# Relative Effects of Pre- and Posteruption Water Fluoride on Caries Experience of Permanent First Molars

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## Abstract

***Objectives:*** *Previous studies have attributed the caries-preventive effects of preeruption (PRE) and posteruption (POST) exposure to fluoridated water based on data collected before and after the commencement or discontinuation of water fluoridation. This study aims to determine the relative pre- and posteruption exposure effects of fluoridated water on caries experience of 6–15-year-old Australian children based on individual residential histories.* ***Methods:*** *Parental questionnaires covering residential history of participants were linked to their oral examinations conducted between June 1991 and May 1992 by the School Dental Services of South Australia and Queensland. Percentage of lifetime exposed to optimally fluoridated water PRE and POST was calculated with respect to the eruption age for first permanent molars. Combined pre- and posteruption categories were created to test PRE against POST exposure: PRE & POST=0, PRE<POST, PRE=POST in the range 0–90 percent of lifetime exposure, PRE>POST, and PRE & POST≥90 percent lifetime exposure. These categories were used as indicator variables with PRE and POST=0 as reference in an analysis of first permanent molar DMFS scores. The linear regression model controlled for important potential confounders.* ***Results:*** *Participation rates were 69.7 percent in South Australia and 55.6 percent in Queensland with 9,690 and 10,195 participants, respectively. Pre- and posteruption exposures were strongly correlated (r=.74; P<.01). Compared to the reference, the categories PRE>POST, PRE=POST in the range 0–90 percent, and PRE and POST≥90 percent showed significantly lower caries levels.* ***Conclusions:*** *The findings indicated that preeruption exposure was required for a caries-preventive effect and that exposure after eruption alone did not lower caries levels significantly. However, the maximum caries-preventive effects of fluoridated water were achieved by high pre- and posteruption exposure. [J Public Health Dent 2003;63(1):11-19]*

*Key Words: water fluoridation, dental caries, children.*

Opinions conflict on the relative effects of preeruption (PRE) and posteruption (POST) exposure to fluoridated water on dental caries experience of permanent teeth in children. A number of fluoridation studies in the 1950s, 1960s, and 1970s separated the caries-preventive effects of PRE exposure to fluoridated water from that of POST exposure by examining caries differences before and after the commencement and discontinuation of water fluoridation (1-9). Calculation of exposure was based on period of residence and it was assumed that all children of any one age cohort had similar exposure, so the analysis was restricted to the aggregate exposure data. Individual level data linking caries with exposure for each subject would provide a more powerful tool in determining the association.

By the early 1970s there were multiple sources of fluoride available, particularly fluoridated toothpaste. The Tiel-Culemborg study recognized this and presented the distribution of use of these discretionary sources. Their use also varied across the duration of the study. In 1969, for example, 10-15 percent of the toothpaste was available with fluoride in the Netherlands (10). A questionnaire sent home to the clinically examined children revealed that by 1983 about 95 percent of the children in Tiel and Culemborg used fluoridated toothpastes and 3 percent used fluoride tablets (9). However, the use of discretionary sources of fluoride and the variation in usage was not controlled for in the analysis of the Tiel-Culemborg study. In addition, other potential confounders such as socioeconomic status (SES) and dietary factors associated with caries levels and exposure were not controlled for in the analyses of these early studies (1-9). These could have contributed to a bias in the results.

Most of these fluoridation studies were conducted during periods of high caries levels. In the late 1970s it became evident that a marked reduction in caries experience among the children and young adults was underway in most developed countries (11). Most researchers have linked the decline to greater use of fluorides in the 1970s (11,12). Fluoridation studies investigating relative pre- and posteruption water fluoridation effects did not use a cutoff age (i.e., eruption age) before and after which exposure could be measured as pre- and posteruption exposure levels, respectively. This would have been a more precise estimate. For the above reasons, it is necessary to evaluate the relative pre- and posteruption exposure effects on low caries experience at the individual level in a population study, controlling for multiple fluoride sources as well as a range of potential confounders.

At present there are multiple means of fluoride exposure, most of which have differential patterns of PRE and POST exposure and therefore potential caries-prevention roles. Water fluoridation can provide caries-pre-

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ventive benefits through both PRE and POST exposure, although it is a recognized source of exposure before eruption through systemic ingestion, whereas other sources such as fluoridated toothpaste are meant to be a source of posteruptive exposure through topical application. With the availability of other fluoride vehicles, the use of water fluoridation is sometimes questioned. The relative benefit of pre- and posteruption exposure is thus important in informing oral health policy on the prevention of caries, particularly policy on fluoridating public water supplies.

