

## Applying Modern Survival Analysis Methods to Longitudinal Dental Caries Studies

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## ABSTRACT

Before the 1960s, tooth-specific caries risk was reported to be highest at 2 to 4 years after eruption. We studied the tooth-specific caries risk in three contemporary age cohorts in Finland. All together, 4072 boys and girls were followed annually from age 6 to age 18+ years in three age cohorts born in the 1960s, 1970s, and 1980s. We used a survival model and Bayesian inferential methods in the statistical analyses to establish the secular changes during this period. The analysis was based on the caries risk in individual teeth as a function of tooth age instead of summary measures, such as DMFS values. Our first finding was a marked overall decrease of caries. Moreover, analyses of the 1960 and 1970 cohorts revealed that the risk in molar teeth was highest immediately after eruption; in the youngest cohort, however, the risks of individual teeth were so low that no such dependencies on tooth age could be established.

**KEY WORDS:** dental caries, Bayesian inference, intensity model, measurement model, survival analysis.

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A supplemental appendix to this article is published electronically only at <http://www.dentalresearch.org>.

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## INTRODUCTION

Well-known indices for dental health, such as DMF(S), are summary measures of the entire dentition and therefore not particularly well-suited for describing the caries process at the level of an individual tooth or surface. This is because such indices do not distinguish between different subjects, different teeth, variations in the numbers of teeth at risk, or dental age. The classic reference for dental health determination based on dental age is the study by Carlos and Gittelssohn (1965) in which life table methods were used to estimate the risk of tooth failure due to caries separately for each tooth and as a function of tooth age. They reported that the caries risk was highest about two years after eruption in the second permanent molars, and one or two years later in all the other teeth.

There has been a significant improvement in dental health in several economically developed countries. Both the level and the pattern of caries attack have changed: Caries in canines and mandibular incisors has virtually disappeared in young adults (Suni *et al.*, 1998), and there is no longer any post-eruptive lag period for molar caries (Larmas *et al.*, 1995).

In this study, the teeth of Finnish boys and girls in three contemporary birth cohorts were compared by means of a Bayesian intensity model. (A more general discussion of the application of Bayesian ideas to dental research is given in Gilthorpe *et al.*, 2000.) Our model is somewhat simpler than that described in Härkänen *et al.* (2000), corresponding to our focus on secular trends rather than on individuals in a heterogeneous population.

We addressed the following main hypotheses: (i) There is an overall decrease of dental caries from the older age cohort, born in the 1960s, to the younger cohorts, born in the 1970s and 1980s; (ii) in molar teeth, the highest risk of failure occurs immediately after eruption in the 1960 and 1970 cohorts; and (iii) in the 1980 cohort, the risk is so low that individual variation between different teeth can no longer be established.

## MATERIALS & METHODS

The present analysis is based on several data sets collected in the course of normal dental care in several municipal health centers in Finland, with annual examinations as described by Larmas *et al.* (1995; Appendix, [www.dentalresearch.org](http://www.dentalresearch.org)). The use of dental records for scientific analyses was approved by the Ethical Committee of the Medical Faculty of the University of Oulu. We considered three age cohorts of boys and girls ( $n = 4072$ ) born in the 1960s, 1970s, and 1980s and followed annually from age 6 to age 18+ years (see Table and Appendix, [www.dentalresearch.org](http://www.dentalresearch.org)). The failure time of a tooth was determined as the time from eruption to the point at which a dentist made a decision, based on the WHO criteria, to fill a caries lesion which had reached dentin (Larmas *et al.*, 1995).

The statistical model and estimation have been described by Härkänen *et al.* (2000). Here, only a short description without mathematical details is provided. The distribution of failure times is expressed in terms of positive-valued

intensity functions  $\lambda(t)$ , where  $t$  denotes subject age in years. Then,  $\lambda(t) dt$  is (approximately) the probability that a tooth which has not failed by age  $t$  will fail during the age interval  $[t, t+dt)$ , where  $dt$  is a small positive constant. After the failure, the intensity function has the value of zero, which is compatible with the fact that a previously failed tooth is no longer intact and therefore cannot fail again "for the first time". The intensity is also zero before tooth emergence, because teeth cannot fail prior to their eruption. High intensity function values reflect a high risk of failure.

