Villa et al. (1998) and shows CMI enamel fluorosis status by age of subject when water fluoridation began. Groups I and II had a higher percentage of cases than Group III (5 and 3 times more cases, respectively).

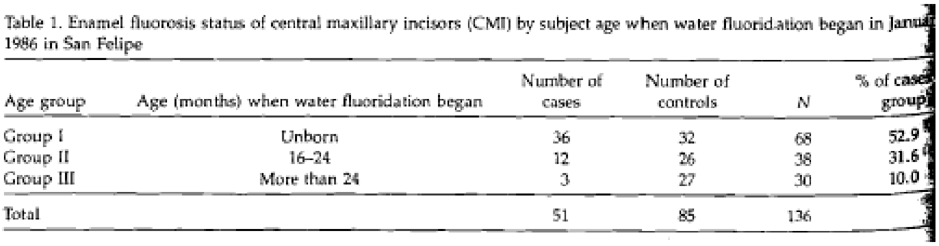


Table 1. Enamel fluorosis status of central maxillary incisors (CMI) by subject age when water fluoridation began in Janu
1986 in San Felipe

Age group	Age (months) when water fluoridation began	Number of cases	Number of controls	N	% of case group
Group I	Unborn	36	32	68	52.9
Group II	16–24	12	26	38	31.6
Group III	More than 24	3	27	30	10.0
Total		51	85	136	

Table 2 also was copied directly from Villa et al. (1998) and shows the adjusted odds ratios with 95% confidence intervals for CMI enamel fluorosis. Group I and II children presented a statistically significant increase (OR=20.44 and 4.15, respectively) in the odds of CMI fluorosis compared with Group III children.

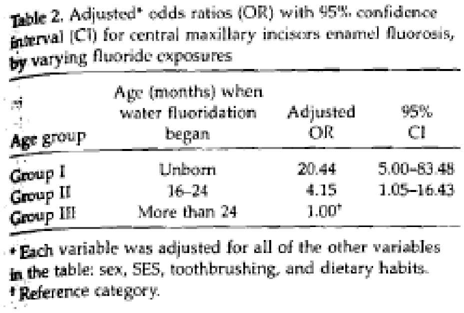


Table 2. Adjusted* odds ratios (OR) with 95% confidence interval (CI) for central maxillary incisors enamel fluorosis, by varying fluoride exposures

Age group	Age (months) when water fluoridation began	Adjusted OR	95% CI
Group I	Unborn	20.44	5.00–83.48
Group II	16–24	4.15	1.05–16.43
Group III	More than 24	1.00†	

* Each variable was adjusted for all of the other variables in the table: sex, SES, toothbrushing, and dietary habits.
† Reference category.

TECHNICAL REVIEWER’S NOTE: Table images inserted above are from best available copies.

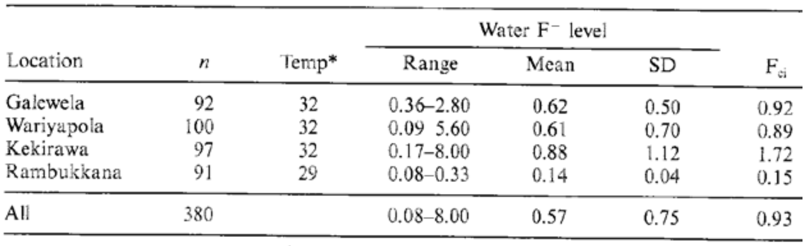
Exclusive breast-feeding was a statistically significant protective factor in the Group I children with a 14% significant decrease in the likelihood of CMI fluorosis (OR=0.86; CI: 0.75-0.98). An increase in the prevalence of enamel fluorosis in the posterior teeth (first molars excluded) of children in Groups II and III was non-significantly related to the amount of tea ingested and to an increased daily frequency of tooth brushing when subjects were pre-schoolers.

PROFILER’S NOTE: The profiler agrees that there was an increased percentage of cases of CMI enamel fluorosis in Groups I and II compared to Group III; however the degree of

		statistical significance should have been included. The profiler also agrees that the risk of developing fluorosis differed depending on the age of the subject when water fluoridation was implemented, and decreased with exclusive breast feeding (average breast-feeding duration of 5.5 months).
STUDY AUTHORS' CONCLUSIONS:		Very mild to moderate enamel fluorosis of permanent CMI was strongly associated both with the age of the subjects when water fluoridation began and with breast-feeding duration for children of Group I. Children born when the drinking water was already fluoridated (Group I) had a higher risk of CMI fluorosis (OR=20.44; 95% CI: 5.00-93.48) compared to those older than 24 months when fluoridation was implemented (Group III) while the group 16-24 months old when water fluoridation was initiated (Group II) had an intermediate increased risk of fluorosis (OR= 4.15; 95% CI: 1.05-16.43). An extended period of exclusive breast-feeding appears to be a protective factor for the Group I children (OR=0.86; 95% CI: 0.75-0.98) but not for the Group III children, who did not ingest fluoridated water during their first 24 months of life. Tea ingestion and the use of fluoridated dentifrice started at similar average ages (32-35 months old). Fluoride supplement use was almost negligible. No significant differences were observed between children with high or low socio-economic status, possibly because there were no differences in use of reconstituted powdered milk. The current results suggest that under Chilean conditions, the increased prevalence of CMI fluorosis may be associated with fluoridated water (0.9 mg/L, with range of 0.65 to 1.42 mg F/L) intake during the first 2 years of life.
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		CMI= central maxillary incisors Russell, A.L. (1961). The differential diagnosis of fluoride and non-fluoride enamel opacities. *Journal of Public Health Dentistry* **21**, 143-146. World Health Organization (1987). Oral Health Surveys: Basic Methods. 3rd ed. WHO, Geneva.
PROFILER'S REMARKS	***Initials/date: SJG/ 1/15/07***	The study was well-conducted and had adequate study design. However, the study was not designed for development of a dose response to fluoride as the emphasis was on establishing risk factors for fluorosis in children born before and after the addition of fluoride in the water supply (1986). Further, the sample size of this study population (n=68, 38, and 30 per group) seems relatively small. The risk of developing CMI enamel fluorosis increased in children exposed to fluoridated water from birth (OR=20.44) compared to those exposed after 24 months of age. However, it is important to note that this does not indicate a cause-effect relationship. The risks of dental fluorosis of teeth other than CMI and first molars that mineralize later in life, and which may be associated with tea ingestion and frequent tooth brushing with fluoridated toothpaste, could not be evaluated in the current study.
PROFILER'S ESTIM. NOEL/NOAEL		Study design was not suitable for development of a NOAEL for fluorosis.
PROFILER'S ESTIM. LOEL/ LOAEL		Study design was not suitable for development of a LOAEL for fluorosis.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor (_), Medium (_), Strong (_) While the study was well-conducted, the study design was not conducive to provide data for a dose-response; however, it does provide some information that will contribute to identifying the sensitive exposure window. The study indicated odds ratios for CMI dental fluorosis in children residing in San Felipe, Chile, dependent on age when water

	fluoridation was implemented. The study did not address any issues of dental caries, plaque or gingivitis.
CRITICAL EFFECT(S):	Prevalence of dental fluorosis in central maxillary incisors.

Warnakulasuriya, K.A.A.S., S. Balasuriya, P.A.J. Perera, and L.C. Peiris. 1992. Determining optimal levels of fluoride in drinking water for hot, dry climates – a case study in Sri Lanka. Commun. Dent. Oral Epidemiol. 20: 364-367.

<table>
<tr><td></td><td></td></tr>
<tr><td>ENDPOINT STUDIED:</td><td>Dental fluorosis, in conjunction with dental caries (DMFT: decayed, missing, and filled permanent teeth index)</td></tr>
<tr><td></td><td></td></tr>
<tr><td>TYPE OF STUDY:</td><td>Case control, retrospective</td></tr>
<tr><td></td><td></td></tr>
<tr><td>POPULATION STUDIED:</td><td>Asia/Sri Lanka: 380 children 14 years old (191 male, 189 female) who lived in rural districts of similar socioeconomic status in four geographic areas (Galewela, Wariyapola, Kekirawa, and Rambukkana). The areas had similar altitudes, with annual maximum temperature of 29-32°C.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>CONTROL POPULATION:</td><td>The reference (i.e., control) groups were: (1) 211 children (of the 380 total) exposed to <0.4 ppm in their drinking water, for evaluating caries status vs. water fluoride levels; (2) 200 children with Dean’s fluorosis index of 0 or 1, for evaluating the fluorosis index vs. water fluoride levels; and (3) 156 children with normal teeth (fluorosis index of 0), for evaluating the mean DMFT vs. the dental fluorosis index.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE PERIOD:</td><td>1972-1986; from birth to 14 years old</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE GROUPS:</td><td>Schoolchildren aged 14 (grades 8 and 9) who lived their entire life in the four selected geographic areas in Sri Lanka, and lived within 15 miles of their secondary school at the time of the dental examination.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>EXPOSURE ASSESSMENT:</td><td>Drinking water fluoride concentrations in 380 domestic samples provided by the children from the four geographic areas, and the community dental fluorosis index (F_{ci}) are shown in Table 1.
Table 1. Distribution of water fluoride level (ppm) in four areas