Opponents of water fluoridation in Australia have claimed that any small benefit of water fluoride is due to its topical action (13). Review articles have credited the anticariogenic effect of fluoride to be a primarily topical action through the promotion of remineralization of previously demineralized tooth hard tissues (14,15), although a preeruptive role continues to be suggested (16). There exists a need to study relative beneficial effects of pre- and posteruptive exposure using more recent data with detailed information on residential and, thereby, fluoride history and other fluoride exposures as well as control for socioeconomic variation (17). This study aimed to determine the pre- and posteruption exposure effects of fluoridated water in the prevention of caries on first permanent molars of Australian children aged 6–15 years, based on individual exposure histories and controlling for the effect of potential confounders.

## Methods

This project used baseline data from the Australian Child Fluoride Study (CFS), a multisite, three-year prospective, longitudinal study of caries in children. The data were collected between June 1991 and May 1992 through clinical examinations and parental questionnaires (18). Each individual's entire residential history of exposure to fluoridated water from birth to current age was determined along with his or her caries experience at the time of examination.

This study used data from two contrasting exposure sites, with South Australia having 70 percent of its population of 1.5 million people living in fluoridated areas and Queensland having only 5.1 percent of its population of 3.1 million people living in fluoridated areas (19). The rationale for this approach was to provide a large range of variation in fluoride exposure levels. The mobility of each individual during his or her lifetime also contributed to different exposure levels.

**Sampling:** All subjects enrolled in the CFS received school dental services in the states of South Australia and Queensland. School dental services in the two states provided periodic dental examinations as well as preventive, restorative, and other nonspecialist dental services (e.g., professional fluoride applications, pit and fissure sealants). The subjects of the CFS were sampled through a random sampling scheme according to their day of birth in any month. There were four strata, two in each state: metropolitan Adelaide and the rest of South Australia in South Australia, and metropolitan Brisbane and the rural city Townsville in Queensland. The sampling scheme of the four strata helped provide similar numbers from each of the four strata and has been described in an earlier paper (19). The children attending the school dental services during the period between June 1, 1991, and May 31, 1992, for a routine examination were sampled for the study (18). Each child was issued a study kit containing a consent form and questionnaire for completion by their parents. Completed parental questionnaires were returned in prepaid envelopes.

**Oral Examinations.** School dental practitioners or providers/clinical staff (i.e., dental therapists and dentists) examined the sampled children following the World Health Organization criteria for decayed, missing, and filled indices in primary (dmfs) and permanent (DMFS) teeth (20). A surface-based assessment was used, with additional coding for surfaces that were sound and unrestored, or fissure sealed. All examiners were given written descriptions of the criteria and procedures and the supervising staff met with the researchers for criteria discussions. Because of the large numbers of clinical staff involved, no additional procedures for standardization of examiners or assessment of examiner reliability through replicate examinations were performed (19).

**Parental Questionnaires.** The parental questionnaire asked about the child's residential history since birth. The date of birth was required and areas of residence starting from the current one were listed in reverse order. All areas lived in for longer than six months were recorded along with their respective usual sources of drinking water. SES measures and use of discretionary sources of fluoride were included in the questionnaire. The parents of sampled children who hadn't responded by completing and sending in the questionnaires were sent up to two reminder notices (21). Prior to data collection for the main study, pretesting of the questionnaire was carried out on a small convenience sample.

**Data Analysis:** DMFS for the first permanent molars (DMFS6) was the dependent variable in the analysis of tooth surface level data. A cut-off or threshold age was required before and after which PRE and POST exposure could be calculated for each subject. The average age of eruption of the first permanent molars was used based on the results of a South Australian study (22), revealing different eruption dates for males and females. Thus, the threshold ages were 80 months (6.67 years) and 78 months (6.50 years) for males and females, respectively. The period of life before and after the threshold ages represent preeruption and posteruption periods, respectively. For subjects whose age was less than or equal to the threshold age posteruption exposure was taken as 0. Subjects with missing residential history information (i.e., whose total residence history available did not add up to the current age) were excluded from the analysis since it was not always known whether the missing period was pre- or posteruption. There were 2.3 percent of the respondents to the questionnaire with missing residential history information who were excluded.

The information from the questionnaires revealed the source of water intake at home, which could be one or more of the following: public supply, tank water, and/or some other source. Tank water refers to rainwater stored in tanks of houses and which contains negligible fluoride. Public supply, which refers to tap water, was the only potential source of fluoride from water since nonpublic sources such as tanks, bores, and bottled water were assumed to have less than 0.3 ppm. Information on the fluoride level of the public water supply was collected from the water authority of each region. Although source of water intake was collected, there was no specific question on quantity of water consumed because it was assumed there would be no systematic bias in volume of water consumed by fluoridation status. A related issue was the assumed level of optimal exposure to water fluoride in the two states of South Australia and Queensland, which have different climates. However, further analyses showed that reassigning different values for optimal exposure had little effect on parameter estimates (19).

