A Model for the Study of Development Processes in Dental Research

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In studying developmental processes in dental research, variables other than chronological age must often be taken into account if we are to characterize differences in the developmental patterns of the groups under consideration. In particular, in addition to age, appropriate developmental models may have to incorporate cohort, time-of-measurement, and learning effects. One such model is described in this article and applied to caries development and gingival condition in the Nymegen Growth Study.

Dental research is often concerned with and frustrated by the manifold difficulties inherent in the problem of measuring change.[1] Despite a long-standing interest in developmental data (for a good review, see Moorrees[2] who cites a study by Fauchard dealing with the developmental sequence of the deciduous and permanent dentitions dating back to 1728), a number of promising questions in dental research continue to go unanswered because of deficiencies in statistical methods.[3-5] At least part of the problem can be traced to the design of developmental studies which, with few exceptions,[4] have been limited to but a scant few basic approaches. These include the conventional cross-sectional and longitudinal approaches as well as a third, frequently overlooked but equally important, method that we refer to as the time-lag method.

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The basic differences between the cross-sectional and longitudinal designs may be put simply as follows: in the cross-sectional design, we gather information using different (independent) samples of individuals at each of several points on an age or time scales, whereas in the longitudinal design we gather information using the same sample of individuals at each point. Thus, in a cross-sectional study, if change with age is the object of inference, the study would consist of different groups of individuals at selected points along the age scale. If changes over the calendar time scale (secular trends) are of interest, another type of cross-sectional study would consist of different groups of individuals of one particular age, each group being examined at a different point of time (the so-called time-lag design). In longitudinal studies, which are invariably concerned with individual[6-9] or group[10-13] development or both, the same individuals are measured at each point on the age scale. Each of these designs have been used in a variety of growth and development contexts and the pros and cons of the cross-sectional vs the longitudinal method have been the center of much discussion (and considerable controversy) in the literature of a number of disciplines.[14,15] It is not our intention to present a detailed recapitulation of this material. For the purposes of the present discussion, it suffices to recognize each of these designs as special cases of a more general developmental model and to point out the limitations of these methods in this more general context.

We begin, following the methods of Kessen,[16] by agreeing that "a characteristic is said to be *developmental* if it can be related to age in an orderly or lawful way" and propose a general developmental model that holds that development is a function of the age of the individual, the cohort to which the individual belongs, and the time at which the measurement is taken.[17-21] Here the term cohort refers to a group of individuals all born at the same point or (small) interval of time and the concept of time-of-measurement is meant to include all those environmental effects (for example, seasonal fluctuation) that may influence the value of a measurement taken at a given temporal point. In this terminology, the inadequacies of the classical designs for the study of development may be conveniently summarized as follows:[19]

1. The cross-sectional method measures age differences but confounds differences in developmental status with cohort differences.
2. The longitudinal method measures age changes but confounds differences in developmental status with environmental treatment effects.
3. The time-lag method measures cultural change but confounds environmental treatment effects with differences between generations.

What all this means is that although each of these designs can be used to measure changes resulting from certain specified effects, these effects cannot be isolated for separate study (that is, they are confounded) when only these simple models are used.[5,17] Thus, for example, if a cross-sectional study shows that two age groups are different, it is impossible to tell if this difference is due to growth (developmental status) or to differences between the cohorts. As stated by Anastasi,[22] "Differences between 20- and 40-year olds tested simultaneously . . . would reflect age changes plus cultural differentials, especially differences in the conditions under which the two age groups were reared." In the context of the properties of cross-sectional and longitudinal designs, these considerations imply that, when cohort differences exist (1) it is necessary to qualify the concept of age by specification of cohort membership, (2) the age effects of a cross-sectional study are confounded with the cohort effects, and (3) the age effects of a longitudinal study may not be generalized to other cohorts.[20] Thus, Campbell and Stanley[23] would not classify either approach as a "true experimental design." Baltes[24] went so far as to assert "If one considers the process of making at least one controlled comparison as the basis of securing scientific evidence, both conventional designs have such a total absence of control as to be of almost no scientific value."