<table>
<tr><th></th><th></th><th></th><th colspan="3">Water F⁻ level</th><th></th></tr>
<tr><th>Location</th><th><i>n</i></th><th>Temp*</th><th>Range</th><th>Mean</th><th>SD</th><th>F_{ci}</th></tr>
<tr><td>Galewela</td><td>92</td><td>32</td><td>0.36–2.80</td><td>0.62</td><td>0.50</td><td>0.92</td></tr>
<tr><td>Wariyapola</td><td>100</td><td>32</td><td>0.09 5.60</td><td>0.61</td><td>0.70</td><td>0.89</td></tr>
<tr><td>Kekirawa</td><td>97</td><td>32</td><td>0.17–8.00</td><td>0.88</td><td>1.12</td><td>1.72</td></tr>
<tr><td>Rambukkana</td><td>91</td><td>29</td><td>0.08–0.33</td><td>0.14</td><td>0.04</td><td>0.15</td></tr>
<tr><td>All</td><td>380</td><td></td><td>0.08–8.00</td><td>0.57</td><td>0.75</td><td>0.93</td></tr>
</table>
* Mean annual maximum daily temperature in °C.
F_{ci} – Community index of dental fluorosis.
The children had not used fluoride-containing toothpaste of any other fluoride therapies during the time of their permanent tooth development (age not specified, presumably up to age 6).</td></tr>
<tr><td></td><td></td></tr>
<tr><td>ANALYTICAL METHODS:</td><td>Water fluoride concentrations were measured using an (Orion) ion-specific electrode. The water ionic strength was controlled with unspecified buffer of pH 5.0-5.5. All measurements were made within 2-3 weeks of sample collection. Data were not provided for any other water quality parameters.</td></tr>
<tr><td></td><td></td></tr>
<tr><td>STUDY DESIGN</td><td>The four geographic regions were selected after pilot studies to give a wide range of ground water fluoride concentrations. Children aged 14, and who had lived their entire life within their four geographic areas, were examined in November and December 1986 at each of their (four) schools. Teeth were examined using indirect natural daylight as the only illumination, plane dental mirrors, and #23 explorers. The criteria of Russell (1961) were used to distinguish between fluorosis and nonfluoride enamel</td></tr>
</table>

opacities, and the degree of fluorosis was classified by Dean's (1942) dental fluorosis index. Fluorosis was assessed in buccal and occlusal tooth surfaces of all teeth, and the more severe score was assigned to a given tooth. The classification for a given person was based on the most severe fluorosis seen for two or more teeth.

Fluorosis was determined in the children by one dentist, and another dentist examined each child for dental caries using the DMFT index and the criteria of Radike (1972). Missing teeth were assumed to have been extracted due to dental caries, unless informed otherwise. Intra-examiner consistency scores was evaluated by duplicate examination of 10% of the subjects each day, which found complete agreement in 66% of the cases and agreement within 1 score in 92% of the cases for fluorosis, and the mean DMFT score within 90.5% of the first examination.

Drinking water fluoride concentrations of the children were determined in 300 mL water samples provided by the children from their domestic drinking water. If the children had moved within their geographic areas, they were asked to provide, if possible, a sample of their drinking water up to age 6.

PARAMETERS MONITORED:

Dental fluorosis was assessed using Dean's classification system and the criteria of Russell (1961) to distinguish between fluorosis and nonfluoride enamel opacities. For the Dean's Index, the authors used a score of 1 instead of 0.5 for questionable results, thus the more severe categories ranged from 2-5. Each child was examined for dental caries using the DMFT index.

STATISTICAL METHODS:

Differences in the percent of children that were caries-free or were fluorosis-free at various water fluoride levels were evaluated using the Chi square non-parametric test. Differences in the mean DMFT index at various water fluoride levels were evaluated by one-way ANOVA.

RESULTS:

Dental caries (DMFT)

There were statistically significant differences in the percent children that were caries-free, and in the mean DMFT scores, at five different fluoride levels (Table 2). The differences were mainly due to the 0.6-0.79 ppm water fluoride group, which had the lowest DMFT (1.91) and greatest percentage of caries-free children (37.5%). Significant differences were not seen among the other four exposure groups. [Note that in Table 2, the lowest fluoride concentration should be <0.4 ppm instead of <0.04 ppm.]

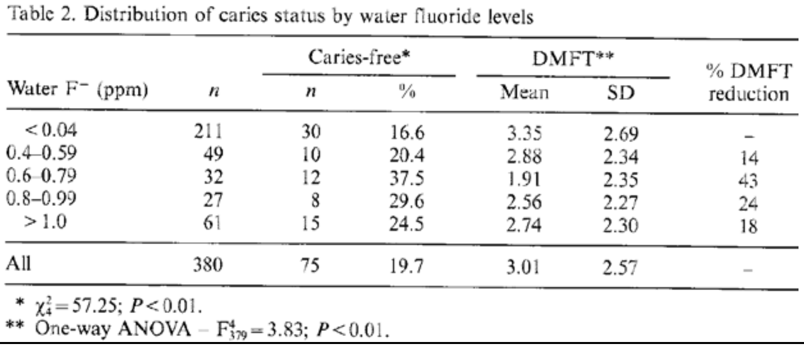


Table 2. Distribution of caries status by water fluoride levels

Water F^- (ppm)	n	Caries-free*		DMFT**		% DMFT reduction
		n	%	Mean	SD	
< 0.04	211	30	16.6	3.35	2.69	–
0.4–0.59	49	10	20.4	2.88	2.34	14
0.6–0.79	32	12	37.5	1.91	2.35	43
0.8–0.99	27	8	29.6	2.56	2.27	24
> 1.0	61	15	24.5	2.74	2.30	18
All	380	75	19.7	3.01	2.57	–

* $\chi^2_4 = 57.25$; $P < 0.01$.

** One-way ANOVA – $F^4_{379} = 3.83$; $P < 0.01$.

Dental fluorosis

Dental fluorosis (Dean's fluorosis index scores combined as 0-1; 2-3; and 4-5) increased in parallel with the water fluoride levels, differing statistically among the exposure groups. Results are shown in Table 3. As shown in Table 1, the CFI also increased with the water fluoridation levels. Children exposed to <0.4 ppm were most often fluorosis-free (69%, 25%, and 6% had score of 0-1, 2-3, and 4-5, respectively), whereas at >1.0 ppm, 20%, 49%, and 31% had scores of 0-1, 2-3, and 4-5, respectively.

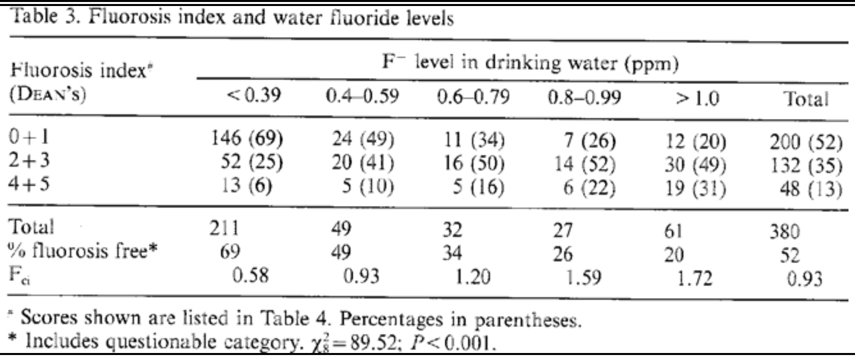


Table 3. Fluorosis index and water fluoride levels

Fluorosis index[a] (Dean's)	F⁻ level in drinking water (ppm)					
	< 0.39	0.4–0.59	0.6–0.79	0.8–0.99	> 1.0	Total
0+1	146 (69)	24 (49)	11 (34)	7 (26)	12 (20)	200 (52)
2+3	52 (25)	20 (41)	16 (50)	14 (52)	30 (49)	132 (35)
4+5	13 (6)	5 (10)	5 (16)	6 (22)	19 (31)	48 (13)
Total	211	49	32	27	61	380
% fluorosis free*	69	49	34	26	20	52
F_{ci}	0.58	0.93	1.20	1.59	1.72	0.93

[a] Scores shown are listed in Table 4. Percentages in parentheses.

* Includes questionable category. $\chi^2_8 = 89.52$; $P < 0.001$.

Effect of dental fluorosis on dental caries (DMFT)

A comparison of the mean DMFT scores with the Dean's fluorosis index showed no statistically significant differences in the groups, as shown in Table 4. The DMFT scores were slightly lower in children with questionable or mild a fluorosis (index of 1 or 2), suggesting a mild protective effect against dental caries in these groups.