Let index  $i$  correspond to a subject,  $j$  to a tooth,  $k \in \{1960, 1970, 1980\}$  to a birth cohort, and  $l \in \{\text{boy, girl}\}$  to gender. The cohort-specific intensity function for tooth failure is then assumed to be of the form:

$$\lambda_{ij}^{(c)}(t) = h_{jkl}(t - \alpha_{ij}) 1\{\alpha_{ij} < t \leq b_{ij}\} \quad (1)$$

where (omitting the indices)  $h$  is called the *baseline hazard (rate)*, expressing the failure risk as a function of tooth age,  $a$  is the eruption time,  $b$  is the failure time,  $1\{a < t \leq b\} = 1$  for  $a < t \leq b$ , and  $1\{a < t \leq b\} = 0$  otherwise, ensuring that the intensity function is zero before eruption and again after failure. A similar model is assumed for tooth eruption times:

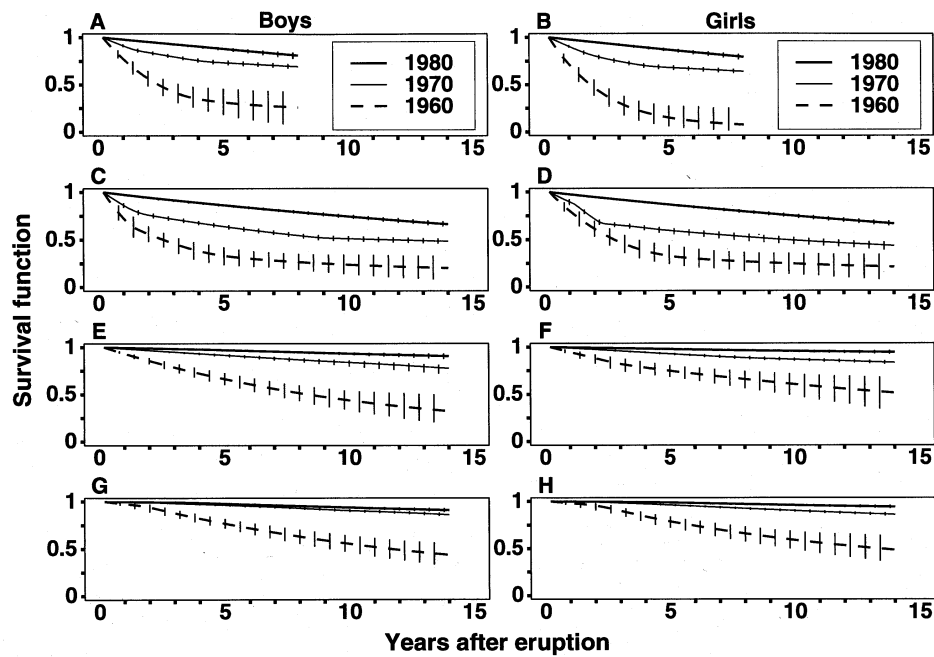
$$\lambda_{if}^{(e)}(t) = f_{ij}(t - \eta_i) 1\{\eta_i < t \leq a_{ij}\} \quad (2)$$

where  $\eta_i$  models the between-subject variation: In some subjects, teeth erupt later (earlier), and for those subjects,  $\eta_i$  gets larger (smaller) values. Although a weak secular trend in the median age of eruption of some teeth was seen between the cohorts, it was assumed that the eruption processes were similar in the three birth cohorts, but possibly different between the genders (Virtanen *et al.*, 1994).

The value of the *survival function* at time  $t$  represents the probability that a newly erupted tooth will survive for at least  $t$  years after eruption, that is,  $b_{ij} > a_{ij} + t$  (Andersen *et al.*, 1993). The survival function depends on the cumulative risk experienced, being a function of the integrated hazard rate, and it is therefore not sensitive to local changes in the risk level. Consequently, we use both hazard rates and survival functions in reporting our empirical results.

In Bayesian inference, the *posterior* distribution of model parameters can be viewed as an expression of the uncertainty regarding their true values, given the *prior* information and the observed evidence contained in the data (Gelman *et al.*, 1995). Due to the large amount of data in this study, the choice of the prior distributions of the parameters  $h$  and  $f$  is likely to have a negligible effect on the results. The software for the estimation is available at <http://www.rni.helsinki.fi/~tth/bite.html>.