In view of these difficulties, more general models for the study of growth and development have been proposed—primarily by Schaie[17-20] and Schaie and Strother[21]—but applications of these methods have, to date, been limited to psychometric investigations.[24-31] It is the purpose of the present article to describe this class of models and to illustrate their application to the study of dental developmental processes in the Nymegen Growth Study.[4] Although strictly mathematical arguments are kept to a minimum, the data-analytic aspects of this exposition will involve some of the techniques of the *Analysis of Variance* and the reader is referred to Chilton[32] for the necessary background in this area.

Materials and Methods

In order to adequately describe the growth and development of a particular characteristic measured on each of a group of individuals, we propose the following model:

$$G = B + A + C + T + L \qquad (1)$$

where G, the average value of the measurement under consideration in the specified group is taken to be (additively) related to five factors, or effects, described in turn as follows:

B is baseline value for the measurement in question, that is, the value that G would assume in the absence of any variability between the groups as a result of differences in age, cohort, time-of-measurement or learning (testing) effects or both. Otherwise stated, the value of B can be viewed as a constant for all of the groups included in the study and differences observed in the value of G for these groups ascribed to differences in the values of the other factors comprising the model.

A is age effect. Here the value of G is made to depend on the age of the individuals comprising the group. In the context of dental developmental studies, this would include such group differences as higher DMF indexes and more advanced dental development in older children.

C is cohort effect. Here the value of G is seen to be effected by possible cohort differences. It is assumed that the value of C is the same for all groups of the same cohort and is independent of age. Examples of cohort effects include differences between generations caused by changes in nutritional status, differential exposure to fluoridation, etc.

T is time-of-measurement effect. Time of measurement effects are viewed as any departures from the baseline value, B, caused by short-term or fluctuating conditions influencing the value of the measurement under consideration. These include seasonal effects (for example, summer vs winter dietary habits) and changes in the measurement procedure itself as may be caused by changes in equipment, observers, etc.

L is learning (or testing) effect. This is the contribution of changes in the value of G induced by participation in the study. Groups that have been repeatedly measured or otherwise influenced by certain treatment effects or both (for example, instruction in proper dental hygiene methods) will often differ from matched control groups simply by virtue of the fact that they are a part of an experimental situation.

Given this model, and recognizing that in any study of development we are primarily interested in the effects of age, that is, the cohort, time-of-measurement, and learning effects are generally viewed as "nuisance parameters" interfering with our ability to directly study the developmental process, we now propose to use this model in such a way as to estimate and correct for these disturbing effects. Since the traditional cross-sectional, longitudinal, and time-lag designs have already been shown to be inadequate for this purpose, we consider instead a design that may be viewed as a convenient compromise between the traditional designs,[4] namely, a mixed-longitudinal design,[17] with overlapping cohorts. The strategy consists of taking a sample of individuals at age A_1 and observing them for a specified number, y, of years; another sample at age $A_2 < A_1 + y$ and observing them for y years, etc. The study can then be completed in y years' time and provides, for each of the groups under consideration, estimates of the average growth curves in the overlapping time intervals $(A_1, A_1 + y)$, $(A_2, A_2 + y)$, . . . $(A_k, A_k + y)$ where, typically, y is chosen to be small relative to $A_k - A_1$. If there are k cohorts each followed longitudinally for y years with x years of overlap, the total coverage is $Y = k(y - x) = A_k + y - A_1$ years.

The structure of such a design, ignoring for the moment the inclusion of a learning effect in equation (1), is shown in Figure 1 for the case of seven groups (labeled G_1 through G_7) corresponding to the various possible combinations of group structure when three cohorts (with the values of the corresponding effects labeled O, c, and C, respectively) are measured at three different times (effects labeled O, t, and T) at three different ages (effects labeled O, a, and A). Thus, for example $G_3 = B + A + t$ corresponds to the group, comprised of the first cohort (so $C = O$), that is measured for the second time at the third age level. Here, for convenience, and without loss of generality, we have scaled the measurements so that the first level of each of the factors, cohort, age, and time-measurement, produces zero effect. (The effect is, simply, absorbed into the constant B. It is always possible to scale the effects in such a way that a particular level of these effects has the value zero.) With this

