Session IV: Analytical Methods—John W. Fertig, Chairman

Analysis of Covariance in Dental Caries Clinical Trials

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Introduction.

There are three theoretical reasons for interest in analysis of covariance in clinical trials of a caries-inhibiting agent: (1) increasing the efficiency of the trial, (2) adjustment for group differences in variables correlated to increment, and (3) provision of insight into the treatment mechanism. The latter is not pursued in this paper. In spite of these potential advantages, analysis of covariance has not been exploited in caries clinical trials. This is a report of exploration of covariance in clinical trials over a period of nearly ten years, during which many covariables have been tested. Important contributions on this topic have been published by Adkins[1], Downer[2], Kingman[3], Lu[4], and Slakter[5]. Most of the findings are excellently summarized by Worthington.[6]

Success in the past has been modest, except when covariance was applied to groups of quite similar age (Adkins[1], 12-year-olds, and Downer[2], 14- and 15-year-olds). This is not practical when the inferences of efficacy of a control agent must apply at least to all the younger and most caries-active population ages. It has been necessary to search for universally available factors by developing knowledge of the occurrence of caries increments within wider age spans over relatively short intervals of time (from one to three years). Analysis of covariance is somewhat restricted in caries clinical trials because of problems arising out of the nature of dental caries data. The body of this report describes the degree to which we have been able to cope with the problems.

Source of data and selection of covariables.

The data sets used represent placebo and fluoride groups from four dentifrice trials. The age ranges were approximately 6-12 years. Sample sizes were large, all exceeding 190 subjects. The caries increments studied were two- to three-year, based on visual-tactile examinations supplemented by adequate radiographic findings.

All the traditional covariables – age, sex, initial dental age, final dental age, and initial DMFS – were included in the battery. In addition to these, we searched for covariables which would be useful in studies involving the wide age ranges used in North America. (Supplementary information on some of the indices described below is given in the Appendix.)

Symmetry index. – It is common knowledge that tooth decay is bilaterally symmetrical in the mouth. Also, because of a similar local environment, it has been shown that tooth surfaces facing into the same approximal space tend to decay jointly. Thus, it was considered likely that if one surface of either a bilateral pair, or of a pair of surfaces making up an approximal space, is decayed initially, the other was likely to decay soon – probably within the term of the clinical trial. Therefore, a score of unmatched pairs (*i.e.*, bilateral or approximal surfaces where one but not the other is decayed) was generated as a covariable. Substantiation of this item as a useful covariable is given in Table 1 for the item termed "symmetry index".

Hierarchy index. – This index is based on the caries hierarchy concept (Grainger[7]), whereby a subject is rated according to the group of tooth surfaces affected. Zero score represents no previous caries, and 1, 2, 3, etc., indicate that caries is present on fissure surfaces, posterior proximal surfaces, anterior proximal surfaces, etc., respectively. Table 2 shows the relation of hierarchy scores to caries increments. Hierarchy levels 3, 4, and 5 occur less frequently in modern caries data than they did when the concept was originated. Although all scores were maintained in the present analysis, some thought has been given to merging scores 3, 4, and 5 as 3 for future use.

Kingman[3] has done further work on this index using scores weighted according to the number of surfaces affected at each level. While Kingman's approach was not utilized in the present work, we consider it well worth future research.

First molar fissure caries index. – The literature contains much evidence that fissure surface caries differs markedly from smooth surface caries, if not entirely in etiology, at least in frequency of occurrence. Therefore, the initial number of decayed fissures on the first permanent molars was selected as a trial covariable. The second molar surfaces were not included because they would not be present in all subjects. Table 3 shows caries increments according to this factor.