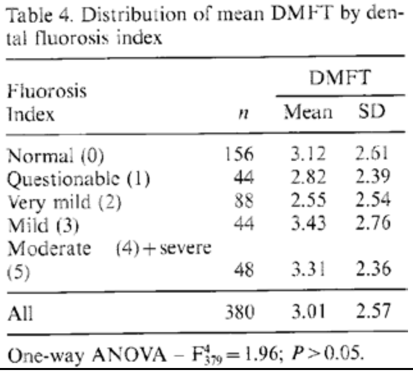


Table 4. Distribution of mean DMFT by dental fluorosis index

Fluorosis Index	*n*	DMFT	
		Mean	SD
Normal (0)	156	3.12	2.61
Questionable (1)	44	2.82	2.39
Very mild (2)	88	2.55	2.54
Mild (3)	44	3.43	2.76
Moderate (4) + severe (5)	48	3.31	2.36
All	380	3.01	2.57

One-way ANOVA – $F^4_{379} = 1.96$; $P > 0.05$.

STUDY AUTHORS' CONCLUSIONS:

Warnakulasuriya et al. (1992) concluded that 0.6-0.79 ppm in the drinking water provided the maximal water protection against caries in these four regions in Sri Lanka (43% lower DMFT than at <0.4 ppm fluoride, per Table 2). The authors assert that drinking water guidelines in temperate climates, and those set by the World Health Organization (1.5 ppm), were too high for developing countries with hot, dry climates like Sri Lanka, and recommend 0.8 ppm as an upper limit for these populations.

Increasing the water fluoride level was associated with an increased prevalence and severity of fluorosis, but the dose-response relationship had no threshold since fluorosis was seen in all groups of children. Fluorosis was prevalent even at the lowest water fluoride concentration, i.e. <0.39 ppm, as 31% of the children had definite fluorosis (Dean's index of 2-5). At the optimal water fluoride concentration of 0.6-0.79 ppm, only 34% of the children were fluorosis-free (Dean's index of 0-1). The study authors speculate that the high fluorosis index may be in part due to the high consumption of locally grown tea rich in fluoride, or that there may be differences in the nutritional status of the children that could influence fluoride metabolism.

The authors note that the study results may have been influenced by the mobility of children within a given geographic region, and by the consumption of water from schools, because wells within 15 miles of each other sometimes had 10-fold different water fluoride concentrations.

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

Radike, A.W. 1972. Criteria for diagnosis of dental caries. In: Proceedings of the Conference on the Clinical Testing of Cariostatic Agents. Chicago, American Dental Association, 87-88.

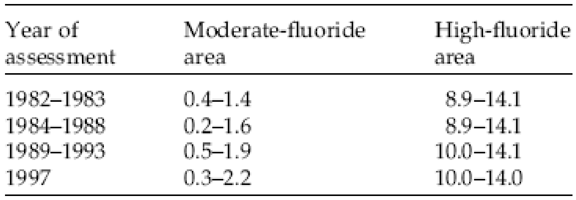
Russell, A.L. 1961. The differential diagnosis of fluoride and nonfluoride opacities. J. Pub. Health Dent. 21: 143-146.

PROFILER'S REMARKS	***Initials/date SM/1/09/07***	A significant finding of this study is that fluoride drinking water guidelines developed for temperate climates in Western countries may not be appropriate for populations from developing countries in hot, dry climates. The study authors did not discuss the reason for these differences, but presumably these may include the fact that these people may drink more water and have dietary differences that significantly impact their total fluoride intake. A definitive relationship could not be drawn between the severity of dental fluorosis and dental caries (DMFT score), as Table 4 showed there was no statistical difference between the fluorosis index and the mean DMFT. Two major methodological shortcoming of the study were (1) the water fluoride concentrations were disproportionately distributed into three very narrow ranges (0.4-0.59, 0.6-0.79, and 0.8-0.99 ppm) and two very broad ranges (<0.4 and >1.0 ppm); the high concentration group, in particular, should have been subdivided into 2 or more groups, and (2) there were too many uncertainties regarding the children's fluoride exposure (potential confounders included drinking tea high in fluoride, differences in nutritional status, and one person obtaining water from sources with vastly different water fluoride concentrations), thus precluding the ability to establish a dose-response for fluoride exposure vs. fluorosis.
PROFILER'S ESTIM. NOEL/NOAEL		A NOAEL for fluorosis could not be established, as even the lowest water fluoride concentration was associated with fluorosis in 34% of the subjects.
PROFILER'S ESTIM. LOEL/ LOAEL		A LOAEL was not identified for fluorosis (or for dental caries due to fluorosis).
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable ( ), Poor ( ), Medium (X), Strong ( ) Increased water fluoride concentration was correlated with increased dental fluorosis, although there were many uncertainties regarding the children's fluoride exposure (potential confounders included drinking tea high in fluoride, differences in nutritional status, and one person obtaining water from sources with vastly different water fluoride concentrations). Also, the fact that there is fluorosis at all levels, even the <0.4 mg/L, raises a question about the source of the fluoride. However, Table 3 does demonstrate that the portion of the population with the severe fluorosis increases as the concentration of the water increases so there is some dose response.
CRITICAL EFFECT(S):		Dental fluorosis

Wondwossen, F., A.N. Åstrøm, K. Bjorvatn, and A. Bårdsen. 2004. The relationship between dental caries and dental fluorosis in areas with moderate- and high fluoride drinking water in Ethiopia. Community Dent. Oral Epidemiol. 32:337-344.

ENDPOINT STUDIED:	Dental fluorosis and dental caries
TYPE OF STUDY:	Prevalence survey
POPULATION STUDIED:	Ethiopia/Rift Valley. 306 Ethiopian children 12-15 yrs old (152 girls, mean age 13.5 yrs, and 154 boys, mean age 13.1 yrs), from three neighboring villages in the Rift Valley; the 3 villages are all within the Wonji Shoa Sugar Estate and are stated by Wondwossen et al (2004) to be of approximate same size and socioeconomic condition. Informed consent was obtained from participating children, their parents and local authorities. The authors point out that boys and girls were unevenly represented in the two study areas (but equally represented in the total sample).
CONTROL POPULATION:	None
EXPOSURE PERIOD:	Beginning in 1982, and lasting for 12-15 years; the dental examinations took place in 1997.
EXPOSURE GROUPS:	The children were grouped into two exposure categories based on fluoride drinking water levels measured in water wells in the three villages, as shown in the Table 1 taken from Wondwossen et al. (2004).

Table 1. Average fluoride concentration (mg/l) measured in the drinking water of the moderate- and high-fluoride area



Year of assessment	Moderate-fluoride area	High-fluoride area
1982–1983	0.4–1.4	8.9–14.1
1984–1988	0.2–1.6	8.9–14.1
1989–1993	0.5–1.9	10.0–14.1
1997	0.3–2.2	10.0–14.0

EXPOSURE ASSESSMENT:	The children in the study population resided in villages that relied on local ground water sources for their drinking water. Exposure to fluoride through other routes such as air or diet, were not assessed in this study; therefore, total fluoride intake was not reported.
ANALYTICAL METHODS:	Not reported. Fluoride levels in ground water sources were assessed between 1982 and 1997.
STUDY DESIGN	Dental fluorosis and caries incidence were evaluated in 306 children 12-15 yrs old, from three neighboring villages in the Rift Valley, Ethiopia. The children were grouped into two exposure categories based on well-water fluoride concentrations measured in 1982-1997 (average values 0.4-1.4 mg/L to 0.3-2.2 mg/l for the moderate exposure group and 0.89-14.1 mg/L to 10.0-14.0 mg/L for the high exposure group). Dental fluorosis was scored using the Thylstrup-Fejerskov (TF) Index, and dental caries was measured with DMFS indices and DMFT scores. Statistical analysis consisted of bivariate analyses using cross-tabulation, chi square statistics, independent sample t test, one-way ANOVA, Spearman's correlation coefficient (γ_s), and the Kruskal-Wallis test.
PARAMETERS MONITORED:	Scoring for fluorosis was based on the Thylstrup-Fejerskov (TF) Index (see Section 2) and assessed on the vestibular, occlusal and lingual surfaces; scoring for dental caries was based

on the DMFS indices and DMFT scores as described by WHO Oral Health Survey system (see Section 2). DMFT scores for each individual were established by summing highest DMFS scores across all permanent teeth.

STATISTICAL METHODS:

Data were analyzed using the Statistical Package for the Social Sciences (SPSS v. 10.0). Bivariate analyses were performed using cross-tabulation, chi square statistics, independent sample t test, one-way ANOVA, Spearman's correlation coefficient (γ_s), and the Kruskal-Wallis test. Dental caries prevalence was regressed on TF scores and area of residence, controlling for confounding factors by the use of multiple logistics regression analyses. Ninety-five percent confidence interval (95% CI) was given for the odds ratio.