A postcode-fluoride database was used to map fluoride exposure to residential history. There was variation in the precision with which fluoride concentrations were specified due to the nature of the sources of information available to compile the database. Therefore, the fluoride concentrations in the public water supply were categorized as 0 ppm (where the listed concentration was less than 0.3 ppm), 0.5 ppm (listed concentrations in the range 0.3–0.7 ppm) or 1 ppm (listed concentrations above 0.7 ppm), which was optimal exposure (19). Besides drinking water, water could be consumed indirectly for cooking purposes, or in beverages and soft drinks. In addition, most manufactured foods themselves contain a fraction of water that is derived from the public water supply of the area. Therefore, if a person lived in an area that was optimally fluoridated and drank tank water, they would still be exposed to fluoride through prepared foods and beverages. Estimates of the fluoride intake attributed to drinking water and dietary sources other than drinking water were based on those adopted by the National Health and Medical Research Council (NHMRC) (23) for a 2-year-old living in that area (24-26). This age was selected because 2-year-olds have the maximum intake of fluoride per kilogram of body weight due to their low body weight. There were nine possible percentages of fluoride exposure based on area of residence and source of water intake using the NHMRC guidelines (Table 1).

With the knowledge of the period of residence at different places, fluoride exposure (Table 1), and the age of the child, the percentage of lifetime exposure pre- and posteruption could be calculated by using the threshold age. Percentage of lifetime pre- and posteruptive exposure to optimally fluoridated water were calculated by the following formulas:

preeruptive:

Eq. 1

$\Sigma$ time of residency (until subject was of threshold age) × percentage of fluoride exposure (fluoride concentration of public water supply of that area and water source(s) used) ÷ [threshold age]

posteruptive:

Eq. 2

$\Sigma$ time of residency (threshold to current age) × percentage of fluoride exposure (fluoride concentration of public water supply of that area and water source(s) used) ÷ [age – threshold age]

The products of time periods in different residential locations by their percentage of fluoride exposure were summed and divided by the total preeruptive or posteruptive periods. The resulting figure represented the fraction of pre- or posteruptive period with optimal water fluoride exposure. This figure was expressed as a percentage. Two examples on calculating pre- and posteruptive exposure are given.

**TABLE 1**
**Percentage of Exposure to Fluoride by Water Source and Fluoride Concentration**

| Fluoride Concentration of Residence Area | Water Source Used: Public Only | Tank/Other | Tank & Public |
|---|---|---|---|
| 1.0 ppm | 100% | 70% | 85% |
| 0.5 ppm | 50% | 35% | 43% |
| 0.0 ppm | 0% | 0% | 0% |

Example 1: In a female child (threshold age=78 months) aged 138 months who first lived for 22 months in a place where her exposure was 0 ppm, then in the next place for 72 months where her exposure was again 0 ppm, then for the next 43.5 months in a place where it was 1 ppm and then 0.5 months where she is still living it was 1 ppm, the pre- and posteruptive exposure would be:

preeruptive = {22×0} + {(78–22)×0} ÷ 78
=0.00=0% lifetime exposure

posteruptive= {(72–56) × 0} + {43.5×1} + {0.5×1} ÷ (138–78)
=0.7333=73.33% lifetime exposure

Example 2: In a male child (threshold age=80 months) aged 178 months who first lived for 120 months in a place where his exposure was 0.35 ppm, then in the next place for 10.5 months where his exposure was 1 ppm, and then 47.5 months where he is still living it was 0 ppm, the pre- and posteruptive exposure would be:

preeruptive={80×0.35}÷ 80
=0.35=35% lifetime exposure

posteruptive={(120–80)×0.35}+ {10.5×1} + {47.5× 0} ÷ (178–80 )
= 0.25= 25.00% lifetime exposure

The condition pre- greater than posteruption exposure would imply that a greater percentage of the preeruptive period had optimal water fluoride exposure than the posteruptive period. On the other hand, the condition pre- less than posteruption exposure would imply that a greater percentage of the posteruptive period had optimal water fluoride exposure than the preeruptive period. A 100 percent lifetime exposure represented the maximum exposure so that a 100 percent preeruptive exposure would mean optimum exposure throughout the preeruptive period (i.e., until the child reaches threshold age) and 100 percent posteruptive exposure would mean optimum exposure from the threshold age to the current age.

Pre- and posteruption lifetime percentages of exposure to optimally fluoridated water were grouped into six categories: 0 percent, >0 – <30 percent, 30 – <60 percent, 60 – <90 percent, 90 – <100 percent, and 100 percent lifetime exposure. The rationale for the coding of these groups was influenced by the actual distribution of the values with the desire to obtain sufficient numbers in each category and to have categories that represented an even range of values across the distribution. The large numbers of subjects with exposure values of 0 percent and 100 percent dictated that these be coded as discrete exposure categories. The category 90–<100 percent was chosen on conceptual grounds to provide a high exposure group that could be differentiated and compared against the 100 percent category. The remaining categories in the range >0 percent and <90 percent were coded to obtain equal intervals of exposure.

