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CARIES PATTERNS IN 7 YEAR OLD CHILDREN IN
BELGIUM: THE SIGNAL TANDMOBIEL® PROJECT.

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CARIES PATTERNS IN 7 YEAR OLD CHILDREN IN BELGIUM: THE SIGNAL TANDMOBIEL® PROJECT.

By

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ABSTRACT

CARIES PATTERNS IN 7 YEAR OLD CHILDREN IN BELGIUM: THE SIGNAL TANDMOBIEL® PROJECT.

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Dental caries or tooth decay is the most common oral health problem. Although it is quite preventable, it still remains the most common chronic disease of children aged 5 to 17 years, and has been linked with poor academic performance, low self confidence and poor peer interactions.

Despite the many epidemiologic studies conducted to assess the intra-oral pattern of dental caries, there are still some unanswered questions. There are four quadrants in the mouth believed to be inter-correlated and it is widely believed that dental caries develop symmetrically within the mouth but much statistical results are still needed. Most of the previous studies have relied on the usage of the decayed, missing, and filled (DMF) index developed in the 1930s, to analyze dental caries outcomes. It has its limitations in explaining the development of caries and is unable to measure tooth-specific problems such as caries patterns. It is speculated that a more effective manner to study the spatial distribution of dental caries may be to analyze using adequate statistical models such as generalizing estimated equations (GEE), and Alternating Logistic Regression (ALR). Such models can be used to determine tooth surface susceptibility to caries formation and to answer questions regarding dental caries spatial distribution that may exist in the mouth. These findings should enable dentists/hygienists to detect dental caries at earlier stages and provide more subject specific treatment plans.

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I extend my deepest gratitude to my parents and siblings for their unending love and great support in helping me with my academic pursuits and with life. Especially for instilling in me a strong foundation of faith in God, from which I draw my strength in life.

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CHAPTER 1

Introduction

1.1 Background and objectives

Dental caries is a leading cause of tooth loss, which can affect chewing, and food intake selection. In the children population especially where nutrients are needed for growth, this can lead to an increased risk of systemic diseases such as cardiovascular conditions at an adult age.

Dental caries is defined as "the dynamic de- and re-mineralizing processes resulting from microbial metabolism on the tooth surface. Overtime this may result in the net loss of mineral and subsequently possibly, but not always, will lead to cavitations" (Fejerskov, 1997). Dental caries occurs as a result of the interplay of three main factors over time: dietary carbohydrates, bacteria within dental plaque, and susceptible hard tooth surfaces. The hard tissues of the crown (coronal, enamel, and dentine) and root (cementum, dentine) surfaces of teeth are affected in the demineralization process, which is caused by acids produced by bacteria. There are a number of bacteria linked to dental caries namely *mutans Streptococci* and possibly *Lactobacilli.* Each carious process begins with the formation of biofilms on the surface of the tooth involved. The biofilm is able to form on any surface where there is adequate supply of water and nutrients such as the oral cavity. The pellicle of the tooth surface present on enamel, dentine and cementum is the key location where the biofilm initiates (Kidd and Fejerskov, 2004). The formation of biofilm and plaque is a stage wise process, where each stage shows a more complex colonization of the bacteria, increased selectiveness of the biofilm regarding bacteria, and an advanced level of organization in the biofilm. Over time, the film hardens with the deposition of minerals and the secretions produced by the bacteria. The constant metabolic activity of these bacteria ensures constant multiplication and thereby increased thickness of the plaque, which in turn requires constant nutritional support (Kidd and Fejerskov, 2004). Most of this support is met by the food and liquid intake via the oral cavity into the mouth, with saliva being the medium of nutrition transport. The bacterial secretions produced drop the pH to around 5.3, and causes demineralization of the tooth surfaces. This leads to "softening" of the tooth structure, which gives way to cavity formation (Kidd and Fejerskov, 2004).