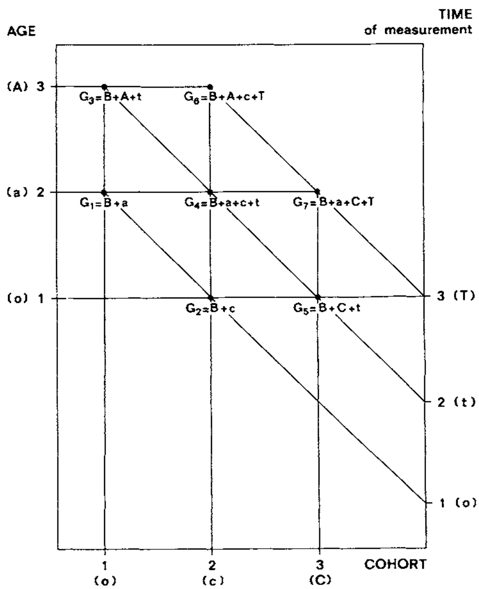

FIG 1.—Diagrammatic representation of mixed-longitudinal design, seven groups being defined by various combinations of factors: age, cohort, and time-of-measurement. Each factor is present at three levels and value of effects corresponding to these levels are indicated in parentheses.

formulation, the source of the controversies that have arisen in connection with the application of this design[19,24,31] is immediately evident in that although we have seven equations (Fig 1) relating seven unknown parameters (namely, the effects B, a, A, c, C, t, and T) the system is not solvable since the equations are not independent (because the group values are related by the equation $G_2 + G_3 + G_7 = G_1 + G_5 + G_6 = 3B + a + A + c + C + \mathrm{t} + T$). Thus, in order to get a solution, it is necessary to impose additional assumptions regarding the absence or equality or both of certain of the effects. This may, at first glance, appear to be a distinct disadvantage of the mixed-longitudinal approach. However, the use of any of the more traditional designs involves the implicit making of even more stringent assumptions or the hopeless confounding of the effects included in the model. Thus, the mixed-longitudinal approach, which forces the explicit recognition of the assumptions necessary to achieve a solution, has the advantages that can be expected to accrue whenever the investigator is forced to carefully consider the structure of his data. In addition, equation (1) can also be used to obtain at least a partial validation of the Schaie model. In the context of the current example (Figure 1), this model implies as noted earlier that $G_2 + G_3 + G_7 = G_1 + G_5 + G_6$ and this can be tested to see whether or not the additive model (1) is appropriate.

It should not be concluded from Figure 1 that seven groups are necessary to use a model of the form of model (1). Indeed, Schaie[17] has suggested that the "most efficient design for a developmental study" consists of the groups G_1 through G_5. Here, since only two times of measurement are involved, sampling attrition in the repeated measurement part of the study is held to a minimum[33-34] and several of these designs could, of course, still be "strung together" to cover a wide age range, using but two times of measurement on each of the groups. In this case, the five equations relate six unknown parameters (B, a, A, c, C, and t) so that, again, additional assumptions must be invoked to obtain a usable solution, but, if suitable control groups are used, the model is easily validated and the attendant test procedures provide considerable guidance toward the making of reasonable assumptions.[17]

The use of a Schaie-type model in the Nymegen Growth Study[4] will now be illustrated. The structure of the design of the complete study, in which six cohorts are each studied longitudinally for a period of five years providing information relevant to the growth and development of Dutch children from 4 to 14 years of age, is shown in Figure 2. There are, in addition to these experimental groups, several control or test groups (denoted by T or T_g in the figure) that are included so that we may be able to estimate possible learning or testing effects within the study population (those denoted by T) and validate the application of the Schaie mixed-longitudinal developmental model (those denoted by T_g).

Our illustration is based on a subset of this complete design which should be sufficient to demonstrate the principles involved and the power of the method. We concentrate on but two variables, namely, gingival condition and caries development, as ob-

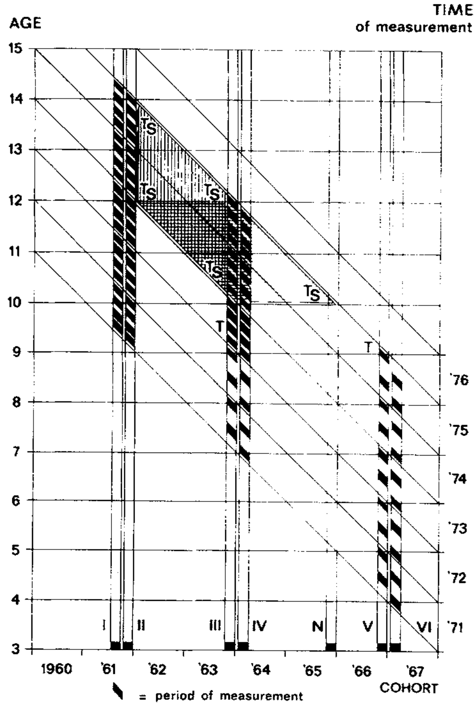

FIG 2.—Diagrammatic representation of mixed-longitudinal design of Nymegen Growth Study, where six cohorts are followed longitudinally for period of five years. Symbol T is used to denote points at which control groups are compared with experimental groups.