Attack risk product indices. – Lu[4] suggested a product function index,

$$S/N\ (1-S/N)$$

TABLE 1
TWO-YEAR CARIES INCREMENTS ACCORDING TO SYMMETRY INDEX

Symmetry Index Score	Set 1 Placebo			Set 2 Placebo		
	N	$\bar{X}$	SE	N	$\bar{X}$	SE
0	14	2.71	0.80	52	2.44	0.36
1-2	50	3.06	0.53	65	2.86	0.39
3-4	52	3.75	0.75	44	3.20	0.65
5-6	41	4.48	0.84	46	3.26	0.72
7 & over	45	9.82	1.34	21	10.33	1.85

TABLE 2
TWO-YEAR CARIES INCREMENTS ACCORDING TO HIERARCHY INDEX SCORES

Hierarchy Level	Score	Set 1 Placebo			Set 2 Placebo		
		N	$\bar{X}$	SE	N	$\bar{X}$	SE
No caries	0	15	2.20	0.69	49	2.82	0.37
Fissure caries	1	76	3.38	0.43	87	2.97	0.41
Posterior proximal	2	90	5.03	0.65	75	3.55	0.55
Maxillary anterior proximal	3	7	12.71	1.74	5	18.20	4.49
Mandibular anterior proximal	4	1	13.00	–	0	–	–
Buccal or lingual	5	16	11.25	3.25	12	5.67	2.03

TABLE 3
TWO-YEAR CARIES INCREMENTS ACCORDING TO INITIAL FISSURE CARIES IN FIRST PERMANENT MOLARS

Fissure Surfaces Decayed	Set 1 Placebo			Set 2 Placebo		
	N	$\bar{X}$	SE	N	$\bar{X}$	SE
0-1	19	2.32	0.71	65	3.62	0.50
2-4	79	3.61	0.45	83	3.41	0.47
5-7	101	5.94	0.71	75	3.95	0.71
8 & over	6	16.00	5.76	5	1.40	1.36

where S is the number of surfaces decayed, and N the total number of erupted surfaces. This form of index would appear to be very useful in a trial that involved individuals having similar numbers of teeth present. It is less useful where N differs from subject to subject not only in value but also in the specific teeth present.

Along the same line, Adkins[1] suggested using six covariables representing subgroups of teeth which erupt at similar ages. The subgroups he suggested and used in an older age group (12 years) were : (1) lower first bicuspids, (2) upper first and upper and lower second bicuspids, (3) first permanent molars, (4) second permanent molars, (5) incisors, and (6) canines. These covariables could not be used where studies include younger individuals not having all the teeth erupted, because incomplete data would be encountered.

In 1976, at the October meeting of the Task Force, Grainger and Lehnhoff[8] described another product function more useful at all ages:

$$(\text{IDMFS/Age})\ \Sigma_1^n\ p_i$$

where p_i is the relative caries attack rate for each tooth surface still at risk (Reid and Grainger[9]). This function provides IDMFS/Age as an estimate of a subject's demonstrated caries susceptibility which (by extrapolation) would be expected to produce caries according to the degree of risk present. The prediction would be for low increments when either the previous caries experience was low, or the risk probability was low. Most new caries would be expected when previous caries experience was high and there still remained sufficient susceptible surfaces at risk.

We would like to suggest that the modifying factor IDMFS/Age, derived from past experience, is the resultant of all the individual subject's characteristics (tooth quality, oral hygiene, bacterial flora, diet, etc.) that determine the subject's inherent tendency to have tooth decay. At present, we can only extrapolate from the past, but future research might result in ways to estimate a subject's current caries activity mechanism level during the time interval of the clinical trial. This approach – modifying the surface specific risk by the subject's inherent susceptibility – seems to be the most promising road to follow.

Two product functions, one using chronological age and the other dental age in the denominator, are shown in relation to caries increments in Tables 4 and 5.

The set of covariables selected for this paper were as follows (some more detailed description is given in the Appendix):

(1) initial chronological age,
(2) initial dental age (number of erupted teeth),
(3) re-ordered dental age group (switch groups 1 and 2),
(4) initial mesial and distal carious surface,
(5) initial fissure caries on first molars,
(6) initial decayed, missing, and filled surface total,

TABLE 4
TWO-YEAR INCREMENTS BY PRODUCT FUNCTION – (IDMFS/CHRONOLOGICAL AGE) ΣP_i

Range	Set 1 Placebo			Set 2 Placebo		
	N	$\bar{X}$	SE	N	$\bar{X}$	SE
0-0.9	41	2.15	0.48	86	2.64	0.28
1-1.9	59	2.27	0.35	61	2.70	0.53
2-2.9	32	4.47	0.84	33	4.06	0.88
3-3.9	29	6.76	1.33	23	4.44	1.22
4-4.9	20	8.95	2.00	15	8.53	2.54
5 & over	24	11.88	1.80	10	6.50	1.69