The plaque and saliva are saturated with calcium and phosphate ions, so if the pH returns fairly rapidly above the 5.3 levels, ions will re-enter the enamel and re-crystallize. The process of re-mineralization takes longer in an acidic environment, but is rapid if the fluid next to the enamel is neutral or even alkaline. It is therefore uncommon to find caries in those parts of the mouth near the outflow of salivary glands, like the lower incisors, where the environment is filled with buffers and concentrated calcium ions of saliva (Manji et al, 1991). Thus saliva flow rate and composition can influence the progression rate of caries lesions (Melberg, 1986). If the total outflow of saliva is increased, there is a lower risk of caries development. Caries develop when the process of re-mineralization is slower than the process of demineralization.

1.2 Literature review

Previous studies have shown that certain teeth are more susceptible to dental caries than others. The maxillary incisors are more prone to developing caries than the mandibular incisors. Posterior teeth which have pit-and-fissure (occlusal) surfaces are more prone to dental caries formation than anterior teeth with smooth (labial and lingual) surfaces (Reid and Grainger, 1955). A recent study of caries susceptibility has replicated previous findings that teeth can be placed in the order of susceptibility from greatest to least, as follows: 1) mandibular (lower) second molars, 2) mandibular first molars, 3) maxillary (upper) second premolars, 4) maxillary first premolars, 5) maxillary central and lateral incisors, 6) maxillary and mandibular canines and 7) mandibular central and lateral incisors (Macek *et al.*, 2003)

While understanding the caries susceptibility of teeth is informative, it does not provide information regarding the progression of the disease. Dental caries has unique characteristics in that it represents both past and current disease processes. When a person goes to the dental clinic for a routine examination, it would be beneficial for the dentist to have an understanding regarding caries patterns to help suggest subject specific preventive measures. The traditional DMFT/S "Decayed/ Missing/ Filled Teeth/Surface" index is a well known method for analyzing the prevalence of caries. It was introduced by Klein *et al.* (1938) and provides aggregated scores which provide a summary of mouth-level caries information for each individual at tooth level or tooth surface level. It counts the number of decayed teeth within the individual's mouth. It is beneficial in the evaluation and comparison of dental caries risks among different population groups but it does not give detailed information among individuals regarding which specific teeth is decayed (Todem, 2007). For a dentist, counting the number of decayed, missing and filled teeth alone does not help address intra-oral caries incidence pattern. When a patient comes for a routine dental examination and a caries lesion is found on a specific tooth in a quadrant, a dentist with knowledge of intra-oral caries distribution patterns will be able to predict the next tooth with a high risk of developing caries. It has been suggested that the use of tooth-level models should enhance the interpretation of complex dependent data generated from studies in dental research.

The initial attempt at understanding the caries experience was to establish first whether the patterns observed are symmetric or asymmetric in nature. Recent studies have helped identify three more categories of carious lesions based on their location. The "random" caries series is one where the lesions have equal opportunity of developing in the contra-lateral sides of the mouth (Vanobbergen *et al.*, 2007). The "aggregated" pattern of caries shows the concentration of carious lesions on one side of the mouth, while the "regular" pattern shows a more symmetrical distribution of caries on both sides of the mouth (Vanobbergen *et al.*, 2007). Using the data from the National Survey of Oral Health (1985-1986), the Hujoel *et al* (1994) study investigated three different caries patterns (random, aggregated, and regular) seen in 12,776 subjects. From the study they determined that the distribution of caries lesions on the teeth and surfaces were not random but rather aggregated or clustered ($P<0.0001$) across the different subgroups. A two-sided test was performed, which resulted in a large calculated z-score rejecting the null hypothesis of a random pattern, in favor of an aggregated pattern. This result confirmed previous findings that adjacent pairs have a higher risk of developing caries. The study by Hujoel *et. al.,* (1994), provided possible explanations that might explain this aggregated caries pattern, one of which suggests that the neighboring teeth are infected by the proximity of the caries lesions regardless of it being on the right or left side (Hujoel *et al,* 1994).

