Determinants of Dropout in a Community Intervention Trial on the Caries-preventive Effect of Chewing Gums

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Abstract

Objectives: *This study describes determinants of dropout in a three-year community intervention trial of the effects of sugar-substituted chewing gums on caries progression rates.* ***Methods:*** *A total of 602 children aged 9–14 years from 28 school classes in five secondary schools in Kaunas, Lithuania, were given a clinical and radiographic baseline caries examination. The schools were assigned randomly to one of the following interventions: sorbitol/carbamide gum, sorbitol gum, xylitol gum, placebo gum, or no gum. Children in the four intervention schools were asked to chew at least five pieces of chewing gum per day, preferably after meals. The children were reexamined clinically after one, two, and three years of study, and radiographically after three years.* ***Results:*** *A total of 33 children (6%) had dropped out before the one-year clinical examination, an additional 29 children (5%) dropped out before the two-year examination, and a further 108 children (18%) dropped out before the final three-year clinical examination. A total of 230 children (39%) were not available or refused to participate in the three-year radiographic examination. Analyses using random effect logit models showed that, irrespective of time of follow-up, most of the cluster variation in dropout was related to school classes within the primary randomization units, the schools. The most important predictors of individual dropout were age and baseline caries experience, whereas sex was not associated with dropout.* ***Conclusions:*** *The results show that a community intervention trial of chewing gums carried out among schoolchildren is subject to cluster effects. Dropout was not primarily related to the randomization units themselves, i.e. the schools, but rather to subclusters of classes within the schools. These findings should be considered when designing community intervention trials and practical preventive programs among schoolchildren. [J Public Health Dent 2002;62(1):21-7]*

Key Words: dental caries, clinical trial, design, dropout, chewing gum, prevention.

Dental caries is known to be associated with sucrose consumption, and much interest therefore has focused on the possible caries-preventive effects of sugar substitutes when such substitutes are added to sweets and chewing gums. Many of the clinical studies on the effect of sugar substitutes, however, have suffered from a considerable loss of study subjects during the intervention period. Hence, the dropout rates reported in previous studies of two to three years' duration are in the order of magnitude of 11–52 percent (1-5). This constitutes a potentially serious problem, as the loss of subjects might be related to the determinants of the outcome of the study—e.g., the interventions or the baseline caries experience—thereby introducing a bias in the estimation of the effects (6). Furthermore, in practical preventive programs, the loss of subjects may lead to a reduced potential for healthy outcomes.

In previous caries-preventive trials, it has often been stated that the loss of study subjects could be ascribed to factors extraneous to the study (3,4,7), implying that the dropout reflects a real-life situation and therefore may be disregarded in scientific studies. However, this argument does not hold, as most trials involve regular follow-up examination and intensive supervision of interventions by schoolteachers, dental health care workers, parents, and study organizers (2-5,7,8). Moreover, comparisons of dropout subjects with subjects retained in the study indicate that the baseline caries levels differ between these groups (2,5,7). This could have led to a bias in the estimation of the effects of the caries-preventive interventions, as it might be expected that the subjects who could benefit the most from the interventions would be subjects with a high caries activity. Hence, it is important to identify the determinants of dropout to be able to take into account such factors in the analysis and interpretation of the results (9-11), as well as in the design of future studies.

The purpose of the present paper was to identify determinants of dropout in a three-year community intervention trial on the effect of sugar-substituted chewing gums on dental caries increments among Lithuanian schoolchildren.

Methods

Setting. The present community intervention trial was carried out during 1994–97 in the city of Kaunas, Lithuania, which has a population of approximately 350,000 inhabitants. A total of 602 children, aged 9–14 years, from 28 classes (grades 5 through 7) in five schools, were included in the study. The five schools were selected among 55 secondary schools in Kaunas based on (1) the willingness of the teachers to participate in a three-year caries-preventive clinical trial with chewing gums, and (2) the availability of at least four sixth grade classes in the school. School dental health serv-

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ices were available free of charge in all the selected schools.