The eruption and failure times were *interval-censored* in

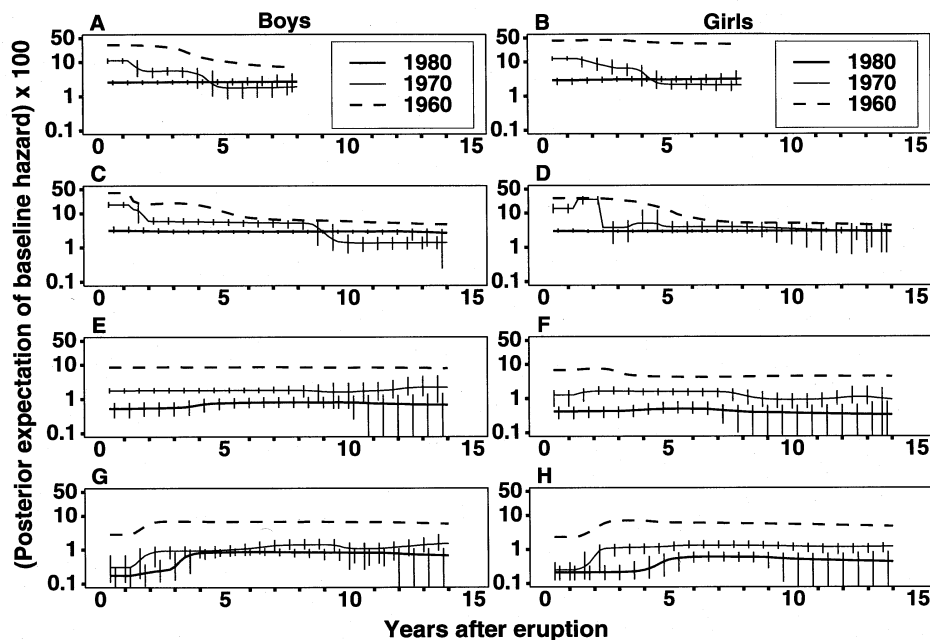


**Figure 1.** Posterior expectation of survival function of maxillary molar and incisor teeth with 95% pointwise credibility intervals. The dashed line corresponds to the 1960 cohort ( $n = 193$ ), the thin solid line to the 1970 cohort ( $n = 1927$ ), and the thick solid line to the 1980 cohort ( $n = 1952$ ). The vertical lines correspond to the 95% pointwise credibility intervals. The panels A, C, E, and G represent boys, and B, D, F, and H girls. The panels A and B stand for second molars, C and D for first molars, E and F for lateral incisors, and G and H for central incisors.

the data: In each case, only the first examination time at which a newly erupted tooth or a new failure was found was recorded. Since the models (1) and (2) are expressed in terms of exact eruption and failure times, the original interval-censored data were augmented (Tanner and Wong, 1987) by the sampling of such times from the Poisson likelihoods defined by (1) and (2). The data augmentation as well as the estimation of the functions  $h$  and  $f$  in (1) and (2) were done iteratively by the generation of a large sample of the missing eruption and failure times and parameter values from the targeted posterior distribution of these variables, given the data. All *posterior probabilities* and *expectations* can then be approximated by suitable averages computed from that sample. For example, the posterior expectation of the unknown survival function corresponds to the mean value of that function, given the statistical model and the evidence contained in the data. For simplicity, we have here chosen to ignore in our statistical model the frailty parameters, which were used by Härkänen *et al.* (2000) for modeling the within-subject correlation of the failure times. In the test runs, this had only a small effect on the width of the credibility intervals.

## RESULTS

Our results show that caries has decreased dramatically during the study period, in view of the tooth survival probabilities in the three cohorts. The difference of survival functions between the 1960 and 1970 cohorts was somewhat larger than that between the 1970 and 1980 cohorts (Fig. 1). The 95% credibility intervals do not overlap, and the differences can therefore be considered statistically significant. In all cohorts, the molar teeth were the most vulnerable, and in the 1960 cohort, up to 80-90% of the molars became carious by the end of the follow-up. In the 1980



**Figure 2.** Posterior expectations of the failure hazard rates of maxillary molar and incisor teeth. The dashed line corresponds to the 1960 cohort (n = 193), the thin solid line to the 1970 cohort (n = 1927), and the thick solid line to the 1980 cohort (n = 1952). The vertical lines correspond to the 95% pointwise credibility intervals (excluding the 1960 cohort due to small sample size). The panels A, C, E, and G represent boys, and B, D, F, and H girls. The panels A and B stand for second molars, C and D for first molars, E and F for lateral incisors, and G and H for central incisors. In the 1980 cohort, the risk of failure is constant, except in central incisors, and the age of the tooth thus does not affect the risk of failure. (Log-scale on the vertical axis ranges from 0.1 to 50.)

cohort, up to 30% of the molars and less than 10% of the other teeth were carious (Fig. 1). The corresponding teeth in the mandible and the maxilla had very similar survival probabilities, except that very few lower incisors became carious.