RESULTS:

Prevalence of dental fluorosis (TF>1) was 91.8% in the moderate fluoride areas and 100% in the high fluoride area. When compared with 12-year olds with TF scores 0-4, odds ratios for DMFT ≥ 1 was 3.0 (95% CI = 1.6-5.7). For children 13-15 years olds with TF scores ≥ 5, odds ratio for DMFT ≥ 1 was 2.0 (95% CI = 1.2-3.2). No statistically significant interaction effect on caries was identified for the term TF scores and place of residence, indicating that the strength of association between dental caries and dental fluorosis did not systematically vary between moderate and high-fluoride areas.

Dental fluorosis

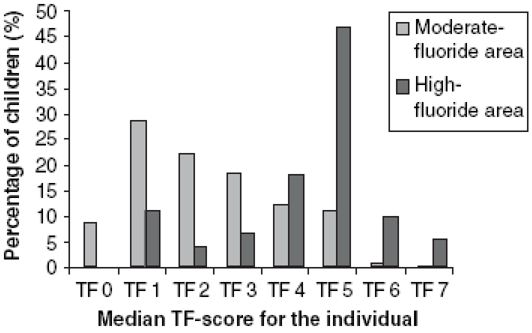


Fig. 1. The percentage distribution of adolescents according to median TF-score for the individual (all teeth) in moderate- and high-fluoride areas.

See also Tables 4 and 5 (below) for additional information on fluorosis (and author comparisons with caries).

REVIEWER'S NOTE: An earlier study (Olsson 1979) also evaluated dental fluorosis among schoolchildren in villages from the Wonji area of the Shoa province. Olsson (1979) pointed out that some Wonji-area villages (as well as the living quarters of the local sugar factory) were supplied with defluoridated water. It is unclear if any participants in the present study by Wondwossen et al (2004) were also supplied with such defluoridated drinking water.

Other effects

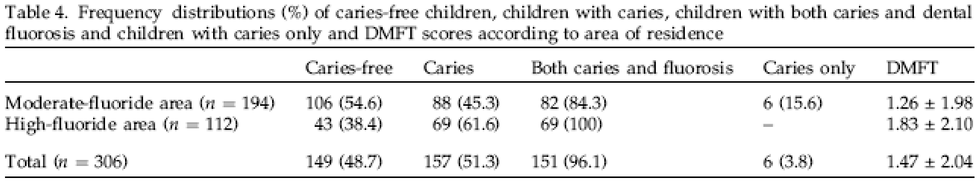


Table 4. Frequency distributions (%) of caries-free children, children with caries, children with both caries and dental fluorosis and children with caries only and DMFT scores according to area of residence

	Caries-free	Caries	Both caries and fluorosis	Caries only	DMFT
Moderate-fluoride area (n = 194)	106 (54.6)	88 (45.3)	82 (84.3)	6 (15.6)	1.26 ± 1.98
High-fluoride area (n = 112)	43 (38.4)	69 (61.6)	69 (100)	–	1.83 ± 2.10
Total (n = 306)	149 (48.7)	157 (51.3)	151 (96.1)	6 (3.8)	1.47 ± 2.04

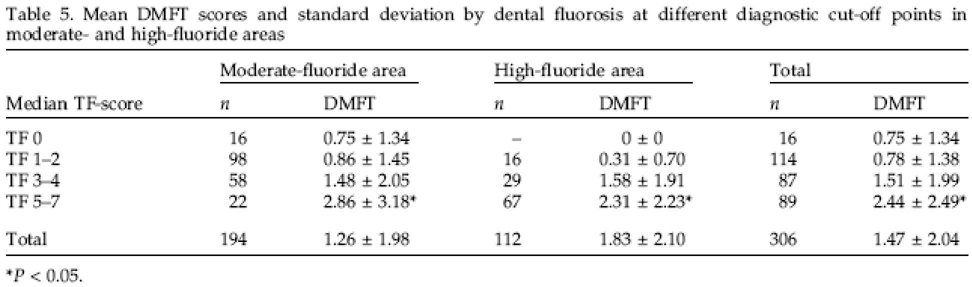


Table 5. Mean DMFT scores and standard deviation by dental fluorosis at different diagnostic cut-off points in moderate- and high-fluoride areas

	Moderate-fluoride area		High-fluoride area		Total	
Median TF-score	*n*	DMFT	*n*	DMFT	*n*	DMFT
TF 0	16	0.75 ± 1.34	–	0 ± 0	16	0.75 ± 1.34
TF 1–2	98	0.86 ± 1.45	16	0.31 ± 0.70	114	0.78 ± 1.38
TF 3–4	58	1.48 ± 2.05	29	1.58 ± 1.91	87	1.51 ± 1.99
TF 5–7	22	2.86 ± 3.18*	67	2.31 ± 2.23*	89	2.44 ± 2.49*
Total	194	1.26 ± 1.98	112	1.83 ± 2.10	306	1.47 ± 2.04

*$P < 0.05$.

Degree of fluorosis in relationship to tooth type as shown in Figure 2 taken directly from Wondwossen et al., 2004

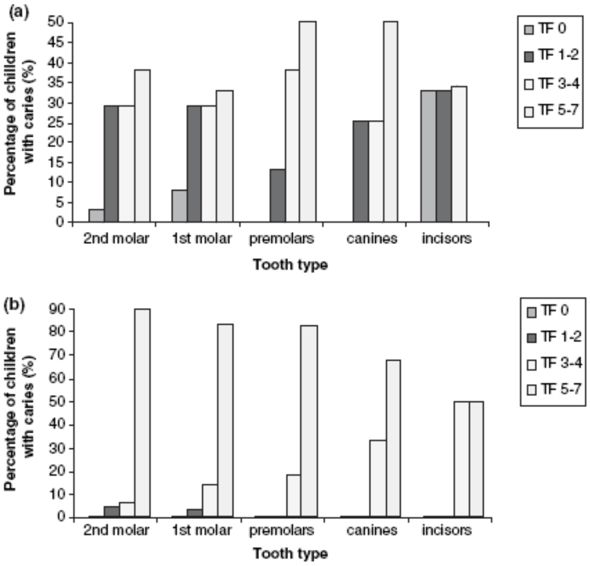


Fig. 2. The percentage distribution of adolescents according to DMFT scores and TF-scores by tooth type in the moderate- (a) and high-fluoride (b) areas.

STUDY AUTHORS' CONCLUSIONS:

The prevalence of dental fluorosis (TF ≥ 1) was 91.8% (moderate fluoride area) and 100% (high-fluoride area).

A positive relationship between caries and fluorosis was observed across tooth types in both the moderate- and high-fluoride areas areas. The percentage of children with DMFT ≥ 1 was highest in groups with TF score ≥ 5 in the 2nd molar, followed by the 1st molar. **The 2nd molar was the tooth most severely affected by dental fluorosis in the age group.**

DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)

For definitions and descriptions of scales and indices, please see Section 2 and List of Acronyms.

PROFILER'S REMARKS

DMO 11/14/06 and 12/15/2006

Because of the wide range of fluoride levels identified in the two exposure groups, the data cannot be used to accurately assess dose response relationships. However, assuming that a TFI of 5 and above is equivalent to severe fluorosis, then the proportion of the population showing severe fluorosis can be estimated to have been about 63% in the high fluoride area, and about 13% in the low fluoride area.

A previous dental fluorosis study (Olsson 1979) identified the presence of some defluoridated water supply systems in Wonji-area villages; it is unclear if these defluoridated water supplies have been incorporated into the present study.

PROFILER’S ESTIM. NOEL/NOAEL		Dental fluorosis observed at all fluoride concentrations examined; thus, estimating a NOAEL for fluorosis is not possible from these data.
PROFILER’S ESTIM. LOEL/ LOAEL		TBD
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (_), Poor (_), Medium (X), Strong (_)
CRITICAL EFFECT(S):		Dental fluorosis and caries

Wondwossen, F, A.N. Åstrøm, K. Bjorvatn, and A. Bårdsen. 2006. Sociodemographic and behavioural correlates of severe dental fluorosis. Internat. J. Paed. Dent. 16:95-103.