Intervention. The schools were randomly assigned to a "no gum" group (negative control) (School E), a "placebo gum" group (positive control) (School D), a "xylitol gum" group (School C), a "sorbitol gum" group (School B), and a "sorbitol/carbamide gum" group (School A), respectively. All the gums had the same flavor; however, the flavor of the gum was changed from peppermint to spearmint after two years of study upon request from the children (12). Throughout the study neither the participants, their family members, the school teachers, the school dental health staff, nor the investigators were aware of the type of gum used in any of the schools. All children stayed in the same class during the study period. A detailed description of the study design, calculations of the sample size, and composition of the chewing gums have been reported previously (12).

Prior to the trial, the parents and teachers in every school were informed verbally and in writing about the study by the principal investigator (VM). Written informed consent was obtained from the parents of all the participating children. Twenty children were not allowed by their parents to participate in the study.

Intervention. The participants were instructed to chew five pieces of gum per day, each piece being chewed for at least 10 minutes, preferably immediately after meals. The teachers of each class were given responsibility for the daily distribution of the chewing gums and for supervision of chewing at school after lunch. During weekends and school vacations, the children were supplied with sufficient amounts of chewing gum to be able to comply with the instructions, and the parents were asked to observe proper use of the gums during these periods. To encourage collaboration with parents, the households of all the participating children were supplied on a weekly basis with an extra package of chewing gum (20 pieces) of the same type as used by the children. Throughout the entire study period, the principal investigator (VM) met regularly with the teachers (once a month) and with the children (every six months) in the intervention schools to stimulate compliance with the study protocol.

Clinical and Radiographic Examinations. All participating children were given an annual clinical caries examination during the study period. Furthermore, two sets of posterior bitewing radiographs were obtained from each child: one at baseline and one at the three-year follow-up examination. The diagnostic criteria used in the clinical and radiographic examinations have been described previously (12).

Statistical Analysis. Four questions were addressed: (1) Which was the most informative categorization of the school classes for the prediction of dropout from the clinical examinations at year 1, year 2, or year 3, respectively?; (2) Which was the most informative categorization of the school classes for predicting dropout from the radiographic examinations at year 3?; (3) Did age, sex and baseline clinical caries experience influence new dropouts from the clinical examination at year 1, year 2, or year 3, respectively?; and (4) Did age, sex, and baseline radiographic caries experience influence dropout from the radiographic caries examination at year 3? As the variables school, grade within school, and school class have a hierarchical structure, such that school classes are nested within grades, and grades are nested within schools, the first two questions were addressed by means of fitting a series of logit models using school (five levels), grades within schools (11 levels), and school class (28 levels), respectively, as random effect variables. These models allow for excess variation between levels of the random factors (the clusters), thereby introducing correlation between observations from the same cluster. This correlation, ρ, may also be interpreted as the proportion of the total variance contributed by these clustering variables. These analyses were carried out using procedure xtlogit of STATA (13). Questions 3 and 4 were addressed by means of logistic regression analyses using procedure logit of STATA (13) of age, sex, and baseline caries experience as predictors of dropout (14), using option "cluster" to account for the interdependence of observations within the clusters as determined above, and option "robust" to obtain robust variance estimates.

Two different measures of baseline clinical caries experience were considered as potential predictors of dropout from the clinical caries examinations: (1) DMFS including both cavitated and noncavitated caries diagnoses, and (2) DMFS including only clinically cavitated stages of lesion formation. The measure of baseline radiographic caries experience considered as a predictor of dropout from the radiographic caries examination was the DMFS as assessed in posterior bitewing radiographs. DMFS scores were expressed as relative scores (DMFS*100/Number of erupted and recordable surfaces). The baseline caries variables were categorized using the quartiles as cutpoints.

As logistic regression analyses showed that the variable percent DMFS including all stages of lesion formation had a higher predictive power, as assessed by the deviance, than had the percent DMFS including only cavitated stages, the former was used in the logistic regression analyses of individual predictors of dropout from the clinical examinations.

Ethical Considerations. The study was approved by the Independent Board of Ethics of Kaunas Medical Academy, Kaunas, Lithuania, as well as by the Ethical Committee of Medical Science, Aarhus, Denmark.