TABLE 5
TWO-YEAR INCREMENTS BY PRODUCT FUNCTION – (IDMFS/NO. OF TEETH) ΣP_i

Range	Set 1 Placebo			Set 2 Placebo		
	N	$\bar{X}$	SE	N	$\bar{X}$	SE
0-0.9	67	2.49	0.39	119	3.06	0.31
1-1.9	81	4.89	0.71	77	4.49	0.74
2-2.9	36	7.61	1.28	19	2.26	0.96
3-3.9	12	8.25	2.72	10	3.60	1.06
4 & over	9	9.89	2.71	3	10.67	4.05

(7) Symmetry index,
(8) base time sum of probabilities for surfaces at risk,
(9) hierarchy score,
(10) product function (IDMFS/chronological age) Σp_i,
(11) product function (IDMFS/No. of teeth) Σp_i, and
(12) final dental age.

The dependent variable was the final DMFS score minus the initial DMFS score.

Findings.

The product moment correlation matrices of the selected variables are given in Tables 6 and 7 for two clinical trials. The placebo and treatment groups are merged in the Tables to permit comparison of coefficients. Perusal of column 13 shows how primary relationships differ between placebo and treatment groups. If a treatment was perfectly successful (all increments zero), all correlations with increment would be zero, and hence, the degree to which treatment relationships are degenerated may provide evidence of treatment success. It is also apparent in the matrices that there are strong correlations among the selected variables.

The results of stepwise multiple regression, forced multiple regression of 12 variables, and stepwise regression of all powers to the 4th for the 12 variables are given in Table 8 for four placebo groups. In most cases tried, the multiple correlation coefficients for treatment groups were lower than those for control groups. The introduction of powers, intended to provide for non-linearity, did increase the magnitude of the R squares even above those when forcing 12 observed variables, but the similarity of selections among the groups was lost. Furthermore, a tendency for selection of only 3rd or 4th powers was not easily interpretable, so we have reported only the more conservative approach. In the stepwise analysis, $p = 0.05$ was used as the cut-off for inclusion. When a clinical trial involves hundreds of subjects, the forcing of 12 variables does not seem to be serious overfitting.

Table 9 displays the complete analysis of covariance results for two clinical trials. It can be seen that the adjust-