Although both pre- and posteruption exposures are independent variables affecting the outcome, it was important to assess the degree of association between them. A strong association would limit the ability to separate the effects of preeruption and posteruption exposure. In the process, one of the two would mask the effect of the other. The Pearson correlation coefficient was calculated between the continuous variables measuring percentage lifetime of pre- and posteruption exposure. A value equal to or greater than 0.7 indicates a high correlation, thus suggesting a marked relationship between the variables (27).

Matrices were formulated by the cross-tabulation between the frequencies of the categorical pre- and posteruption exposure variables. As there were six categories in each exposure variable, the number of rows (i) and columns (j) of the resulting array of numbers were six each, respectively. In this way, a symmetric matrix was formed (28). The exposure frequencies could be either lying on the diagonal (i=j) or off the diagonal (i≠j), giving an indication of the correlation between preeruption and posteruption exposure. A combined variable for PRE and POST exposure was created. The combined exposure variable was coded into five categories. The rationale behind the coding adopted was to create a set of ordered categories with varying degrees of exposure that would allow comparison of PRE and POST exposure while maintaining sufficient numbers in each category for analysis. The five categories thus created were basic to the requirement to test PRE against POST exposure.

The five categories were defined in increasing order of PRE exposure: (1) both PRE and POST exposure of 0 percent lifetime; (2) PRE<POST exposure; (3) PRE=POST exposure; (4) PRE>POST exposure; (5) maximum exposure for PRE and POST. The second and fourth categories were created to test PRE against POST exposure. For a subject to belong to the second category the PRE exposure could be in the range 0–<90 percent, whereas POST exposure was in the range >0–100 percent with the condition that PRE<POST exposure. The subjects belonging to the third category were coded to have PRE and POST exposure in the range >0–<90 percent with the condition that PRE=POST. The actual range of exposure after coding was 35–85 percent in the third category. The fourth category had reverse conditions from the second category for PRE and POST exposure. Category V had the combination of maximum PRE and POST exposure in the range ≥90–100 percent. The coding schema for the development of the combined variable is shown in Figure 1.

Apart from the main exposure variable of interest, there were potential confounders such as age, SES, and discretionary fluoride sources. SES was measured by including questions on the annual pretax income, highest level of educational attainment, and occupation in the parental questionnaire. Among the three SES measures, parental income was selected for reasons of parsimony using stepwise methods prior to inclusion in the multivariate model. Exposure to fluoride through sources other than fluoridated water such as fluoride toothpastes, tablets/drops, infant formulas, and mouthrinses were taken as potential confounders.

The questionnaire asked about current brushing frequency and mouthrinsing. In the analysis they have been expressed as categorical variables representing the frequency (fluoride tablets/drops, toothpastes, and mouthrinses) and duration (fluoride tablets/drops and mouthrinses) of their usage. Frequency of brushing, expressed as an ordinal variable, was included in the analysis as average number of times being brushed per day. For the purpose of the analysis they were grouped into three categories: less than once a day, once to less than twice, twice or more. Professional fluoride treatment was also included as an explanatory variable, as it could potentially alter the relationship between exposure to fluoridated water and caries experience.

Age at which the child participant started toothbrushing was an indicator of dental behavior. Fluoridated toothpastes were assumed to be a source of posteruption exposure to fluoride, although inadvertent swallowing by young children could contribute to a preeruptive effect. In the analysis, this variable was expressed categorically as: 0–<2 years, 2–4 years, and >4 years of age. Another potential confounder in the association was use of fissure sealants that was described by the number of surfaces fissure sealed with categories: 0, 1–2, and 3–8 surfaces.

Indicator variables were created from the combined lifetime exposure to fluoridated water variable and potential confounders of age, parental income, age at which the child started brushing, frequency of brushing with