The goal of the Ananth and Kantor (2004) study was to assess if caries aggregated within a subject. This complex dataset utilized a radiographic efficacy National Institutes of Health (NIH) data with multiple levels of nesting. In this study, they investigated the clustering of caries on each of the 16 tooth surfaces per subject. There was a complex multiple levels of nesting: tooth surfaces within an interproximal (IP) regions, IP rejoins within a jaw, and jaws within a subject. It was reported that caries lesions appear to aggregate strongly within subjects with a spatially distributed risk ($p<0.05$).

Using data from two Belgium surveys: the Signal Tandmobiel® (ST) project and the Tandje de Voorste-Smile for Life (TDV) project, the Vannobergen et al (2007) study investigated the distribution and spatial correlation of caries lesions. This sample covered 1,291 3-year old and 1,315 5-year old children from the TDV project and 4,468 7-year old Flemish school children from the ST project. A symmetrical pattern was noted at the population level, left-right caries distribution patterns appearing strongest in the mandible. At an individual level, randomness of caries patterns could be rejected, as caries tended to cluster on one side of the mouth ($p=0.0005$).

The prevailing hypothesis remains that there is indeed a spatial distribution of dental caries, and a need for statistical models that allow for such evaluations. To answer this question, there is a need for data collected at the tooth or tooth-surface level (Hujoel *et al.,* 1994).

CHAPTER 2

Population and Methods

2.1 *Study Population: The Signal Tandmobiel® Project*

2.1.1 Introduction

The Signal Tandmobiel® project is an extensive longitudinal and cross-sectional study carried out from 1996 till 2001, and conducted with the support of three Flemish universities (Catholic University at Leuven, University of Gent, Free University at Brussels), the Association of Flemish Dentists (VVT), the Flemish scientific Association for Youth Health (VWVJ) and the industry (LeverElida). The Signal Tandmobiel® project's objectives were to carefully examine the oral hygiene of the school children ages 7 to 12 year old over six years, and assess the effect of yearly oral hygiene education conducted at the random schools. The three parts of the study were: (1) oral health condition screening, (2) obtaining health information and education, and (3) a scientific contribution.

2.1.2 Study Design

The study included 4468 Flemish children in Belgium, who were selected by a stratified clustered random sample. The children were born in 1989, and followed throughout elementary school. At enrollment, children were about 7 years of age, and by the end of the study, they were 12 to 13 years of age. An equal number of boys and girls were examined. The selected schools were divided into three groups known as samples A, B and C. Group A consists of a cohort of children who were followed longitudinally during their 6-year period in elementary school from 1996 to 2001 and were examined yearly and also subjected to a yearly educational program. The cohort of children in Group B, were examined in the first and last year of the study. Those in Group C were sampled yearly, starting from the second year, to allow a cross-sectional comparison with group A. Group B was used as a control in assessing the effect of the examinations and educational program in group A. Group B is identical to Group C in year 1. Schools, instead of children, were selected randomly with a probability proportional to the number of children in school. The sampling was done after stratification for educational system and province. This stratification allows that the group of children is representative of the population. Whenever a school was selected, all children in the first grade of the selected school were allowed to participate. Selecting individual children instead of schools would not be feasible for practical and economical reasons and it would be unfair to allow only some of the children from the same school to participate.

2.1.3 Project Conduct

The children were examined by trained dentists in a mobile dental clinic (Tandmobiel), using the standardized and well established diagnostic criteria of the World Health Organization (WHO) and the British Association for the Study of Community Dentistry (BASCD). There were 16 dentists in the "Tandmobiel" who had been trained and evaluated on a yearly basis to conduct the dental examination. The examination was divided into three main parts; the evaluation of the dental hygiene, the evaluation of the gingival health status and the examination of hard dental tissue for the presence of caries and fillings. In addition to the examinations, questionnaires were also administered; there was a parental questionnaire that addressed specific questions regarding the child's oral hygiene, fluoride exposure, visits to a dentist, dietary habits and dental trauma. A medical center questionnaire was completed for each child by a physician at the medical center that provided name, date of birth, gender, nationality, school, class, socioeconomic status, region and medical precedents. A preventive health education program was an important component of the project, and was adapted each year to fit the age of the children. The message was conveyed through the use of slides, tapes, brochures, and a reward. Study results were not directly reported to the child but in considerable details to the medical center and by means of a letter to the parents for possible preventive instructions, advise, treatment or referral to their dentist.