TABLE 6
CORRELATION MATRIX FOR SET 1 FOR PLACEBO AND TREATMENT GROUP

Item		1	2	3	4	5	6	7	8	9	10	11	12	13
1 Chronologic Age	P	1.000	0.779	0.622	0.443	0.384	0.553	0.517	0.530	0.437	0.539	0.409	0.786	0.408
	T	1.000	0.825	0.695	0.496	0.138	0.492	0.531	0.587	0.385	0.533	0.337	0.826	0.256
2 Dent. Age	P	0.779	1.000	0.859	0.546	0.360	0.669	0.653	0.749	0.414	0.592	0.258	0.806	0.507
	T	0.825	1.000	0.841	0.576	0.200	0.641	0.641	0.721	0.448	0.629	0.271	0.846	0.363
3 DA Group	P	0.622	0.859	1.000	0.485	0.267	0.586	0.554	0.547	0.339	0.582	0.250	0.723	0.550
	T	0.695	0.841	1.000	0.474	0.191	0.542	0.563	0.537	0.331	0.651	0.379	0.784	0.441
4 MES + DIS	P	0.443	0.546	0.485	1.000	0.452	0.852	0.862	0.061	0.641	0.702	0.532	0.457	0.504
	T	0.496	0.576	0.474	1.000	0.312	0.854	0.855	0.052	0.615	0.598	0.462	0.487	0.288
5 1st Molar	P	0.384	0.360	0.267	0.452	1.000	0.746	0.400	−0.061	0.559	0.652	0.652	0.349	0.277
	T	0.138	0.200	0.191	0.312	1.000	0.664	0.253	−0.241	0.484	0.564	0.607	0.161	0.193
6 IDMFS	P	0.553	0.669	0.586	0.852	0.746	1.000	0.794	0.150	0.697	0.794	0.609	0.543	0.524
	T	0.492	0.641	0.542	0.854	0.664	1.000	0.777	0.063	0.706	0.731	0.577	0.503	0.343
7 Symmetry	P	0.517	0.653	0.554	0.862	0.400	0.794	1.000	0.257	0.609	0.641	0.428	0.516	0.474
	T	0.531	0.641	0.563	0.855	0.253	0.777	1.000	0.231	0.608	0.639	0.481	0.531	0.355
8 Sum Risk	P	0.530	0.749	0.547	0.061	−0.061	0.150	0.257	1.000	0.021	0.104	−0.160	0.507	0.195
	T	0.587	0.721	0.537	0.052	−0.241	0.063	0.231	1.000	0.062	0.146	−0.154	0.556	0.099
9 Hierarchy	P	0.437	0.414	0.339	0.641	0.559	0.697	0.609	0.021	1.000	0.605	0.540	0.365	0.373
	T	0.385	0.448	0.331	0.615	0.484	0.706	0.608	0.062	1.000	0.673	0.614	0.426	0.213
10 (C/A) Σp	P	0.539	0.592	0.582	0.702	0.652	0.794	0.641	0.104	0.605	1.000	0.886	0.736	0.527
	T	0.533	0.629	0.651	0.598	0.564	0.731	0.639	0.146	0.673	1.000	0.882	0.733	0.488
11 (C/DA) Σp	P	0.409	0.258	0.250	0.532	0.652	0.609	0.428	−0.160	0.540	0.886	1.000	0.568	0.340
	T	0.337	0.271	0.379	0.462	0.607	0.577	0.481	−0.154	0.614	0.882	1.000	0.509	0.343
12 FDA	P	0.786	0.806	0.723	0.457	0.349	0.543	0.516	0.507	0.365	0.736	0.568	1.000	0.474
	T	0.826	0.846	0.784	0.487	0.161	0.503	0.531	0.556	0.426	0.733	0.509	1.000	0.386
13 DMFS Increment	P	0.408	0.507	0.550	0.504	0.277	0.524	0.474	0.195	0.373	0.527	0.340	0.474	1.000
	T	0.256	0.363	0.441	0.288	0.193	0.343	0.355	0.099	0.213	0.488	0.343	0.386	1.000