ENDPOINT STUDIED:	Dental fluorosis
TYPE OF STUDY:	Prevalence survey; continuation of a study reported by Wondwossen et al 2004.
POPULATION STUDIED:	Ethiopia/Rift Valley: 306 Ethiopian children 12-15 yrs old (152 girls, mean age 13.5 yrs, and 154 boys, mean age 13.1 yrs), from three neighboring villages in the Rift Valley; the 3 villages are all within the Wonji Shoa Sugar Estate (WSSE) and, according to Wondwossen et al (2004), are of approximate the same size and socioeconomic condition. The dental examinations took place in 1997. Informed consent was obtained from participating children, their parents and local authorities.
CONTROL POPULATION:	None
EXPOSURE PERIOD:	Lifetime, up until the time of the dental examinations in 1997.
EXPOSURE GROUPS:	The study population was separated into two groups; villages A and M were in the moderate fluoride area with fluoride levels ranging from 0.3 to 2.2 mg/L; and village K was considered to be in a high fluoride area with fluoride levels of 10 and 14 mg/L. The authors point out that boys and girls were unevenly represented in the two study groups, but equally represented in the total sample.
EXPOSURE ASSESSMENT:	Factors evaluated included fluoride concentration in drinking water derived from wells; use of fluoride supplements and dentifrices; diet, including tea and fish consumption; breast-feeding; and use of clay cooking pots. Total fluoride intake, however, was not estimated.
ANALYTICAL METHODS:	Information on fluoride levels in drinking water (obtained from drilled wells) was provided by the medical service of the WSSE; however, analytical methods were not reported.
PARAMETERS MONITORED:	Fluorosis was assessed on the buccal, occlusal and lingual surfaces according to the Thylstrup-Fejerskov (TF) Index (see Section 2 for description).
STATISTICAL METHODS:	The SPSS (Statistical package for Social Sciences) software for PC, Version 10·0, computer program was used in the analysis. Bivariate analyses were performed using cross-tabulation, chi-square statistics and one-way analysis of variance. The Mann–Whitney *U* -test and Kruskal–Wallis test were used when comparing severity according to selected independent variables. Multiple logistic regression analysis was used to estimate the risk for severe dental fluorosis, calculating odds ratio (ORs) and 95% confidence interval (CI). Collinearity between the independent variables was checked by means of the variance inflation factor (VIF), using x_i as the dependent variable in regression on the other independent variables. All analyses are based on the total number of participating mother/child pairs (*n*= 233).
RESULTS:	
Caries	Not evaluated
Dental fluorosis	Fluorosis, as measured by the TFI scores, was significantly greater (p<0.001) in the high fluoride area, as indicated in Table 2 taken from Wondwossen et al (2006). Higher levels of fluorosis were also associated with: 1) shorter periods of breast feeding, tea and fish consumption; and storage of drinking water in non-clay containers.

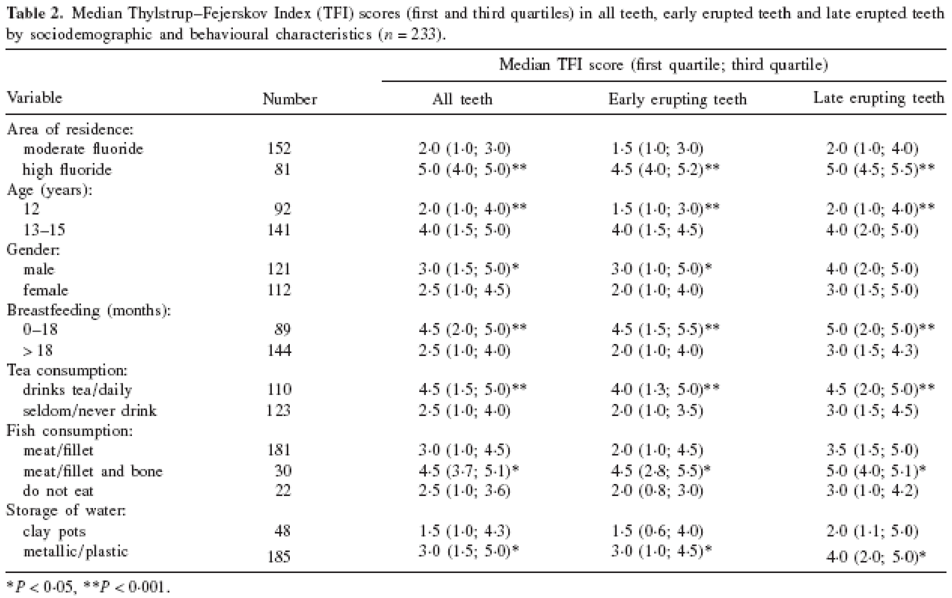


Table 2. Median Thylstrup–Fejerskov Index (TFI) scores (first and third quartiles) in all teeth, early erupted teeth and late erupted teeth by sociodemographic and behavioural characteristics ($n = 233$).

		Median TFI score (first quartile; third quartile)		
Variable	Number	All teeth	Early erupting teeth	Late erupting teeth
Area of residence:				
moderate fluoride	152	2·0 (1·0; 3·0)	1·5 (1·0; 3·0)	2·0 (1·0; 4·0)
high fluoride	81	5·0 (4·0; 5·0)**	4·5 (4·0; 5·2)**	5·0 (4·5; 5·5)**
Age (years):				
12	92	2·0 (1·0; 4·0)**	1·5 (1·0; 3·0)**	2·0 (1·0; 4·0)**
13–15	141	4·0 (1·5; 5·0)	4·0 (1·5; 4·5)	4·0 (2·0; 5·0)
Gender:				
male	121	3·0 (1·5; 5·0)*	3·0 (1·0; 5·0)*	4·0 (2·0; 5·0)
female	112	2·5 (1·0; 4·5)	2·0 (1·0; 4·0)	3·0 (1·5; 5·0)
Breastfeeding (months):				
0–18	89	4·5 (2·0; 5·0)**	4·5 (1·5; 5·5)**	5·0 (2·0; 5·0)**
> 18	144	2·5 (1·0; 4·0)	2·0 (1·0; 4·0)	3·0 (1·5; 4·3)
Tea consumption:				
drinks tea/daily	110	4·5 (1·5; 5·0)**	4·0 (1·3; 5·0)**	4·5 (2·0; 5·0)**
seldom/never drink	123	2·5 (1·0; 4·0)	2·0 (1·0; 3·5)	3·0 (1·5; 4·5)
Fish consumption:				
meat/fillet	181	3·0 (1·0; 4·5)	2·0 (1·0; 4·5)	3·5 (1·5; 5·0)
meat/fillet and bone	30	4·5 (3·7; 5·1)*	4·5 (2·8; 5·5)*	5·0 (4·0; 5·1)*
do not eat	22	2·5 (1·0; 3·6)	2·0 (0·8; 3·0)	3·0 (1·0; 4·2)
Storage of water:				
clay pots	48	1·5 (1·0; 4·3)	1·5 (0·6; 4·0)	2·0 (1·1; 5·0)
metallic/plastic	185	3·0 (1·5; 5·0)*	3·0 (1·0; 4·5)*	4·0 (2·0; 5·0)*

*$P < 0·05$, **$P < 0·001$.

Among the 233 children, the prevalence of severe dental fluorosis (TFI ≥ 5) was 24.1% and 75.9% in the moderate- and high-fluoride areas, respectively (see Table 3, copied directly from Wondwossen et al 2006):

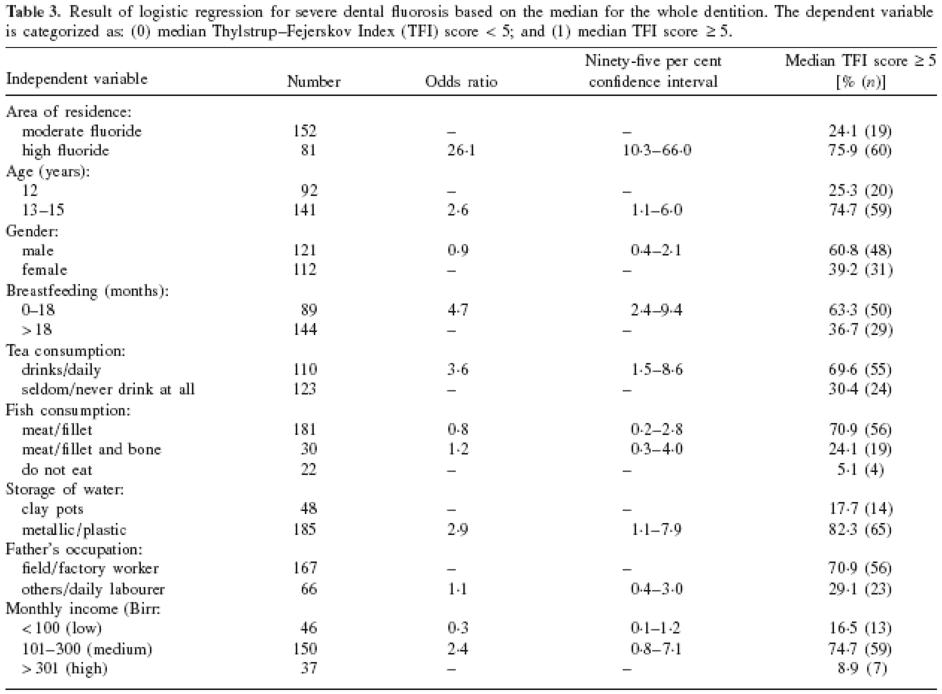


Table 3. Result of logistic regression for severe dental fluorosis based on the median for the whole dentition. The dependent variable is categorized as: (0) median Thylstrup–Fejerskov Index (TFI) score < 5; and (1) median TFI score ≥ 5.