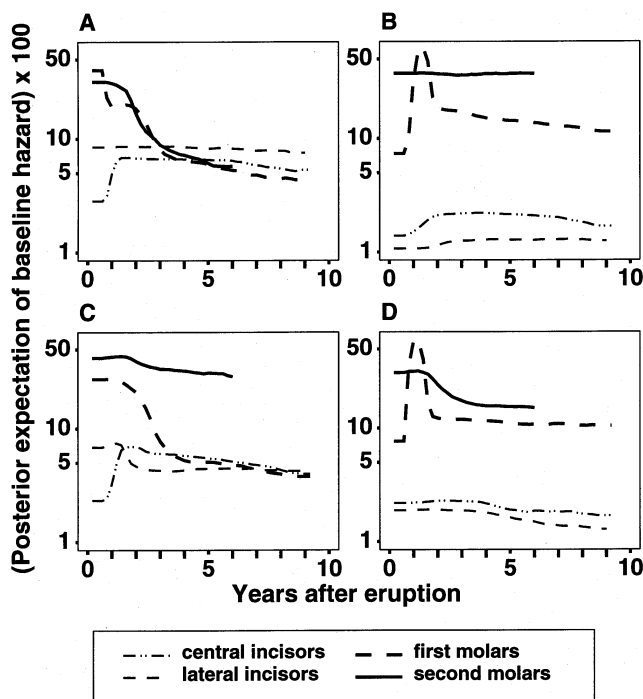
The molar teeth also had much larger failure risks in terms of posterior expectations of the hazard rates in the 1960 cohort (Fig. 3), but the small amount of data in that cohort resulted in wide credibility intervals. (For this reason, they are not presented in Fig. 2.) The risk was generally highest immediately after eruption, but in the mandibular first molars, the highest risk occurred about two years after eruption (Fig. 3). After five years, the failure risks were more similar in all cohorts (Fig. 2). In the 1970 cohort, the overall risk decreased during the 7-8 years after the eruption of the first molars, whereas in the 1980 cohort the overall caries risk seemed to remain almost constant. A peculiar finding was

that the hazard rates for the maxillary first molars of boys in the 1970 cohort were significantly below those in the 1980 cohort at later tooth ages, having been clearly higher after eruption (Fig. 2c).

**DISCUSSION**

The classic reference for longitudinal dental caries studies in adolescents has been Carlos and Gittelsohn (1965). Their report was based on a clinical trial conducted in two towns (n = 6400) in the state of New York, USA. Their survival estimates were found to be similar to our estimates (Fig. 1) for the 1960 cohort. However, one should bear in mind that, here, we followed dental caries to a later stage and did not include enamel lesions (Larmas *et al.*, 1995). This indicates that the progression of enamel lesions to dentin was rapid.

It is not clear how many of the differences in the observed patterns of caries attack between the 1960 and 1970 cohorts compared with the 1980 cohort are real changes in caries, and to what extent they should be attributed to new practices in disease prevention and treatment. The emphasis placed on preventive treatment, such as school-based fluoride rinses, the use of fissure sealants, increased use of fluoridated tooth paste, etc., in Finland had reduced the caries risk in the 1970 and especially in the 1980 cohorts. It is also probable that, as caries has diminished, the decisions to restore have been postponed (Espelid *et al.*, 2001). The peculiar difference in the failure risk in some molar teeth (Figs. 1, 2) may also be a consequence of a selection mechanism: In the 1970 cohort, the teeth of high-risk subjects remained at risk only for a few years after they had erupted, and only the healthiest subjects



**Figure 3.** Posterior expectations of the failure hazard rates for the 1960 cohort containing boys (n = 103) and girls (n = 90). The panels A and B represent boys, and C and D girls. The panels A and C stand for the maxilla, and B and D for the mandible. Molar teeth have the highest failure risk after eruption, with the exception of mandibular first molars, which have the highest risk approximately two years after eruption. (Log-scale on the vertical axis ranges from 1 to 50.)

were hence used for assessing the caries risk at the later tooth ages, while in the 1980 cohort the high-risk subjects also remained at risk for a longer period.

When the tooth-specific hazard rates were considered as functions of tooth age, some striking differences were found between our results (Fig. 3) and the life table estimates of annual probabilities of caries attack (Carlos and Gittelsohn, 1965). The life table estimates of logarithmic failure intensities of different teeth seem to have the approximate form of a downward parabola, with the highest risk at 2 to 4 years after eruption. Our results, in contrast, indicate that the risk was highest immediately after eruption and then decreased monotonically in the molars, except in the mandibular first molars. The risk in the other teeth was approximately constant, or the curve had a slightly downward parabolic shape.