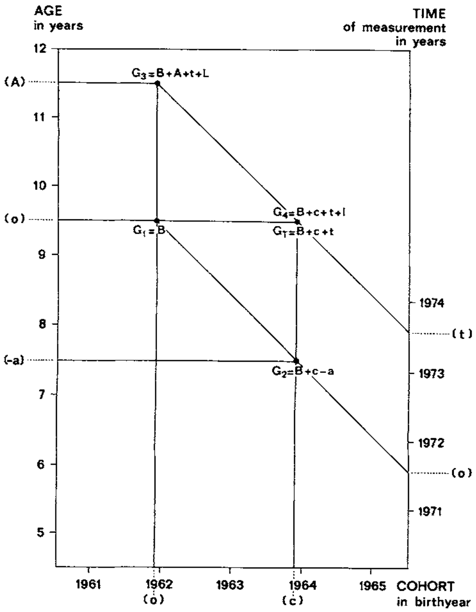

FIG 3.—Part of Nymegen Growth Study used in our study of gingival condition and caries development for two cohorts and two times-of-measurement. G_T represents control group used to assess possible learning and time-of-measurement effects among four experimental groups.

served among the females in the study, for two cohorts and two times-of-measurement as shown in Figure 3. Here, recalling that we can always scale the effects so that the values of the effects corresponding to a particular level of the factors are all zero, we have scaled the age effects $-a$, O and A to facilitate the drawing of this graph. Gingival condition is measured on the six-point scale devised by Parfitt.[35,36] Six sites in the mouth are examined and the mean of these scores is taken to represent the condition of the gingiva; the higher the score, the worse the condition. Caries development is based on changes in the number of DMF surfaces of permanent teeth as observed under standardized conditions using an explorer and mirror.

Referring now to Figure 3, we note that in this situation we have but five equations (one for each of the experimental groups G_1 through G_4 and the control group, G_T) to be used in estimating the seven parameters (B, a, A, c, t, l, L). It is therefore necessary to find two additional, independent equations if we are to be able to solve this system, that is, we need to make two additional assumptions concerning the absence or equality of two of these effects. The first may be realized by assuming that the generational difference of just two years is too small to produce a significant cohort effect, that is, we take $c = O$. The second is that since the length of time the two cohorts actively participated in the study was the same, the learning effects for the two cohorts are equal, that is, $L = l$.

Assuming this for both gingival condition and caries development, the equations can be written as

$$\begin{aligned} G_1 &= B \\ G_2 &= B - a \\ G_3 &= B + A + \mathrm{t} + l \\ G_4 &= B + \mathrm{t} + l \\ G_T &= B + \mathrm{t} \quad , \end{aligned}$$

in which the unknown parameters are B, baseline value; a, age effect from 7.5 to 9.5 years; A, age effect from 9.5 to 11.5 years; $l\,(=L)$, learning effect from two years' participation in the study; and t, the time-of-measurement effect, that is, possible differences in being measured in 1971 as compared with 1973.

Then, the effects included in the model can be estimated by comparing the groups indicated below:

$$\begin{aligned} a&\text{: compare } G_1 \text{ and } G_2 \\ A&\text{: compare } G_3 \text{ and } G_4 \\ l = L&\text{: compare } G_4 \text{ and } G_T \\ \mathrm{t}&\text{: compare } G_1 \text{ and } G_T \\ B&\text{: look at } G_1 \quad . \end{aligned}$$

These groups can be compared in a variety of ways. The hypothesis for the absence of these effects, for example, can be tested using Student's t test or Wilcoxon's two-sample rank sum test.[32]