Independent variable	Number	Odds ratio	Ninety-five per cent confidence interval	Median TFI score ≥ 5 [% (*n*)]
Area of residence:				
moderate fluoride	152	–	–	24·1 (19)
high fluoride	81	26·1	10·3–66·0	75·9 (60)
Age (years):				
12	92	–	–	25·3 (20)
13–15	141	2·6	1·1–6·0	74·7 (59)
Gender:				
male	121	0·9	0·4–2·1	60·8 (48)
female	112	–	–	39·2 (31)
Breastfeeding (months):				
0–18	89	4·7	2·4–9·4	63·3 (50)
> 18	144	–	–	36·7 (29)
Tea consumption:				
drinks/daily	110	3·6	1·5–8·6	69·6 (55)
seldom/never drink at all	123	–	–	30·4 (24)
Fish consumption:				
meat/fillet	181	0·8	0·2–2·8	70·9 (56)
meat/fillet and bone	30	1·2	0·3–4·0	24·1 (19)
do not eat	22	–	–	5·1 (4)
Storage of water:				
clay pots	48	–	–	17·7 (14)
metallic/plastic	185	2·9	1·1–7·9	82·3 (65)
Father's occupation:				
field/factory worker	167	–	–	70·9 (56)
others/daily labourer	66	1·1	0·4–3·0	29·1 (23)
Monthly income (Birr:				
< 100 (low)	46	0·3	0·1–1·2	16·5 (13)
101–300 (medium)	150	2·4	0·8–7·1	74·7 (59)
> 301 (high)	37	–	–	8·9 (7)

According to bivariate as well as multivariate analyses, a number of sociodemographic and behavioural factors were related to severe fluorosis. The odds for having severe fluorosis varied according to the fluoride concentration of the drinking water, age, consumption of tea, length of breastfeeding and method of storing water. The adjusted odds ratios ranged from 2.6 to 26.1. Breastfeeding for >18 months and the use of clay pots for storing drinking water was associated with significantly lower TFI scores. Bivariate analyses indicated that being male and consuming fish might be associated with higher TFI scores.

STUDY AUTHORS' CONCLUSIONS:

In order to avoid dental fluorosis, low-fluoride drinking water should be provided in the relevant villages. A prolonged period of breastfeeding, the use of clay pots for storing water, and possibly a reduced intake of tea and whole fish in infants might also help to avoid severe fluorosis in children growing up in traditionally fluoride-endemic areas. The authors consider this report to be the first

		documentation of a relationship between clinical dental fluorosis and use of clay pots for water storage (e.g., fluoride binding capacity of various clays) Bjorvatn et al (2003).
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)		Bjortn, K., Reimann, C., Østvold, S.H., Tekle-Haimanot, R., Melaku, Z. Siewers, U. 2003. High fluoride drinking water. A health problem in the Ethiopian Rift Valley. 1 Assessment of lateritic soils as defloridating agents. Oral Health and Preventive Dentistry 1:141-148.
PROFILER'S REMARKS	***Initials/date DMO/1/12/07***	The study showed that fluoride levels of 10 and 14.1 mg/L in drinking water were associated with the occurrence of severe fluorosis (TFI score > 5) in 75% of the exposed population.
PROFILER'S ESTIM. NOEL/NOAEL		Can not be determined
PROFILER'S ESTIM. LOEL/ LOAEL		Severe fluorosis (median TFI of 5) occurred in the high fluoride area, associated with fluoride levels in drinking water of 10 and 14.1 mg/L.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable ( ), Poor (X), Medium ( ), Strong ( ) Only two exposure groups were evaluated, and the one for the moderate fluoride area included a range of fluoride drinking water levels (0.3 to 2.2 mg/L) too wide to be useful in a dose-response analysis.
CRITICAL EFFECT(S):		Dental fluorosis

Yoder, K.M., Mabelya, L., Robison, V.A., Dunipace, A.J., Brizendine, E.J., Stookey, G.K. 1998. Severe dental fluorosis in a Tanzanian population consuming water with negligible fluoride concentration. Community Dent. Oral Epidemiol. Dec; 26(6):382-93.

ENDPOINT STUDIED:	Dental fluorosis and caries
TYPE OF STUDY:	Cohort
CONTROL POPULATION: (Site 1)	84 school children of heterogeneous tribal ethnicity (≥12 tribes represented), ages 9-19 years old, from the Chanika school in Tanzania near sea level (100 m), where the fluoride level in the drinking water is negligible (0.046±0.047 mg/l).
POPULATION STUDIED: (Site 2)	100 school children of heterogeneous tribal ethnicity (≥12 tribes represented), ages 9-19 years old, from the Rundugai school in the plains of Tanzania at 840 m, where the fluoride level in the drinking water is 5.72±4.71 mg/l.
POPULATION STUDIED: (Site 3)	100 school children of homogenous tribal ethnicity (Chagga tribe), ages 9-19 years old, from the Kibosho school located at 1463 m on Mount Kilimanjaro in Tanzania where the fluoride level in the drinking water is negligible (0.18±0.32 mg/l).
EXPOSURE PERIOD:	Subjects were lifelong residents, so exposure period ranged from 9 to 19 years.
EXPOSURE GROUPS:	284 subjects were randomly selected from class rosters from three sites: Chanika School (Site 1, 100 m altitude, negligible water fluoride), Rundugai School (Site 1, 840 m altitude, high water fluoride level), and Kibosho School (Site 3, 1463 m altitude, negligible water fluoride). The residents of all three sites were primarily farmers and not nomadic and were required to be lifelong residents of the study site from which they were recruited, to be in good health, and to consent to participation.
EXPOSURE ASSESSMENT:	Subjects were examined for dental fluorosis and caries. Subjects were interviewed about their food habits, environmental characteristics, and use of a fluoride-containing food tenderizer known locally as magadi. Parents were not questioned.
ANALYTICAL METHODS:	Meal (n=280), urine (n=280), water (n=42) and magadi (n=139) samples supplied by participants were analyzed for fluoride content at the Oral Health Research Institute of Indiana University School of Dentistry. Magadi samples from Sites 1 and 3 (n=2 from each site, randomly selected from 98 total samples) were analyzed for complete element composition at the Indiana State Department of Health, Environmental Laboratory. Water, urine, and magadi were directly analyzed for fluoride using a fluoride ion-specific electrode (Orion Research, Boston, MA). Foods were analyzed by a modification of the diffusion method of Taves (1968). Urine samples also were analyzed for creatinine concentration to enable determination of the urinary fluoride to urinary creatinine ratio as a means of correcting for collecting spot urine specimens rather than 24-hour samples; creatinine was determined at the Indiana University Hospital Endocrinology Laboratory.
STUDY DESIGN	283 school children, ages 9 to 19, were examined in three locations of varying altitude in Tanzania during 1996. Three sites, representing high and low altitude with negligible fluoride and a mid-altitude site with high water fluoride were selected from records of the Ministry of Health and Social Welfare of the United Republic of Tanzania. The children were questioned by a Tanzanian interviewer regarding length of residence at that site; their consumption of tea, fish, and milk; the family's use of magadi; the family's cooking location (inside or outside the home) and type of fuel used; frequency of use of insecticide on crops; and their younger siblings' ingestion of tea and food cooked with magadi. Subjects were asked to list what they ate the previous day in order to survey the types of foods consumed in that village. Information regarding nutritional status, on the district level, was obtained from records of the Regional Maternal and Child Health Office, relating height and weight to WHO standards. Subjects were instructed to bring a sample of their evening meal (as a mixture, excluding drink) and a sample of their first morning urine void in two separate closable 8-oz containers. They also brought a sample

(~tablespoonful) of magadi used in their home. Meal, urine, water and magadi samples were analyzed for fluoride content. Urine samples also were analyzed for creatinine concentration. Four randomly selected magadi samples from Sites 1 and 3 were analyzed for complete element composition.

Examinations: Subjects were examined for dental fluorosis using the Thylstrup and Fejerskov Index (TFI) and the Tooth Surface Index of Fluorosis (TSIF). Dental caries was recorded as decayed, missing and filled permanent surfaces (DMFS) by Radike's criteria. One examiner quantified TFI scores and DMFS rates at all sites; another examiner examined TSIF scores at Site 1 where minimal fluorosis existed; and a third examiner examined for TSIF scores at Sites 2 and 3 where severe fluorosis existed. TSIF examinations were conducted without drying teeth, and then the next examiner used gauze to dry the teeth for the TFI examinations. Intraoral mirrors and explorers and battery-operated head lamps were used. Aseptic procedures were followed. No radiographs were taken during the surveys. Intra-rater reliability for TSIF and TFI fluorosis scoring was measured by random and blind re-examination of 10% of the subjects. Kappa statistic was 0.74, 0.89, and 0.60 for the three examiners regarding fluorosis scores, within acceptable limits.