2.1.4 Data

The collected outcome data comprise information on (1) the caries experience of all deciduous and permanent teeth, including the tooth surfaces affected by caries, (2) the plaque index measured at six locations in the mouth, (3) the gingival condition, etc. Questionnaires on oral hygiene behaviors are distributed yearly to the children, filled out by the parents and returned on the day of the examination in the Tandmobiel. Risk factor information such as the consumption of candy and dry biscuits, the utilization of toothpaste and with or without fluoride, the brushing habit of the child as well as that of her parent, the visit of the child to the dentist, etc, were also collected. Other aggregated information such as the nationality, the province, the urbanization status of the place of residence and the educational system of the child were also collected. More description of the Signal-Tandmobiel® can be found elsewhere (Vanobbergen *et al.,* 2000).

2.2 *Statistical Methods and Design*

2.2.1 Research Questions/Purpose of the study

This study aims to investigate the spatial distribution of dental caries on tooth surfaces in the primary dentition of 7 year olds, using statistical models for correlated data. The data used are from the Signal Tandmobiel® study. Our study sample was restricted to 4351 school children who attained their seventh birthday anniversary during the course of the study. Specifically, in this study, we are interested in the following questions:

- Which tooth surfaces are more susceptible to caries experience?
- With respect to dental caries, is there any spatial association of dental caries at the quadrant level?

An answer to these questions requires the analysis to be performed at the tooth or tooth-surface level. This then necessitates the use of methods for correlated data. In dental research, intra-mouth data present a unique set of challenges to statistical analysis (Leroux *et al.*, 2006). These challenges include, but are not limited to, large cluster sizes (large number of teeth within a mouth); informative cluster sizes and multilevel data structures which generate a very complex correlation structure.

Figure 2.1 is an illustration of the primary dentition. In Europe, these deciduous teeth are numbered with two digits where the first digit represents the quadrant and the second digit the position of the tooth within a quadrant. As an example, tooth 55 represents the last molar of the fifth quadrant. Quadrants V and VI form the maxilla or the upper jaw whereas quadrants VII and VIII form the mandible or the lower jaw. This pictorial representation of the primary dentition exhibits a two-level spatial association structure. The first-level spatial association structure is that among quadrants (V)-(VIII), whereas the second-level spatial association structure is that of teeth nested within a quadrant.

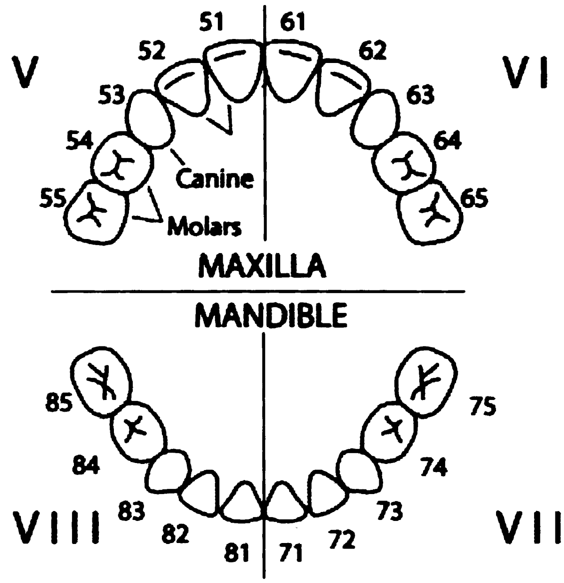

Figure 2.1 The location of the deciduous teeth in the mouth (adapted from Bogaerts et al. 2002).