TABLE 7
CORRELATION MATRIX FOR SET 2 FOR PLACEBO AND TREATMENT GROUP

Item		1	2	3	4	5	6	7	8	9	10	11	12	13
1 Chronologic Age	P	1.000	0.778	0.705	0.314	0.252	0.418	0.355	0.520	0.303	0.411	0.304	0.798	0.349
	T	1.000	0.734	0.645	0.328	0.293	0.431	0.424	0.439	0.399	0.379	0.323	0.735	0.196
2 Dent. Age	P	0.778	1.000	0.858	0.325	0.160	0.412	0.397	0.817	0.339	0.388	0.094	0.802	0.476
	T	0.734	1.000	0.854	0.402	0.270	0.520	0.523	0.713	0.379	0.473	0.222	0.793	0.400
3 DA Group	P	0.705	0.858	1.000	0.277	0.109	0.348	0.330	0.633	0.267	0.375	0.109	0.746	0.462
	T	0.645	0.854	1.000	0.350	0.256	0.456	0.463	0.520	0.347	0.507	0.293	0.787	0.368
4 MES + DIS	P	0.314	0.325	0.277	1.000	0.196	0.674	0.867	0.030	0.512	0.510	0.404	0.277	0.419
	T	0.328	0.402	0.350	1.000	0.335	0.837	0.845	−0.090	0.615	0.621	0.522	0.356	0.281
5 1st Molar	P	0.252	0.160	0.109	0.196	1.000	0.789	0.290	−0.277	0.485	0.734	0.738	0.233	0.027
	T	0.293	0.270	0.256	0.335	1.000	0.723	0.410	−0.282	0.552	0.698	0.725	0.299	0.150
6 IDMFS	P	0.418	0.412	0.348	0.674	0.789	1.000	0.712	−0.074	0.691	0.853	0.736	0.395	0.328
	T	0.431	0.520	0.456	0.837	0.723	1.000	0.802	−0.102	0.721	0.779	0.673	0.439	0.310
7 Symmetry	P	0.355	0.397	0.330	0.867	0.290	0.712	1.000	0.085	0.594	0.592	0.459	0.342	0.428
	T	0.424	0.523	0.463	0.845	0.410	0.802	1.000	0.409	0.680	0.694	0.578	0.460	0.347
8 Sum Risk	P	0.520	0.817	0.633	0.030	−0.277	−0.074	0.085	1.000	0.045	−0.056	−0.303	0.557	0.349
	T	0.439	0.713	0.520	−0.090	−0.282	−0.102	0.409	1.000	−0.094	−0.113	−0.319	0.452	0.250
9 Hierarchy	P	0.303	0.339	0.267	0.512	0.485	0.691	0.594	0.045	1.000	0.652	0.539	0.315	0.218
	T	0.399	0.379	0.347	0.615	0.552	0.721	0.680	−0.094	1.000	0.658	0.621	0.388	0.219
10 (C/A) Σp	P	0.411	0.388	0.375	0.510	0.734	0.853	0.592	−0.056	0.652	1.000	0.906	0.568	0.301
	T	0.379	0.473	0.507	0.621	0.698	0.779	0.694	−0.113	0.658	1.000	0.915	0.615	0.336
11 (C/DA) Σp	P	0.304	0.094	0.109	0.404	0.738	0.736	0.459	−0.303	0.539	0.906	1.000	0.388	0.133
	T	0.323	0.222	0.293	0.522	0.725	0.673	0.578	−0.319	0.621	0.915	1.000	0.500	0.175
12 FDA	P	0.798	0.802	0.746	0.277	0.233	0.395	0.342	0.557	0.315	0.568	0.388	1.000	0.367
	T	0.735	0.793	0.787	0.356	0.299	0.439	0.460	0.452	0.388	0.615	0.500	1.000	0.315
13 DMFS Increment	P	0.349	0.476	0.462	0.419	0.027	0.328	0.428	0.349	0.218	0.301	0.133	0.367	1.000
	T	0.196	0.400	0.368	0.281	0.150	0.310	0.347	0.250	0.219	0.336	0.175	0.315	1.000

TABLE 8
CUMULATIVE MULTIPLE R^2 FROM STEP-WISE ANALYSIS OF FOUR PLACEBO GROUPS USING 12 COVARIABLES

Method	Selection Order	Set 1 VAR	Set 1 R^2	Set 2 VAR	Set 2 R^2	Set 3 VAR	Set 3 R^2	Set 4 VAR	Set 4 R^2
Step-wise*	1	3	0.302	2	0.226	10	0.223	4	0.282
	2	4	0.376	4	0.304	3	0.291	10	0.305
	3	10	0.389			9	0.318	7	0.326
	4							11	0.351
Forced 12			0.403		0.360		0.346		0.369
Step-wise* 12 Variables through 4th Power	No. Selected	4	0.414	13	0.522	3	0.388	4	0.385

*Selection level for forward entry = 0.05.

TABLE 9
RESULTS OF ANALYSIS OF COVARIANCE FOR TWO CLINICAL TRIALS USING 12 COVARIABLES

	Set 1 DMFS Increments		Set 2 DMFS Increments	
	Observed	Adjusted	Observed	Adjusted
Placebo	5.00	4.93	3.60	3.85
Treatment	3.68	3.65	3.01	2.88
Difference	1.42	1.28	0.59	0.97
% Difference	28.4%	26.0%	16.4%	25.2%
Error Mean Square	38.87	26.25	23.90	17.90
d of f	399	387	681	669
% Reduction in MS		32%		25%

ment of mean increments necessitated by imbalance in one or more of the covariables is substantial. There is also a useful reduction in the error mean square in both sets in the order of 25 to 30%.

Discussion.