The differences raise some questions which are difficult to answer, since we do not have access to the data of Carlos and Gittelsohn (1965). Nevertheless, some of their results can be questioned: First, the follow-up time was divided into four-month *computational intervals*. The risk of caries was then estimated by dividing the number of failures by the subjects' (estimated) total time at risk during that interval. In these computations, interval-censored (unobserved) occurrence times were replaced by the mid-points of the dental examination intervals, which were approximately one year. This may have surprising consequences in the life table estimates, particularly if the computational intervals are much shorter than the examination intervals. If both tooth eruption and caries attack were registered as having occurred during the same examination interval, then the unknown true value of the tooth lifetime was approximated by a value equal to half the length of that interval. As a consequence, the first computational interval can contain a failure time of a tooth only if the corresponding examination interval was less than eight months, and thus, short lifetimes are recorded (approximately) correctly in the life table estimation only if they are associated with short examination intervals. It seems that such intervals were quite rare in the study by Carlos and Gittelsohn (1965). This alone can explain why the short lifetimes were systematically associated with low risk estimates, which also explains partly the "rapid rise in susceptibility" shown by the curves in their Figs. 1 and 2. Our results, which are naturally based on much more elaborate

**Table.** The Representative Samples of Finnish Subjects from Kemi (23,000 inhabitants), Kuopio (95,000), Oulu (110,000), Raahе (18,500), Tornio (23,000), Turku (160,000), Laitila (9,000), Muurame (7,000), and Ylivieska (13,500), and Born in the 1960s, 1970s, and 1980s (Virtanen *et al.*, 1997; Larmas, 1999)

Municipality	Gender	1960	1969	1970	1971	1979	1980	1981	Σ
Kemi	Boys	103		89			104		296
	Girls	90		84			82		256
	Σ	193		173			186		552
Kuopio	Boys			102	101		98	91	392
	Girls			101	102		95	102	400
	Σ			203	203		193	193	792
Oulu	Boys			63	85		96	84	328
	Girls			62	71		97	92	322
	Σ			125	156		193	176	650
Raahе	Boys			7	48		83		178
	Girls			6	59		92		193
	Σ			13	107		175		371
Tornio	Boys			46			83		129
	Girls			71			95		166
	Σ			117			178		295
Turku	Boys			113			68	27	208
	Girls			155			86	19	260
	Σ			268			154	46	468
Laitila	Boys			20	25	3	36	37	121
	Girls			29	15	2	44	29	119
	Σ			49	40	5	80	66	240
Muurame	Boys			42			48		90
	Girls		1	41			60		102
	Σ		1	83			108		192
Ylivieska	Boys			79	74		111		264
	Girls			81	79		88		248
	Σ			160	153		199		512

modeling and computations, do not contain these systematic biases.

Second, Table 1 (in Carlos and Gittelsohn, 1965) indicates that only 2104 children out of approximately 7400 were included in the life table analysis. All permanent teeth that had erupted before the first examination were excluded. It is also unclear why some children had only one or two examinations. It is questionable whether appropriate life table techniques exist for dealing with such situations. The strength of our method is that it does not require intervals of equal length, and that it can also utilize data on children who were examined only a few times.

From a clinical point of view, it is important to notice that our results show that the highest risk of caries attack in the molar teeth occurred soon after eruption in the 1960 and 1970 cohorts, not 2 to 4 years after eruption. Therefore, the most efficient caries-preventive measures for molar teeth were needed during the years immediately following tooth eruption. Similar results can be seen in all the other analyses of carious attack that have been conducted on Finnish children and adolescents after the 1960s (Larmas *et al.*, 1995; Virtanen and Larmas, 1995; Virtanen *et al.*, 1997; Suni *et al.*, 1998). This high-risk period seems to occur at least when the caries prevalence is as high as it was in the USA before 1960 (Carlos and Gittelsohn, 1965) and in Finland in the 1960s.

Although Bayesian intensity models are not the only method

for analyzing survival data (*cf.* Hujoel *et al.*, 1998; Hannigan *et al.*, 2001), they constitute a unified framework for analyzing left-, interval-, or right-censored multivariate data. Frequentist methods could also be used, but non-parametric analysis of interval-censored data is not equally straightforward in that case. From a methodological perspective, the present study supports the proposition that Bayesian modeling and data analysis will become familiar features in the dental literature in the future (Gilthorpe *et al.*, 2000). The drawback of this methodology is that the computational burden in estimation is considerably heavier than when traditional frequentist methods are applied.

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