Vanobbergen *et al.* (2007) have proposed a GEE-based model to answer some of the questions related to the spatial association of dental caries in the mouth. Specifically, these authors have used so-called alternating logistic regression (ALR) to model simultaneously the marginal expectation of each binary outcome and the pair-wise associations between outcomes (Liang, Zeger and Qaqish, 1992). This model was used to circumvent some of the numerical problems related to the second order moments-GEE2 model due to larger cluster sizes. Although the ALR model is known to be numerically stable, its convergence for unstructured second order moments remains an issue for moderately larger cluster sizes. Indeed, when the cluster size is relatively large, one may encounter a numerical difficulty when an unstructured odds ratio model is imposed. This

limitation was the reason for these authors to perform their analysis on a small subset of teeth (8 per mouth). When the ALR model with unstructured odds ratios is attempted on the full dataset (20 teeth per mouth), the algorithm did not converge. To circumvent some of the computational difficulties of the ALR model for larger cluster sizes, we imposed some structure on the odds ratio model. These constraints are carefully chosen, as overly simplistic models may limit our ability and flexibility to study the spatial distribution of dental caries in the mouth. We discuss this in the section below.

2.2.2 Modeling correlated binary data using the alternating logistic regression

Generalized Estimating Equations (GEEs), developed for the analysis of correlated data, provide a flexible method for modeling the marginal mean response while adjusting inferences for correlation. The estimates of the mean response that this approach yields are therefore population-averaged estimates, analogous to those obtained from cross-sectional data. GEE uses a "working correlation" to treat the within-subject correlation, and produces standard error estimates that take into account the correlation of responses within subjects (Liang and Zeger, 1986; and Zeger and Liang, 1986). As a result, the within-subject correlation is not modeled explicitly but adjusted for using the so-called sandwich-based estimator of the variance covariance matrix of the parameter estimates. The classical GEE model treats the intra-oral correlation as a nuisance parameter. This is troublesome since the intra-oral association terms are important in understanding the spatial distribution of dental caries in the mouth.

The so-called Alternating Logistic Regression (ALR) model developed by Carey, Zeger, and Diggle (1993), overcomes this problem by explicitly modeling the association between the intra-oral caries outcomes. The algorithm switches back and forth between the GEE and the logistic regression, hence the name ALR. Another alternative to modeling association using odd ratios is the use of Pearson correlation coefficient. But as pointed by Diggle, Liang, and Zeger (1994) modeling association among binary responses with correlation has a disadvantage, and they propose using the odds ratio instead. We illustrate the application of the ALR model to data on intra-oral caries outcomes. For tooth k in quadrant j of child i, we denote by y_{ijk} a binary response variable taking value 1 if caries is present and 0 if otherwise. The first moment $P(y_{ijk} = 1)$ is modeled as:

$$\log\left(\frac{P(y_{ijk} = 1)}{1 - P(y_{ijk} = 1)}\right) = \gamma_{jk}$$

where γ_{jk} represents the log odds of caries for tooth k in quadrant j. These parameters help estimate the caries prevalence for any tooth at a specific location in the mouth. In this logistic regression model, the position of the tooth in the mouth is treated as the independent variable. Details are given in the Table 2.1.

Note that teeth 71, 72, 81, and 82 were removed from our analyses as these teeth were primarily unaffected by caries. To compare the frequency of dental caries between two teeth, the parameter γ_{jk} is used. As an example, to compare teeth 85 and 75, we consider the following null hypothesis,

$$\gamma_{85} = \gamma_{75}.$$

Table 2.1 Parameter γ_{jk} based on tooth position in the quadrant

QUADRANT	POSITION	TOOTH	γ_{jk} PARAMETER
5	5	**55**	γ_{55}
5	4	**54**	γ_{54}
5	3	**53**	γ_{53}
5	2	**52**	γ_{52}
5	1	**51**	γ_{51}
6	1	**61**	γ_{61}
6	2	**62**	γ_{62}
6	3	**63**	γ_{63}
6	4	**64**	γ_{64}
6	5	**65**	γ_{65}
8	5	**85**	γ_{85}
8	4	**84**	γ_{84}
8	3	**83**	γ_{83}
7	3	**73**	γ_{73}
7	4	**74**	γ_{74}
7	5	**75**	γ_{75}