The 25-30% reductions in error mean square are somewhat modest mathematically, but in modern clinical trials involving thousands of subjects, the gain in efficiency should not be discarded as valueless. Greater reductions in error mean squares may be possible through further refinement of technique, but the nature of dental caries data, *per se,* seems to set some practical limits for the usefulness of analysis of covariance in clinical trials.

As with caries prevalence data (Grainger and Reid[10]), the variances are correlated with the means, but this relationship is not simple, making the use of transformations only marginally effective in overcoming heterogeneity of variances (Worthington[6]). The effect of this is that the larger and more variable data from the older subjects disproportionally influence the product moment correlation coefficients and the slopes upon which covariance depends. Clearly, this phenomenon alone points to stratification rather than covariance as the technique of choice (Korts[11]). But stratification involving more than one variable is in itself a complicated analytical problem.

Recently, Smith[12] has suggested, based on simulated data, that use of log or square root transformations can increase the efficiency of trials. However, we did not use transformations in this project.

Distributions of caries increments are typically skewed, exhibiting variation in excess of that of the Poisson distribution. The negative binomial distributions fitted by Reid and Grainger[9] could result from pooling Poisson data with different means, and indeed such distributions resolve into Poisson when the means are very small. However, means of such small size are unlikely to be encountered in real clinical trials. Lack of normality is frequently ignored in applications of multiple regression, but in the case of caries increments, the problem appears complicated by inconsistencies in the shape of the distributions related to changes in specific surface groups at risk over age. For example, at very young ages, when caries is almost restricted to a finite number of surfaces (10-12 fissures) on first permanent molars, the distributions may more closely resemble the binomial. It is at older ages, when the number of surfaces at risk is large, that the highly skewed Poisson-like distributions appear. The inconsistency of the distributions of increments within the data sets seems incompatible with efficient multiple regression estimation.

The covariables used are not perfectly linear in relation to caries increments. Correction for curvilinearity may be possible in some of our covariables by minor adjustments of the scores recorded and also by use of simple functions such as logarithms or square roots. However, we attempted polynomial powers as a general approach, since no fundamental relationships were known. Our attempts to introduce powers resulted in the step-wise analysis, giving preference to 3rd and 4th powers in an almost haphazard order, with improvement in results (with the exception of one data set) insufficient to warrant increasing the complexity.

As has been common experience in multivariate analyses, minor variations in the product moment correlation coefficients from data set to data set modify the order in which step-wise analysis selects covariables. One can only define some covariables that are very frequently useful. Then the strategy becomes one of providing a set of most frequently useful covariables, such as the twelve used in this research, with an expectation that enough of them will have good correlations.

While caries data are likely to violate the assumptions of the analysis of covariance to some degree, the analysis must be considered a viable option for estimating treatment effects and improving the efficiency of caries clinical trials. A single degree of freedom test of significance of adjusted means, which are adjusted to the means of the covariables, would appear to be an adequate analytical strategy which should provide an improvement over a *t* test of observed means.

Conclusions.

(1) Use of analysis of covariance in clinical trials of caries control agents is somewhat limited by the complexity of the data.

(2) The methods discussed in this paper should provide a reduction of 25-30% in the error mean square and strengthen the conclusions by adjustment of the mean increments.