**FIGURE 1**
**Coding Used in Development of Combined PRE and POST Exposure Variable**

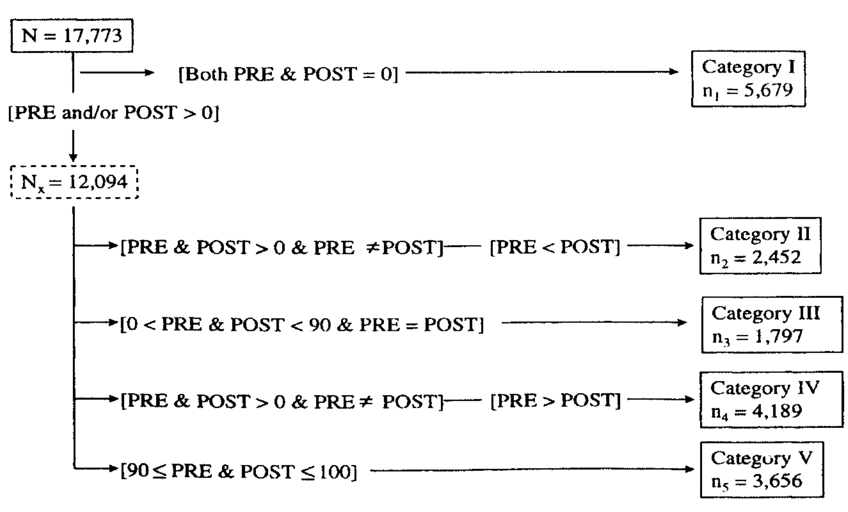

**TABLE 2**
**Cross-tabulation of Pre- versus Posteruption to Fluoridated Water (*N*=17,773)**

| | Posteruption | | | | | |
|---|---|---|---|---|---|---|
| Preeruption | 0% | >0–<30% | 30%–<60% | 60%–<90% | 90%–<100% | 100% |
| 0% | 5,679 | 155 | 139 | 127 | 29 | 10 |
| >0–<30% | 536 | 73 | 126 | 95 | 9 | 235 |
| 30%–<60% | 652 | 100 | 1,064 | 243 | 22 | 310 |
| 60%–<90% | 683 | 88 | 184 | 1,680 | 43 | 545 |
| 90%–<100% | 476 | 8 | 45 | 155 | 17 | 121 |
| 100% | 43 | 120 | 146 | 297 | 68 | 3,450 |

fluoride toothpaste, professional fluoride treatment received, fluoride supplement use, use of infant formula, use of fluoride mouthrinses, and number of surfaces fissure sealed. A reference group for each variable was selected against which significance of the indicator variables was determined using ordinary least squares regression. In this way, beta coefficients of indicator variables were also obtained, indicating the direction and strength of association with respect to the reference group.

**TABLE 3**
**Exposure Categories of Combined Pre- and Posteruption Exposure Variable and Their Mean Percentage of Lifetime Exposed to Fluoridated Water**

| | Coding Criteria with Coding Range | Coded Exposure Category (Mean Exposure) | Range after Coding | |
|---|---|---|---|---|
| | | | Preeruption | Posteruption |
| I | PRE=0.0; POST=0.0 | PRE (0.0)=POST (0.0) | 0.0–0.0 | 0.0–0.0 |
| II | 0.0≤PRE<90.0; 0.0<POST≤100.0 | PRE (40.1)<POST (77.4) | 0.0–90.0 | 1.0–100.0 |
| III | 0.0<PRE<90.0; 0.0<POST<90.0 | PRE (60.0)=POST (60.0) | 35.0–85.0 | 35.0–85.0 |
| IV | 0.0<PRE≤100.0; 0.0≤POST<90.0 | PRE (66.6)>POST (22.6) | 1.0–100.0 | 0.0–90.0 |
| V | 90.0≤PRE≤100.0; 90.0≤POST≤100.0 | PRE (99.8) & POST (99.9)≥90.0 | 90.0–100.0 | 90.0–100.0 |

## Results

**Subject Participation.** The subjects whose parents gave their consent by signing and returning the consent form were regarded as participants. Of the 13,911 children sampled for the study in South Australia, 9,690 (69.7%) participated. In Queensland, the participation rate of the 18,348 children sampled was lower at 55.6 percent, with 10,195 children participating (19). Participation rates varied by age group and strata. In general, participation rates were higher among younger age groups. For example, in Adelaide the participation rate for 5-year-olds was 70.4 percent compared with 59.8 percent for 15-year-olds (19). The majority of children participating in the study were aged younger than 12 years, with an age distribution of 6–7 years (28.8%), 8–9 years (27.3%), 10–11 years (26.4%), 12–13 years (13.2%), and 14–15 years (4.3%). Although 9,690+10,195=19,885 children participated, there were 17,773 children whose returned questionnaires provided complete residential history.

**Caries Distribution.** A frequency distribution of DMFS6 scores across the group was determined. A total of 17,031 participants had one or more first permanent molars. The mean DMFS6 was 0.60 (SD=1.37), with a range of 0 to 20. More than 12,000 subjects had a DMFS6 score of 0. The distribution was highly positively skewed, with a skewness of 3.46.

**PRE and POST Exposure Variables.** The distribution of subjects by PRE and POST and the cross-tabulation of PRE versus POST is given in Table 2. The cell representing 0 percent PRE and POST exposure had the highest count (5,679). The next highest count (3,450) represented those with 100 percent PRE and POST exposure. Not all the subjects of cells lying on the diagonal corresponding to categories <0–<30 percent, 30–<60 percent, and 60–<90 percent of PRE and POST exposure had equal PRE and POST exposure. The cells represent cases whose PRE exposure was in the same range as POST exposure, a subset of which is the cases with equal PRE and POST exposure in the range <0–<90 percent. This subset is a separate category in the combined PRE and POST exposure variable described in the next paragraph. The cross-tabulation between PRE and POST exposure showed that most participants had similar PRE and POST exposure. Thus, PRE exposure was strongly associated with POST exposure. The Pearson correlation coefficient between PRE and POST was 0.74 ($P<0.01$), which suggested a positive, high collinearity, therefore justifying the adoption of a combined exposure variable for PRE and POST as outlined in the *Methods* section to avoid collinearity.