Results

Table 1 shows the percentage distribution of children who dropped out from the clinical and radiographic follow-up examinations by age, sex, and baseline DMFS values. Overall, 33 (6%) of the 602 children given a clinical baseline caries examination had dropped out of the trial at year 1, whereas an additional 29 children (5%) dropped out between year 1 and year 2, and 108 children (18%) dropped out between year 2 and year 3. In three of the 28 classes there was no dropout at all; in 13 classes, there was new dropout at all three time periods considered; in nine classes, dropout was confined to two of the three time periods; and in three classes, dropout was confined to one time period only. A total of 230 children (39%) of the 592 children who were given a baseline radiographic examination were not available for the three-year radiographic follow-up examination.

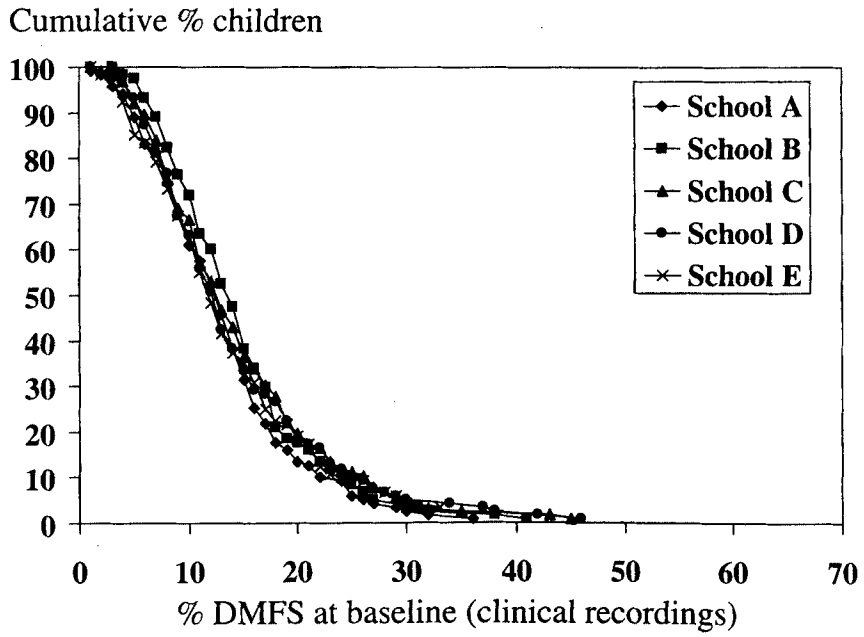
Figures 1–3 show the cumulative frequency distribution for each of the five schools of number of children according to the baseline percent DMFS including noncavitated caries lesions

TABLE 1
Percentage Distribution of Dropout from Clinical Caries Examination at Year 1, Year 2, and Year 3, and from Radiographic Caries Examination at Year 3 by Age, Sex, and Baseline DMFS Values Among 602 Schoolchildren, Kaunas, Lithuania, 1994–97

		Clinical Examination			Radiographic Examination
	*N**	Before Year 1	Between Years 1 and 2	Between Years 2 and 3	Before Year 3
Age (years)					
10	61	1.6	3.3	6.9	32.2
11	328	4.6	4.5	16.1	35.8
12	213	8.0	6.6	30.1	46.3
Sex					
Male	305	5.9	4.5	20.8	41.4
Female	297	5.1	5.7	19.2	36.8
% DMFS (clinical)					
0–7	142	1.4	3.6	14.1	—
8–11	141	6.4	3	23.4	—
12–17	179	8.4	3.7	23.5	—
18+	140	5	10.5	18.5	—
% DMFS (radiographic)					
0–8	144	—	—	—	36.8
9–14	150	—	—	—	39.3
15–21	148	—	—	—	36.5
22+	146	—	—	—	43.8

*Number of children examined at baseline. Percentages calculated based on number of children at risk of dropout.