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APPENDIX

Detailed Description of Covariables

1. *Chronological Age.* – Age in years last birthday was recorded at time of first examination. This permits the assumption that age is on the average the age last birthday plus one-half year.
2. *Dental Age.* – This is the count of erupted permanent teeth. A tooth is recorded as erupted as soon as part of the crown emerges. Teeth erupt in clusters, beginning with the lower central incisors and first permanent molars about age 6. The next group are the upper incisors, followed by the bicuspids. Then, around 12 years, the second permanent molars and cuspids erupt. The range of eruption time about the specific tooth average is in excess of plus-or-minus two years. Because fissure caries tends to occur within months of tooth eruption, fissure caries increments occur at two main times shortly after eruption of the molars. Smooth surface caries requires time to become clinically detectable; hence, caries increments tend to accumulate about two years after tooth eruption, depending on the intensity of the caries attack. For the above reasons, the relation of caries increments to tooth age is curvilinear, with at least two modes.
3. *Re-ordered Dental Age.* – Because of the characteristics of the teeth erupting in the age interval 6-11, the rate of new caries in this age interval is less than before or after. A simple switch of DA 1 and 2 tends to make the relation of increment to dental age roughly linear. The dental age groupings by number of teeth erupted were 0-5, 6-11, 12-19, and 20-28.
4. *Initial Count of Mesial and Distal Surface Caries.* – This score is obvious to compile and is intended to give a measure of degree to which caries has progressed to the smooth surfaces of higher susceptibility. Although 52 surfaces exist clinically, only about 20-30 have real likelihood of decaying in children.
5. *Fissure Surfaces of First Molars.* – This includes the two upper molar lingual surfaces and lower two buccal surfaces, making a total of eight. The index is used with the hope of characterizing the dentition as to susceptibility of fissures. Predictive value is mainly aimed at erupting bicuspids and second molars in which fissures tend to decay either quickly or never.
6. *Initial Total Decayed, Missing, or Filled Surfaces.* – The usefulness of this index has been discussed in the body of the paper. At early ages, when there has been insufficient time for decay to occur, a zero IDMFS can be misleading.
7. *Symmetry Index.* – This index is a count of pairs of bilateral matching surfaces, plus pairs of surfaces facing the same proximal space on the same side in which one but only one of the pairs is decayed. Due to the tendency for these surfaces to have similar susceptibility, new decay is reasonably linear to the count of incomplete match pairs.
8. *Sum of Base Time Risk Probabilities.* – In the paper by Reid and Grainger (1955), under the assumption that attack rate remains constant and caries-producing attacks occur randomly in time, the proportion of surfaces free from decay at age t may be approximated by:

$$P_i = e^{-b(t-a)}$$

where b is a measure of the attack rate, and a is the age at which exposure begins. This expression implies that

$$-\log_e P_i = k + bt.$$

The natural logarithm of the percentage free of decay is linearly related to age. Factor b may then be interpreted as the number of attacks *per* year.

A least-squares estimate of b may be made by the formula

$$b = \Sigma W(y-\bar{y})(t-\bar{t})/\Sigma W(t-\bar{t})^2$$

where $y = -\log_e p_i$ and $W = NP_i/(1-P_i)$, where P_i is the true proportion caries-free, and, since it is unknown, weights are estimated from initial observed values of p or graphic estimates. Iterative calculations are carried out using estimates for P_i from previous cycles until the value of b stabilizes. Two types of surfaces cannot be treated satisfactorily in this way. The first are those with very rare caries for which a

simple average was taken. The second were certain surfaces of erupting teeth that seem to decay so rapidly that no slope could be computed. In the latter case, the level was used.

On the assumption that the slopes represent the relative susceptibility of specific surfaces, the sum of the slopes for surfaces at risk is used as a function of the summed probability for decay. This score can be computed for any dental age above zero.

9. *Simple Hierarchy.* — This is a score 0 to 5, representing the extent to which decay has advanced into the more highly resistant groups of tooth surfaces. This score can be computed for any dental age above zero, although the actual surfaces present may differ.

Hierarchy	Surface Groups With One or More Affected Areas
0	No caries
1	Fissure surfaces
2	Posterior approximal surfaces
3	Approximal surfaces of upper incisors
4	Approximal surfaces of lower incisors
5	Labial or lingual smooth surfaces

Since this score was introduced, caries of levels 3 and 4 have become very rare in North America but are still found. Scores 3, 4, and 5 may be merged as score 3.

10. *(IDMFS/Chronological Age)* ΣP. — As described previously, this index provides a measure of apparent caries susceptibility from past observation to be used as a modifier of the summed risk function 8. When either past experience is low or the summed risk is low, the increment estimate is low.
11. *(IDMFS/Dental Age)* ΣP. — A second product function using dental age (number of teeth erupted) in the denominator. Although the denominator is intended to improve IDMFS as a measure of caries susceptibility by relating it to time, the relation to the number of teeth erupted also seemed to have merit.
12. *Final Dental Age.* — This is the count of teeth present at the final examination of the clinical trial. The difference between final and initial dental age gives a measure of erupting teeth.