The number of subjects in the categories of the combined exposure variable is presented alongside the coding scheme in Figure 1. The category with no exposure to fluoridated water PRE or POST had the highest number of subjects with 5,679. This was followed by the category with PRE > POST exposure with 4,189 subjects. The category with the lowest count of 1,797 subjects had each subject with equal

**TABLE 4**
**Bivariate Linear Regression for Association of DMFS6 with Explanatory Variables**

| Independent Variables | Mean | *P*-value |
|---|---|---|
| Combined exposure groups (% lifetime) | | |
| PRE & POST=0 | 0.67 | Ref. |
| PRE<POST | 0.68 | .723 |
| PRE=POST | 0.63 | .298 |
| PRE>POST | 0.51 | .000 |
| PRE&POST≥90 | 0.48 | .000 |
| Age (years) | | |
| 6–7 | 0.15 | Ref. |
| 8–9 | 0.39 | .000 |
| 10–11 | 0.79 | .000 |
| 12–13 | 1.15 | .000 |
| 14–15 | 1.62 | .000 |
| Parental income | | |
| Up to $20,000 | 0.74 | Ref. |
| $20,001–$30,000 | 0.62 | .000 |
| $30,001–$40,000 | 0.56 | .000 |
| $40,001–$50,000 | 0.48 | .000 |
| Above $50,000 | 0.46 | .000 |
| Age at which child began brushing (years) | | |
| <2 | 0.52 | Ref. |
| 2–4 | 0.72 | .000 |
| >4 | 1.06 | .000 |
| Brushing frequency (per day) | | |
| Less than once | 0.86 | .000 |
| Once to less than twice | 0.67 | .000 |
| Twice or more | 0.54 | Ref. |
| Professional fluoride treatment (times) | | |
| 0 | 0.47 | Ref. |
| 1–2 | 0.55 | .001 |
| 3–4 | 0.73 | .000 |
| 5 or more | 1.06 | .000 |
| Fluoride supplement use (months) | | |
| 0 | 0.58 | Ref. |
| >0–50 | 0.64 | .072 |
| More than 50 | 0.57 | .887 |
| Use of mouthrinse | | |
| Yes | 0.74 | .000 |
| No | 0.59 | Ref. |
| Use of infant formula | | |
| Yes | 0.63 | Ref. |
| No | 0.54 | .000 |
| Number of first molar surfaces fissure sealed | | |
| 0 | 0.54 | Ref. |
| 1–2 | 1.12 | .000 |
| 3–8 | 0.47 | .036 |

Bivariate linear regression against reference (Ref.) group.

PRE and POST exposure in the range >0–<90 percent lifetime. The five categories of the combined variable are described in Table 3.

**DMFS6 Bivariate Linear Regression.** Group means for DMFS first molars by the indicator variables were calculated and bivariate linear regression analyses compared the means with a reference category for each independent variable. Table 4 lists the group means and indicates the significant differences.

Among the exposure variables, the categories with PRE & POST≥90 percent and PRE>POST had significantly lower DMFS scores compared to the reference category of no exposure. Caries experience increased with age, age at which a child started brushing, lower brushing frequency, higher numbers of professional fluoride treatments, mouthrinsing, and use of infant formula, and decreased with increasing parental income. Use of fissure sealants on 1–2 surfaces was associated with significantly increased DMFS6 scores and use on 3–8 surfaces was associated with significantly decreased DMFS6 scores. There was no significant association of DMFS6with fluoride supplement use.

**Testing PRE against POST Exposure in the Multivariate Model.** Table 5 shows the results of ordinary least squares regression for DMFS6 on controlling for potential confounders. The negative beta coefficients of the exposure variables indicate preventive effects compared to the reference of no PRE and POST exposure (Table 5). A decreasing caries experience with increasing PRE exposure (i.e, an exposure-response relationship) was observed. Among the potential confounders, mouthrinsing, use of infant formula, and use of fluoride supplements from >0–50 months were each nonsignificant. The beta coefficients of the variables for professional fluoride treatment showed an increase in strength with increasing number of times of treatment. There was an increase in strength of positive beta coefficients with decrease in brushing frequency compared to the reference of maximum brushing frequency of twice or more times a day. Use of fluoride supplements as drops or tablets for over 50 months' duration was associated with decreased caries levels. Use of fissure sealants in 3 or more surfaces was associated with significantly lower DMFS6 scores and use in 1–2 surfaces with significantly higher DMFS6 scores compared to the reference group of no use of fissure sealants. This suggested that children who were targeted were in need of application as noted by the higher caries scores for those with 1–2 surfaces sealed. The beneficial effects came out on use in 3 or more surfaces indicated by the lower caries scores. Controlling for potential confounders, the lowest caries experience was associated with high PRE and POST exposure and exposure to a higher PRE than POST was more beneficial than exposure to a higher POST than PRE. The model $R^2$ value showed 11.8 percent of the variance in the DMFS first molar score could be explained by the independent variables.