Results

Table 1 gives the means and standard deviations for both gingival condition and DMF surfaces for the five groups of girls included in the illustration. Table 2 gives the magnitudes of the effects and the associated significance levels for Student's t test for the significance of these effects. It is seen that there is a significant age effect for both gingival condition and caries development; and although the other effects comprising the model are nonsignificant factors in caries development, the time-of-measurement and learning effects are highly significant in the

TABLE 1
MEAN VALUES AND SD OF GINGIVAL CONDITION AND CARIES PREVALENCE FOR THE FIVE GROUPS OF GIRLS DEFINED BY FIGURE 3

Group	Age	Sample Size	Cohorts (mo)	Time of Measurement (mo)	Gingival Condition Mean	Gingival Condition *SD*	Caries (DMF) Mean	Caries (DMF) *SD*
G_2	7.5	33	May/December 1963	May/June 1971	0.1	0.3	2.2	2.6
G_1	9.5	46	November/December 1961	May/June 1971	0.4	0.6	5.8	4.0
G_4	9.5	35	November/December 1963	May/June 1973	1.3	0.7	6.9	4.5
G_T	9.5	22	November/December 1963	May/June 1973	1.9	0.6	6.8	4.4
G_3	11.5	50	November/December 1961	May/June 1973	1.6	0.6	12.3	7.1

model for the developmental changes in the gingival condition.

Discussion

Considering first the observed pattern of caries development, we see significant changes between 7.5 and 9.5 years of age and again between 9.5 and 11.5 years of age. No learning or time-of-measurement effects are in evidence and the interpretation of the data is, in this case, entirely straightforward. The observed changes in the gingival condition, however, require a more detailed discussion. Although the learning effect of 0.6 point is readily ascribable to the instruction received by the experimental group during the course of the study, the surprisingly high time-of-measurement effect of 1.5 points dramatically illustrates the extent of the bias the more traditional designs—which confound this effect with the age effect—may contain and points to the power of Schaie's more general developmental model. Faced with the magnitude of this effect, our attention was immediately called to the fact that different observers were used during the measurement periods; a fact that otherwise might have gone unnoticed and, even if recognized, would not have allowed the accurate assessment of the required correction factor.

We reiterate, for emphasis, that the traditional designs would have confounded both the learning and time-of-measurement effects with the age effect, directly interfering with our ability to study the process of primary concern, namely, the relationship between gingival condition and age. Yet, it should be noted that the factors comprising Schaie's developmental model may not always be unambiguously defined and some care must still be exercised in the interpretation of the results obtained. To cite but one simple example, fluoridation of the water supply would constitute a time-of-measurement effect for a cohort that had been measured previously; but for cohorts subsequently introduced into the study (postfluoridation), the fluoridation factor would have to be seen as giving rise to a potential cohort effect in analyses designed to compare the prefluoridation with the postfluoridation generations. In any event, once the relevant factors to the process under consideration have been

TABLE 2
TESTS FOR THE SIGNIFICANCE OF THE EFFECTS COMPRISING SCHAIE'S MODEL FOR THE FIVE GROUPS OF GIRLS SEEN IN FIGURE 3

Effect	Groups	Gingival Condition Magnitude of Effect	Gingival Condition *P**	Caries (DMF) Magnitude of Effect	Caries (DMF) *P*
Age effect					
7.5 vs 9.5 yr	G_2 vs G_1	0.3	0.05	3.6	0.01
9.5 vs 11.5 yr	G_3 vs G_4	0.3	0.05	5.4	0.01
Test effect from 2-yr participation	G_T vs G_4	0.6	0.01	−0.1	*NS*
Time of measurement effect 1971 vs 1973	G_T vs G_1	1.5	0.001	1.0	*NS*

Note: NS, not significant.
* As calculated from Student's two-sample *t* test.

identified, Schaie's model may be used to isolate these factors for separate study and to estimate the magnitudes of their effects.

Conclusions

In studying growth and developmental processes in dental research, variables other than simple chronological age must often be taken into account if we are to adequately characterize differences in the developmental patterns of the groups under consideration. As demonstrated in this article, cohort, time-of-measurement, and learning (testing) effects may significantly interfere with our ability to directly study development if the traditional cross-sectional and longitudinal designs are used. Mixed-longitudinal studies, with well-scheduled control groups, may better serve the dental research community in the design of studies dealing with the measurement of change.

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