PARAMETERS MONITORED:

Dental fluorosis was measured using the Thylstrup and Fejerskov Index (TFI) and the Tooth Surface Index of Fluorosis (TSIF). Dental caries was recorded as decayed, missing and filled permanent surfaces (DMFS) by Radike's criteria. A qualifier (S) was added to both fluorosis indices to indicate an anterior tooth appearing to be artificially abraded for the purpose of removing pitting/discoloration due to fluorosis. A qualifier (A) was added to TSIF scores to indicate an occlusal surface which had more abrasion than would be expected in a child of that age.

STATISTICAL METHODS:

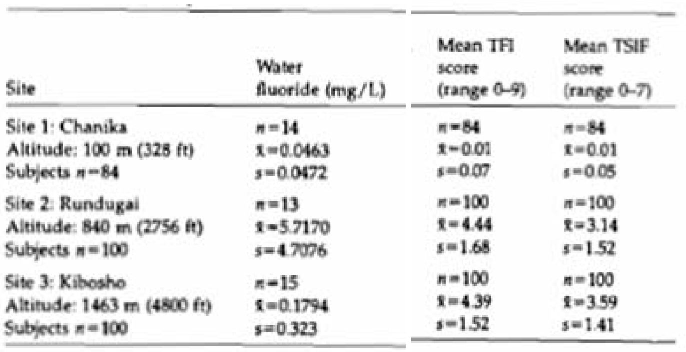
Statistical methods were not reported.

RESULTS:

Dental fluorosis

All tables were copied directly from Yoder et al. (1998). Table 1 was split for size considerations and summarizes specimen fluoride values, urine creatinine values, and mean maximum fluorosis scores (water fluoride concretion and fluorosis scores presented here). Water fluoride concentrations at Site 2 varied dramatically (range: 1.26 to 12.36 mg/L, mean: 5.72 mg/L). Sites 1 and 3 had negligible water fluoride concentrations (0.05 and 0.18 mg/L, respectively). Mean TFI (TSIF) scores were 0.01 (0.01), 4.44 (3.14), and 4.39 (3.59) for Sites 1, 2, and 3, respectively. As expected, subjects from Site 2, who consumed high levels of fluoride in the drinking water, exhibited severe fluorosis. Yet, although both Sites 1 and 3 had negligible water fluoride, Site 1 children had minimal fluorosis while virtually all subjects at Site 3 experienced severe fluorosis.

Table 1



Site	Water fluoride (mg/L)	Mean TFI score (range 0–9)	Mean TSIF score (range 0–7)
Site 1: Chanika	$n=14$	$n=84$	$n=84$
Altitude: 100 m (328 ft)	$\bar{x}=0.0463$	$\bar{x}=0.01$	$\bar{x}=0.01$
Subjects $n=84$	$s=0.0472$	$s=0.07$	$s=0.05$
Site 2: Rundugai	$n=13$	$n=100$	$n=100$
Altitude: 840 m (2756 ft)	$\bar{x}=5.7170$	$\bar{x}=4.44$	$\bar{x}=3.14$
Subjects $n=100$	$s=4.7076$	$s=1.68$	$s=1.52$
Site 3: Kibosho	$n=15$	$n=100$	$n=100$
Altitude: 1463 m (4800 ft)	$\bar{x}=0.1794$	$\bar{x}=4.39$	$\bar{x}=3.59$
Subjects $n=100$	$s=0.323$	$s=1.52$	$s=1.41$

Table 2 reports percentage distribution of TSIF fluorosis scores. At Site 1, less than 1% of subjects had TSIF scores ≥1. Distribution was relatively similar at Sites 2 and 3. 85% of subjects with high TSIF scores (6-7) had ≥4 molars with occlusal surfaces which were excessively abraded by wear; in contrast, subjects with low TSIF scores (≥3) did not have similar abrasion

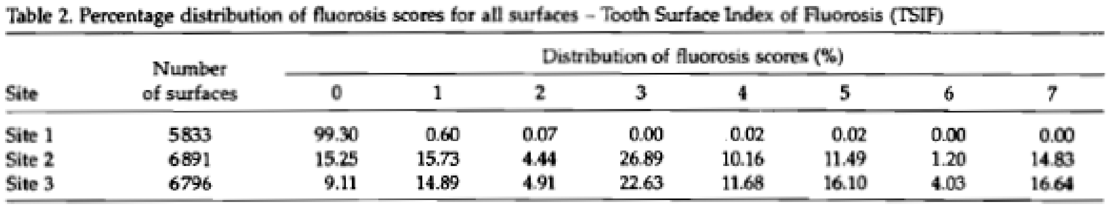


Table 2. Percentage distribution of fluorosis scores for all surfaces – Tooth Surface Index of Fluorosis (TSIF)

Site	Number of surfaces	Distribution of fluorosis scores (%)							
		0	1	2	3	4	5	6	7
Site 1	5833	99.30	0.60	0.07	0.00	0.02	0.02	0.00	0.00
Site 2	6891	15.25	15.73	4.44	26.89	10.16	11.49	1.20	14.83
Site 3	6796	9.11	14.89	4.91	22.63	11.68	16.10	4.03	16.64

Table 3 reports percentage distribution of TFI fluorosis scores. At Site 1, 1% of subjects had TFI scores ≥1. Distribution was relatively similar at Sites 2 and 3. Approximately half of the subjects with high TFI scores (7, 39%; 8, 51%; 9, 60%) artificially abraded their anterior teeth in an attempt to remove pitting and discoloration.

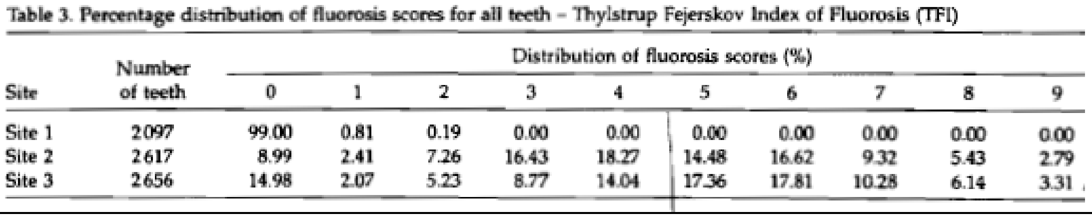


Table 3. Percentage distribution of fluorosis scores for all teeth – Thylstrup Fejerskov Index of Fluorosis (TFI)

Site	Number of teeth	Distribution of fluorosis scores (%)									
		0	1	2	3	4	5	6	7	8	9
Site 1	2097	99.00	0.81	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Site 2	2617	8.99	2.41	7.26	16.43	18.27	14.48	16.62	9.32	5.43	2.79
Site 3	2656	14.98	2.07	5.23	8.77	14.04	17.36	17.81	10.28	6.14	3.31

Caries

Caries experience was low in all three sites; only 43 of the 284 children had DMFS >0. Mean DMFS for all sites combined was 0.52±1.52. At Sites 1, 2, and 3, mean DMFS was 1.39 (±2.45), 0.15 (±0.73), and 0.19 (±0.61), respectively. Sixty percent of caries was detected in the least fluorosed teeth (TFI 0-1) and the next highest percentage of caries (16%) was detected in the most severely fluorosed teeth (TFI 8-9). 71 permanent teeth had 116 decayed surfaces, which were predominately in occlusal surfaces (54%).

PROFILER'S NOTE: A table summarizing caries data was not provided in the article.

Fluoride levels

Table 1 was split for size considerations and summarizes specimen fluoride values, urine creatinine values, and mean maximum fluorosis scores. Mean urinary fluoride concentrations were 0.52, 4.43, and 1.43 mg/L for subjects at Sites 1, 2 and 3, respectively. Children from Site 3 had unexpectedly high mean urinary fluoride (1.43 mg/L) compared with fluoride in the water they consumed (0.18 mg/L), but unexpectedly low urinary fluoride compared with their mean fluorosis scores (TFI, 4.39; TSIF, 3.59). Eight (of 100) subjects at Site 2 had urinary fluoride ≥10 mg/L, which is the reference value described as toxic by SmithKline Beecham (1997-98), and an additional 5 subjects' urinary fluoride levels were 8-10 mg/L.

Magadi fluoride concentrations were highly variable (range 189 to 83,211 mg/L); mean concentrations were 16010, 4113, and 5037 mg/L at Sites 1, 2, and 3, respectively. Fluoride concentration in meals was widely variable, ranging from 0.03 to 22.04 mg/L. Mean fluoride in meal samples was 0.49, 2.47, and 2.14 mg/L at Sites 1, 2, and 3, respectively; meal fluoride was considered high at Sites 2 and 3.

There were statistically significant linear relationships between food fluoride and urine fluoride (r=0.31) as well as between urine fluoride and magadi fluoride ($p \leq 0.0001$) (Pearson correlation coefficient, combining all sites). Thus, urine collected was a good indicator of the fluoride content in the food consumed the previous night.