## Discussion

The results showed an important PRE exposure caries-preventive effect. The categories with high POST exposure and low PRE exposure did not have significantly lower mean caries scores with respect to their reference groups. The category with PRE = POST exposure had mean lifetime percentage of exposure of 60.0 percent for both PRE and POST. Categories with PRE<POST and PRE>POST had mean PRE exposures of 40.1 percent and 66.6 percent, respectively. Correspondingly, there was an increasing strength of beta coefficients with increasing PRE exposure among these three categories, thus exhibiting an exposure-response relationship between PRE exposure and caries. Even though the category PRE<POST had a higher mean POST exposure of 77.4 percent lifetime exposure, the low PRE exposure was associated with a higher, nonsignificant DMFS6 score.

Exposure to fluoridated water in the POST period alone did not suffice in restricting caries to low levels, whereas a PRE exposure alone resulted in lower overall DMFS6 scores. The maximum caries-preventive effect however, was achieved by both high PRE and POST exposure. Thus, the relative importance of preeruptive exposure in this multisite study using individual exposure histories appears greater than the current predominant view (14,15,29).

In the bivariate linear regression analysis, use of infant formula instead of breast milk may be linked to low SES and education, and hence increased caries levels. Subjects with higher risk (reflecting the existing caries level) may have been given professional fluoride treatment and advised to perform mouthrinsing. Of the 10 explanatory variables, the significance and direction of seven were consistent in the bivariate and multivariate analyses. Two were significant in the bivariate and not in the multivariate (mouthrinsing and use of infant formula), while one that was not significant in the bivariate was significant in

**TABLE 5**
**Multiple Linear Regression for Association of DMFS6 with Explanatory Variables**

| Independent Variables | β | *P*-value |
|---|---|---|
| Combined exposure groups (% lifetime) | | |
| PRE & POST=0 | Ref. | Ref. |
| PRE<POST | –0.001 | .936 |
| PRE=POST | –0.028 | .003 |
| PRE>POST | –0.033 | .001 |
| PRE&POST≥90 | –0.055 | .000 |
| Age (years) | | |
| 6–7 | Ref. | .Ref. |
| 8–9 | 0.065 | .000 |
| 10–11 | 0.183 | .000 |
| 12–13 | 0.222 | .000 |
| 14–15 | 0.199 | .000 |
| Parental income | | |
| Up to $20,000 | Ref. | Ref. |
| $20,001–$30,000 | –0.031 | .003 |
| $30,001–$40,000 | –0.039 | .000 |
| $40,001–$50,000 | –0.053 | .000 |
| Above $50,000 | –0.058 | .000 |
| Age at which child began brushing (years) | | |
| <2 | Ref. | Ref. |
| 2–4 | 0.040 | .000 |
| >4 | 0.053 | .000 |
| Brushing frequency (per day) | | |
| Less than once | 0.033 | .000 |
| Once to less than twice | 0.031 | .000 |
| Twice or more | Ref. | Ref. |
| Professional fluoride treatment (times) | | |
| 0 | Ref. | Ref. |
| 1–2 | 0.047 | .000 |
| 3–4 | 0.075 | .000 |
| 5 or more | 0.096 | .000 |
| Fluoride supplement use (months) | | |
| 0 | Ref. | Ref. |
| >0–50 | 0.002 | .841 |
| 5 or more | –0.028 | .001 |
| Use of mouthrinse | | |
| Yes | –0.001 | .904 |
| No | Ref. | Ref. |
| Use of infant formula | | |
| Yes | Ref. | Ref. |
| No | –0.015 | .070 |
| Number of first molar surfaces fissure sealed | | |
| 0 | Ref. | Ref. |
| 1–2 | 0.081 | .000 |
| 3–8 | –0.052 | .000 |

Ordinary least squares regression against reference (Ref.) groups.
Model $R^2$=11.8%.

the multivariate (fluoride supplement use). The difference in the significance between the bivariate and the multivariate analyses reflects control of the full range of confounding factors in the multivariate analysis. Some methodologic issues related to the Child Fluoride Study have been discussed elsewhere (19). A few methodologic issues relevant to the analysis of this study will be discussed in the next few paragraphs.