FIGURE 1
Cumulative Frequency Distributions of 602 Schoolchildren in Kaunas, Lithuania (1994), According to Clinical Baseline % DMFS, Calculated Using All Stages of Lesion Formation (given for each of five schools)



(Figure 1), percent DMFS including only cavitated lesions (Figure 2), and percent DMFS based on recording of posterior bitewing radiographs (Figure 3). The prevalence of caries was 100 percent when all stages of lesion formation was considered (Figure 1), greater than 85 percent when only cavitated lesions were considered (Figure 2), and greater than 90 percent when recordings were based on radiographic evidence (Figure 3). The cumulative frequency distribution of the number of children according to their baseline percent DMFS were essentially identical for the five schools, with the exception that children in school C tended to have a relatively greater proportion of the caries experience in the form of cavitated and filled surfaces than did children in the other schools (compare Figures 1 and 2).

Irrespective of year of dropout, a clear trend was seen for a positive association between age of the children and the dropout proportion, whereas the dropout proportion was similar for boys and girls (Table 1). Dropout from clinical caries examination before year 1 was highest among children with 12–17 percent DMFS (third quartile); dropout between year 1 and year 2 was highest among children with 18+ percent DMFS (upper quartile); and dropout between year 2 and year 3 was highest among children in the interquartile range for the percent DMFS (Table 1). Dropout from the radiographic caries examination was highest among children in the upper quartile of the radiographic percent DMFS distribution.

Table 2 shows that school class was a statistically significant contributor to the variation in dropout before the year 1 clinical examination (ρ=0.4; 95% CI=0.1, 0.8), whereas neither school (ρ=0.1) nor the combination of school and grade (ρ=0.1) were significant sources of variation. None of the random factors considered were important for the prediction of dropout between year 1 and year 2, whereas all three categories of random factors contributed to the total variation in dropout between year 2 and year 3 and in dropout from the radiographic examination at year 3 (Table 2). However, in both instances the correlation relating to school class was the largest (ρ=0.5 and ρ=0.7, respectively).

FIGURE 2
Cumulative Frequency Distributions of 602 Schoolchildren in Kaunas, Lithuania (1994), According to Clinical Baseline % DMFS, Including only Cavitated Stages of Lesion Formation (given for each of five schools)

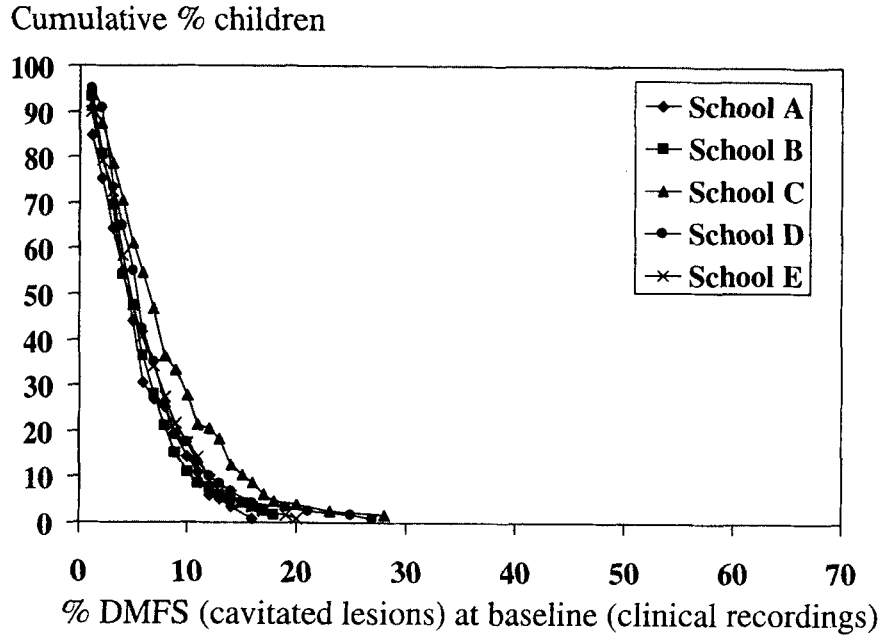


FIGURE 3
Cumulative Frequency Distributions of 602 Schoolchildren in Kaunas, Lithuania (1994), According to Baseline % DMFS, as Assessed on Posterior Bitewing Radiographs (given for each of five schools)