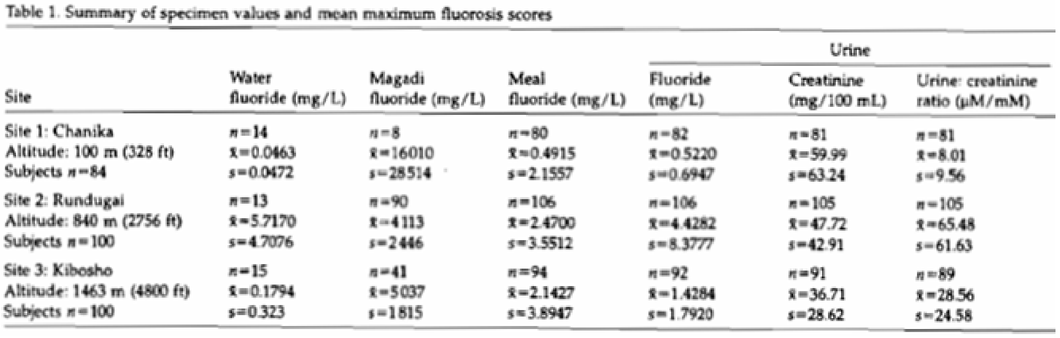


Table 1. Summary of specimen values and mean maximum fluorosis scores

Site	Water fluoride (mg/L)	Magadi fluoride (mg/L)	Meal fluoride (mg/L)	Urine		
				Fluoride (mg/L)	Creatinine (mg/100 mL)	Urine: creatinine ratio (µM/mM)
Site 1: Chanika Altitude: 100 m (328 ft) Subjects n=84	n=14 $\bar{x}$=0.0463 s=0.0472	n=8 $\bar{x}$=16010 s=28514	n=80 $\bar{x}$=0.4915 s=2.1557	n=82 $\bar{x}$=0.5220 s=0.6947	n=81 $\bar{x}$=59.99 s=63.24	n=81 $\bar{x}$=8.01 s=9.56
Site 2: Rundugai Altitude: 840 m (2756 ft) Subjects n=100	n=13 $\bar{x}$=5.7170 s=4.7076	n=90 $\bar{x}$=4113 s=2446	n=106 $\bar{x}$=2.4700 s=3.5512	n=106 $\bar{x}$=4.4282 s=8.3777	n=105 $\bar{x}$=47.72 s=42.91	n=105 $\bar{x}$=65.48 s=61.63
Site 3: Kibosho Altitude: 1463 m (4800 ft) Subjects n=100	n=15 $\bar{x}$=0.1794 s=0.323	n=41 $\bar{x}$=5037 s=1815	n=94 $\bar{x}$=2.1427 s=3.8947	n=92 $\bar{x}$=1.4284 s=1.7920	n=91 $\bar{x}$=36.71 s=28.62	n=89 $\bar{x}$=28.56 s=24.58

Other factors: *dietary*

Consumption of milk, tea and fish varied from site to site, but statistical differences were not reported. Milk

factors, magadi use, nutritional status	consumption appeared most variable with a low of 1.4 half-cups/ week at Site 1 (negligible fluorosis) to a high of 5 half-cups/ week at Site 2. 74% of subjects at Site 1 reported that they never drank milk. Tea consumption ranged from 6.23 (Site 3) to 8.66 (Site 1) cups/week. Fish consumption ranged from 4.24 (Site 3) to 6.42 (Site 2) times/ month. Magadi was used by 77, 96, and 99% of families in Sites 1, 2, and 3, respectively. The families cooked with magadi a mean of 1.50, 2.24, and 3.04 times/week. When asked if babies and toddlers were fed food cooked with magadi, 9.5, 89, and 100% respondents at Sites 1, 2, and 3, respectively, said "yes". Element analysis revealed that some components of magadi were aluminium (Al), iron (Fe), magnesium (Mg), manganese (Mn), molybdenum (Mo), strontium (Sr), and titanium (Ti), with much higher concentrations of these elements in samples from Site 3 as compared with Site 1; Al 7.6 times, Fe 54 times, Mg 5 times, Mn 8 times, Mo 2 times, Sr 4.7 times, and Ti 7.2 times higher in Site 3 as in Site 1. Bioavailability was not determined. Al and Mg are two elements that have potential as risk factors for enamel disturbances (human effects have not yet been proven). Approximately half of the children from the regions of Sites 2 (53%) and 3 (44%) were considered malnourished by WHO standards between 1981 and 1990, which were the years when their permanent teeth would have been forming. Data for Site 1were not available.
STUDY AUTHORS' CONCLUSIONS:	An analysis of covariance model showed that all three communities differed significantly in mean fluorosis scores (p<0.0001). Controlling for urinary fluoride concentration and urinary fluoride: creatinine ratio, location appeared to significantly affect fluorosis severity. Urinary fluoride: creatinine ratio had a stronger correlation than urinary fluoride concentration with mean maximum fluorosis scores (r=0.43 *vs* r=0.25). Fluorosis at Site 3 (high altitude) was more severe than would be expected from the low water and normal urinary fluoride values. Altitude, the elements (including fluoride) contained in magadi, and other nutritional factors may contribute to the severity of fluorosis observed. Although statistical analysis implicated lifelong residence at that location (1436 m altitude) as a risk factor in the severe fluorosis which was observed at Site 3, it is reasonable to expect that other factors may contribute to the high prevalence of fluorosis. The differences observed in the populations which could be potential risk factors for developing severe fluorosis included the following: o Frequency and patterns of use of magadi (fluoride-containing cooking additive) o Elements, besides fluoride, in magadi (which were found in higher concentrations in magadi from Site 3 vs. Site 1) o Altitude of residence since birth o Nutritional factors (malnutrition, tea and insufficient milk consumption) o Genetic factors
DEFINITIONS AND REFERENCES CITED IN PROFILE THAT ARE NOT FOUND IN NRC (2006)	Taves, D.R. (1968). Separation of fluoride by rapid diffusion using hexaamethyedisiloxane. *Talanta* 15: 969-974. SmithKline Beecham Clinical Laboratories (1997-98). Directory of services reference guide. Collegeville, Pennsylvania.
PROFILER'S REMARKS ***Initials/date SJG/ 10/23/07***	The study was well-conducted and had adequate study design. However, the study was not designed for development of a dose response to fluoride as the emphasis was on monitoring dental fluorosis in children and on attempting to explain other factors besides fluoride in the drinking water that may contribute to fluorosis. Not surprisingly, children from Site 1 (Chanika School, low altitude, negligible water fluoride) had very little fluorosis (TFI and TSIF scores= 0.01), but the most caries (DMFS score = 1.39). Urinary fluoride levels (0.52 mg/L) were consistent with water (0.05 mg/L) and meal fluoride levels (0.49 mg/L). The mean magadi fluoride level was high (16010 mg/L), but magadi use was lowest in this group (77% of families, 1.5 times/week) and fewer babies and toddlers were fed food cooked with magadi (9.5% answered 'yes') according to interviews. Children from Site 2 (Rundugai School, mid-altitude, high water fluoride) had moderate fluorosis (TFI = 4.44; TSIF=3.14) and low caries experience (DMFS=0.15). Urinary fluoride levels (4.43 mg/L) were consistent with water (5.72 mg/L) and meal fluoride levels (2.47 mg/L).

		Children from Site 3 (Kibosho School, high altitude, negligible water fluoride) had surprisingly high fluorosis scores (TFI=4.39; TSIF=3.59) and urinary fluoride concentrations (1.43 mg/L) relative to water fluoride levels (0.18 mg/L); however, fluoride from meals contributes to urinary fluoride levels, so urinary fluoride levels actually were not surprising. Several factors that were common to the subjects at Site 3 have been theoretically associated with severe dental fluorosis: residence at high altitude; relatively high magnesium; excessive fluoride in food due to magadi use; and malnutrition. Caries experience also was low (DMFS=0.19). Limitations of the study: o High altitude alters urinary excretion of fluoride, so urine may not be the best body fluid for measuring fluoride body burden; however, blood sampling was not feasible in this study. Urine samples from toddlers (during amelogenesis) could have provided additional information, but this was beyond the scope of the current study. o Element analysis was conducted on only 2 magadi samples each from Sites 1 and 3, so results are suggestive but not conclusive. o Statistics methods were not described. o Malnutrition data were not available for Site 1.
PROFILER'S ESTIM. NOEL/NOAEL		Study design was not suitable for development of a NOAEL for fluorosis or caries.
PROFILER'S ESTIM. LOEL/ LOAEL		Study design was not suitable for development of a LOAEL for fluorosis or caries.
POTENTIAL SUITABILITY FOR DOSE-RESPONSE MODELING:		Not suitable (X), Poor ( ), Medium ( ), Strong ( ) While the study was well-conducted, the study design was not conducive to provide data for a dose-response. The study indicated that factors besides drinking water fluoride levels contribute to fluorosis prevalence and severity (e.g., altitude, food additive, nutrition). The study did not address any issues of plaque or gingivitis.
CRITICAL EFFECT(S):		Severity of dental fluorosis; caries experience