**Eruption Age Data.** Due to absence of information on eruption age of the participants, an estimate was made by taking the average age of eruption separately for males and females using a South Australian longitudinal study on eruption age. There were two advantages of using the data from that study:

- The study population from which the samples were drawn for both the eruption study and the Child Fluoride Study is located in the same geographic area.
- The time at which the studies were done overlaps (i.e, concurrent data).

In addition, the averages of eruption ages for the maxillary and mandibular first permanent molars were taken as the threshold ages for males and females separately to further increase the precision of the eruption age.

On the other hand, use of average age may result in misclassification because eruption ages vary and some of the participants would have had an early eruption and others a later eruption than the threshold ages. However, this misclassification is nondifferential, which would increase the possibility of the results to attenuate toward the null value of no association between exposure and outcome (30). The separate threshold ages taken for males and females were close to individual eruption ages and thus provided a precise estimate of the eruption age.

Another implication of taking an average eruption age as the threshold age was that some of the children whose age at examination was equal to or less than the threshold age, were assumed to have no POST exposure. These children were females aged 72–78 months and males aged 72–80 months. Their risk period was taken as 0 months. For the older children, the risk period could be much greater, increasing up to 102 months for girls and 100 months for boys. This variation in risk period was controlled by taking age as a confounding factor and controlling for it in the multivariate analysis.

**Dietary Patterns.** The CFS questionnaire did not include questions on dietary behavior of the participants such as sugar intake because in a low caries population the sugar-caries relationship is difficult to demonstrate (31).

**Negative Binomial Regression.** When the caries distribution with its skewed DMFS pattern was modeled using negative binomial regression, there was no alteration of the trend in beta coefficients of the exposure indicator variables. Therefore, a standard approach using ordinary least squares regression was used.

**SES Indicators.** Out of the three SES indicators asked in the questionnaire, income was preferred since it was entered prior to the other SES indicators in the stepwise procedure.

**Exposure Categorization into 0, 0.5, and 1 ppm.** Due to variation in precision in the postcode level of fluoride concentrations listed in the database, categorization to 0, 0.5, and 1 ppm was done to avoid a systematic bias. The various fluoride concentrations listed in the database were not random numbers, but select and few values; thus the nondifferential misclassification introduced by categorization was limited.

**Longitudinal Exposure Data.** While the residential history from the questionnaires allowed the calculation of PRE and POST exposure to water fluoride, an assessment of PRE and POST exposure to discretionary sources was not done. The resulting misclassification would be again nondifferential.

The Tiel-Culemborg study, commencing in 1953 with the fluoridation of Tiel, was the most thorough investigation of relative pre- and posteruption exposure benefits of water fluoride. The long study period (investigations being conducted until 1987/88) established the effects of the start and the end of fluoridation on caries levels. Van Eck's (32) investigation of the data showed an important preeruptive effect. The findings from the CFS indicated a greater advantage of a high preeruption exposure and hence were supportive of the findings of the Tiel-Culemborg study.

Researchers have questioned the earlier acceptance of the greater relative importance of preeruption exposure in caries prevention through incorporation of fluoride into enamel and dentin, stating that the difference in fluoride content of dentin and enamel between fluoridated and nonfluoridated areas is insufficient to explain reductions in caries in fluoridated areas. Whereas pure fluorapatite has a fluoride concentration of 38,000 ppm, that of enamel is usually only about 500–1,500 ppm (33). However, a sharp gradient with surface concentrations as high as 5,000 ppm fluoride could be reached in fluoridated areas (34). This may exist as a very thin layer of fluorapatite on the surface of hydroxyapatite crystal, converting crystal surfaces of enamel so that they behave as though they were fluorapatite (33). Consequently, there would be a significant decrease in enamel solubility contributing to the cariostatic effect of fluoride (34).

Although the caries-preventive action of fluoridated water had been established in over a half-century of research, the posteruptive benefits have been considered to outweigh preeruptive exposure effects in recent reviews (11,14,15,29). The use of topical sources has become increasingly important, although water fluoridation remains the most cost-effective method of caries prevention. As caries levels in developed countries have declined considerably in the past couple of decades with the additive effects of topically applied fluorides, the same absolute caries differences in fluoridated and nonfluoridated communities cannot be demonstrated, as they were 20 to 40 years ago (35).

Opponents of water fluoridation claim that the benefits of fluoride are due to its posteruptive (topical) action on teeth so that alternative fluoride vehicles can provide benefit without fluoride being ingested (36). Thus, the answer to the question of the value of preeruptive fluoride in caries prevention is critical to the future of water fluoridation and other systemic fluorides (35). This project separated the pre- and posteruptive effects of fluoride and the findings indicated the importance of a preeruptive exposure to fluoridated water without which there was no significant prevention of caries. The preventive effect was maximized by continuous exposure both before and after eruption. The results supported water fluoridation as a public health measure in view of the need for continuous exposure for the maximum benefit.

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