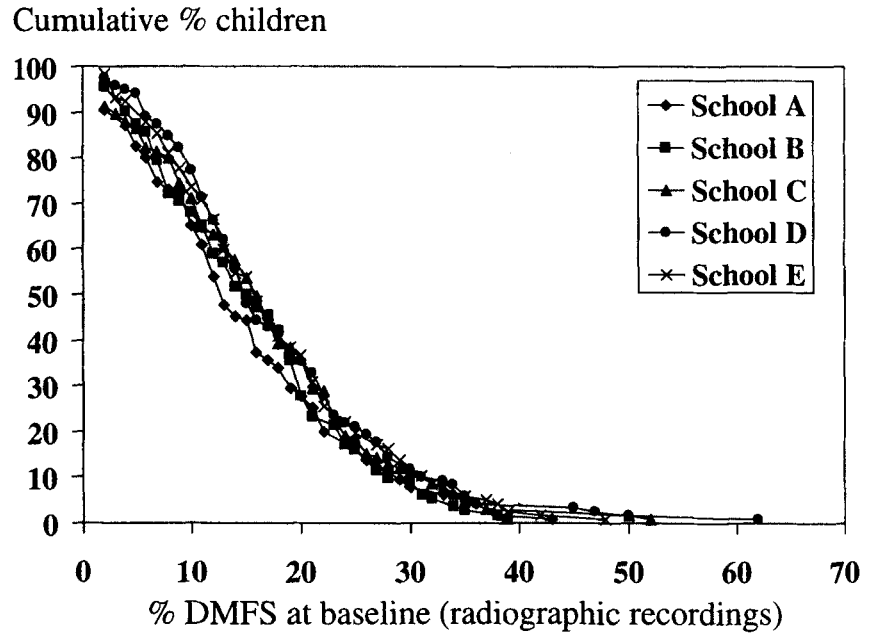


Table 3 shows the results of logistic regression analyses of age, sex, and baseline caries experience, measured as percent DMFS (including all stages of lesion formation), or as percent DMFS (radiographic lesions), as predictors of dropout from the clinical and the radiographic caries examinations. Overall, age was not a statistically significantly contributor to the prediction of dropout before year 1 (P~.07). However, the clinical baseline percent DMFS did provide a statistically significant contribution to the prediction of dropout before year 1 (P<.03), such that children in the interquartile range of the distribution of baseline percent DMFS were more likely to drop out than were the remaining children.

Overall, neither age nor sex provided a significant contribution to the prediction of dropout from the clinical examinations between year 1 and year 2 of the study. However, clinical baseline percent DMFS was a significant predictor such that children in the upper quartile of the distribution of the baseline percent DMFS were statistically significantly more likely to drop out than were children in the lower quartile (Table 3).

Age was a significant individual predictor of dropout from the clinical examinations between year 2 and year 3 (P<.001). Overall, the clinical baseline percent DMFS and sex did not contribute significantly (P>.10); however, children with a baseline percent DMFS in the range from 12–17 percent were statistically significantly more likely to drop out between year 2 and year 3 than were children in the extreme quartiles (Table 3). Age was the only significant individual predictor (P~.04) of dropout from the radiographic caries examination.

Discussion

While there is no *a priori* reason to expect that similar dropout rates will be observed in different studies, it is nevertheless noteworthy that the cumulative dropout rates observed in the present study (11% at year 2 and 28% at year 3 from the clinical follow-up examinations, and 39% from the three-year radiographic follow-up examination) are comparable to those observed in the trials reported by Scheinin et al. (1,2) and Mäkinen et al. (5), but higher than reported by Isokangas (7) and Petersen and Razanamihaja (8), and lower than reported by Kandelman et al. (3) and Kandelman and Gagnon (4). The observation that the dropout from the radiographic examination at year 3 was comparatively higher than that of the three-year clinical examination was due to the fact that some parents were concerned about the radiographic examinations imposing a health hazard to the children. The written information given to the par-

TABLE 2
Proportion of Variance, ρ, Contributed by Random Effect Variables School, Grade within School, and School Class, Used to Determine Most Informative Categorization of School Classes for Predicting Dropout from Intervention Trial Among 602 Schoolchildren in Kaunas, Lithuania, 1994–97

Time of Dropout	Random Effect	ρ	95% CI for ρ
Before year 1	School (5 levels)	0.08	(0.00, 0.79)
	Grade within school (11 levels)	0.13	(0.01, 0.66)
	School class (28 levels)	0.41	(0.14, 0.75)
Between years 1 and 2	School (5 levels)	0.00	—
	Grade within school (11 levels)	0.00	—
	School class (28 levels)	0.00	—
Between years 2 and 3	School (5 levels)	0.32	(0.09, 0.70)
	Grade within school (11 levels)	0.45	(0.26, 0.66)
	School class (28 levels)	0.53	(0.33, 0.72)
Before year 3 (radiographic examination)	School (5 levels)	0.38	(0.28, 0.50)
	Grade within school (11 levels)	0.41	(0.28, 0.55)
	School class (28 levels)	0.67	(0.47, 0.83)

TABLE 3
Results from Multiple Logistic Regression Analyses of Individual Predictors of New Dropout from Clinical Caries Examinations at Year 1, Year 2, and Year 3, and from Radiographic Caries Examination at Year 3, Among 602 Schoolchildren in Kaunas, Lithuania, 1994–97

	Examination			
	Clinical			Radiographic
	Before Year 1	Between Years 1 and 2	Between Years 2 and 3	Before Year 3
Predictor	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (years)				
10	1	1	1	1
11	2.8 (0.4, 18.1)	1.2 (0.3, 4.5)	2.0 (0.7, 6.0)	1.2 (0.6, 2.2)
12	5.2 (0.7, 38.6)	2.0 (0.5, 7.5)	4.6 (1.3, 15.5)	1.8 (0.7, 4.4)
Sex				
Female	1	1	1	1
Male	1.2 (0.6, 2.3)	0.8 (0.3, 2.0)	1.1 (0.7, 1.7)	1.2 (0.8, 1.8)
% DMFS (clinical)				
0–7	1	1	1	—
8–11	4.7 (1.1, 19.0)	0.8 (0.2, 3.3)	1.9 (0.8, 4.4)	—
12–17	6.5 (1.9, 23.0)	1.0 (0.3, 3.5)	2.0 (1.1, 3.9)	—
18+	3.7 (0.8, 16.0)	3.2 (1.2, 8.7)	1.5 (0.7, 3.2)	—
% DMFS (radiographic				1
0–8	—	—	—	
9–14	—	—	—	1.1 (0.7, 1.8)
15–21	—	—	—	1.0 (0.6, 1.6)
22+	—	—	—	1.3 (0.9, 2.0)

OR=odds ratio; CI=conficende interval.

ents prior to the commencement of the study clearly stated that the children were supposed to be examined twice by bitewing radiography (at baseline and after three years). However, as a result of the concerns expressed, all the parents of the participating children were specifically informed prior to the second x-ray examination that another x-ray examination was going to take place, and it was made clear to the children and their parents that participation was optional.

The results of the present study demonstrate that among the three clustering variables considered in the analysis, school, grade within school, or school class, the major source of variation with respect to dropout from the study was attributable to the school class. In other words, the variation in dropout between school classes was larger than between schools or between grades within schools. However, the within-cluster correlations, as represented by ρ, were different depending on time of dropout. For dropout before year 1, only the school class contributed to the variation; whereas neither school nor grades within schools were significant sources of variation. For dropout between year 1 and year 2, all correlations were very close to 0 and nonsignificant. For dropout between year 2 and year 3, the pattern of correlations was more complex, such that all three clustering variables were sources of variation in dropout, although the school class remained the major source of variation.

This more complex pattern of correlations observed for dropout between year 2 and year 3 from the clinical examination, and before the final radiographic examination at year 3 may be explained in part by some children finishing secondary school to go for further education in high schools, and in part by the fact that the propensity for children to follow this educational pattern varied between schools. These results confirm the existence of cluster effects in a community intervention trial as the present. It is noteworthy, however, that these cluster effects were not primarily related to the schools, (i.e., the type of interventions as the school was the randomization unit), but predominantly to subclusters of classes within the randomization units. This indicates that the interventions as such—for example, the

taste and texture of the chewing gums—was not the major reason for discontinuing participation in the study. Rather, the results suggest that norms within the local social network in the classes, which may influence the behavior of the single individual (15), have played a decisive role for sustained participation. Alternatively, differences in the learning environment, such as the teachers' motivation and attitude to the caries-preventive program, may have influenced the children's engagement in the trial (15). Strategies to reduce dropout and thereby increase the effectiveness of caries-preventive trials and programs in settings such as the present should therefore focus on the social context of the children as well as the motivation and commitment of the teachers undertaking the daily supervision of the program.

It is characteristic for most studies carried out among schoolchildren that the children enter the study on the basis of the clusters (classes) to which they belong. This means that the proper dimensions of the study, as determined by the sample size calculations, are usually obtained by selecting a sufficiently large number of classes to cover the necessary number of children. The number of selected classes will typically be substantially lower than the calculated number of children, in the present study by a factor of 21.5. Our finding that the variation with respect to dropout was more closely related to school class than to school would suggest that, from a dropout point of view, selecting 28 classes from five schools to obtain the necessary sample size was as effective as selecting one class from each of 28 schools. However, from the point of view of the interventions carried out, it is clearly preferable to have more than one randomization unit within each intervention category, as this would allow for a determination of the variation of the effect within each intervention category. This in turn means that, from a statistical point of view, classes would be more appropriate randomization units than schools. This fact should, however, be weighted against the impact on the logistics of carrying out such a community intervention trial and the risk of interventions being mixed across the randomization units. Such factors may indeed necessitate that the trial be carried out using a design in which major clusters, such as schools, are the primary randomization units.

An important finding of the study was that the baseline caries experience, including all stages of lesion formation, was predictive of dropout from the clinical examinations, particularly before the year 1 clinical examination. Children with higher baseline caries experiences tend to dropout at a higher frequency than children with lower caries experiences. This indicates that caries-preventive programs may suffer from a selective loss of subjects who could benefit the most from of the intervention. The reason for this phenomenon, which has also been observed in other long-term caries-preventive trials (7,16), remains speculative. However, it is likely that high caries activity is a marker of a lifestyle that cannot easily be interfered with, no matter how simple the intervention. As higher baseline caries levels are known to be associated with higher caries incremental values (17-19), this suggests that the caries increments, as observed clinically, could be biased by a selective dropout of high-caries subjects. This, in turn, requires that baseline caries levels be taken into account when describing caries incremental values. As there was no evidence of a selective dropout from the radiographic follow-up examinations, similar precautions need not be taken in the analyses of radiographic caries incremental values.

Our observation that age was associated with dropout before the three-year follow-up examinations, whether clinical or radiographic, was not surprising, as all the children who dropped out during the third year of the trial did so because they finished secondary school and moved to other schools. This event was particularly pronounced among children attending schools in the downtown areas of Kaunas. Although we considered inviting all of these children to continue in the study, the idea was abandoned due to difficulties in organizing daily supervision of gum chewing.

In summary, the results of the present study show that a community intervention trial in which schools have been randomized to different intervention groups is subject to cluster effects with respect to dropout. However, these cluster effects do not primarily relate to the randomization unit, but rather to subclusters of classes within the randomization units. These findings suggest that from a dropout point of view, the use of schools as the primary randomization unit is as effective as using school classes as the unit of randomization. From the point of view of assessing the effects of intervention, it clearly would be desirable to include several randomization units within each intervention group; however, the logistics of carrying out such a study, as well as the risk of mixing interventions, may indeed necessitate a design in which fewer clusters are randomized. Finally, our data indicate that from a practical prevention perspective, attempts to change the health behavior of schoolchildren specifically should consider the social context of the children in the classes.

Acknowledgment

This study was supported by Aarhus University Research Foundation, and by Dandy (Fertin) A/S, Denmark. Special thanks are due to Professors Michael Vaeth and Anders Foldspang for valuable discussions.

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