In addition to these first moments, we model the association parameters as,

$$\log\left(\frac{P(y_{ijk}=1)/\left(1-P(y_{ijk}=1)\right)}{P(y_{ij^*k^*}=1)/\left(1-P(y_{ij^*k^*}=1)\right)}\right)=\alpha_{u(jk,j^*k^*)}.$$

Here the parameter $\alpha_{u(jk,j^*k^*)}$ measures the log odds of dental caries for tooth k in quadrant j relative to that of tooth k* in quadrant j*. A full description of $\alpha_{u(jk,j^*k^*)}$ is given in Table 2.2. As an example, the parameter α_1 captures the lag 1 association in quadrant 5. This lag 1 association is captured by the pairs of teeth (55,54), (54,53), (53,52), and (52,51) of the fifth quadrant. This model obviously assumes that the odds ratio of dental caries for the pair of teeth (55,54), is the same as that of the pairs (54,53), (53,52) and (52,51). The parameter α_{22} captures the constant log odds ratio between any tooth in quadrant 5 to any tooth in quadrant 8. These constraints may be viewed as restrictive, but as stated in the section above, we have imposed these conditions to ensure convergence of the ALR model. Other restrictions are shown in the Table 2.2.

Table 2. 2 Description of the log odds ratio Parameters $\alpha_{u(jk,j^*k^*)}$

PARAMETERS $\alpha_{u(jk,j^*k^*)}$	QUADRANT POSITION	TOOTH PAIRS $(jk, j^* k^*)$
α1	Q5 lag1	(55,54),(54,53),(53,52),(52,51)
α2	Q5 lag2	(55,53),(54,52),(53,51)
α3	Q5 lag3	(55,52)(54,51)
α4	Q5 lag4	(55,51)
α5	Q6 lag1	(61,62)(62,63)(63,64)(64,65)
α6	Q6 lag2	(61,63)(62,64)(63,65)
α7	Q6 lag3	(61,64)(62,65)
α8	Q6 lag4	(62,65)
α9	Q8 lag1	(85,84)(84,83)
α10	Q8 lag2	(85,83)
α11	Q7 lag1	(73,74)(74,75)
α12	Q7 lag2	(73,75)
α13	Q5Q6lag1	(51,61)
α14	Q5Q6lag2	(52,61)(51,62)
α15	Q5Q6lag3	(53,61)(52,62)(51,63)
α16	Q5Q6lag4	(54,61)(53,62)(52,63)(51,64)
α17	Q5Q6lag5	(55,61)(54,62)(53,63)(52,64)(51,65)
α18	Q5Q6lag6	(55,62)(54,63)(53,64)(52,65)
α19	Q5Q6lag7	(55,63)(54,64)((53,65)
α20	Q5Q6lag8	(55,64)(54,65)
α21	Q5Q6lag9	(55,65)
α22	Q5Q8	(55,85)(55,84)(55,83)(54,85) (54,84)(54,83)((53,85)(53,84) (53,83)(52,85)(52,84)(52,83) (51,85)(51,84)(51,83)
α23	Q5Q7	(55,73)(55,74)(55,75)(54,73) (54,74)(54,75)(53,73)(53,74) (53,75)(52,73)(52,74)(52,75) (51,73)(51,74)(51,75)
α24	Q6Q8	(61,85)(61,84)(61,83)(62,85) (62,84)(62,83)(63,85)(63,84) (63,83)(64,85)(64,84)(64,83) (65,85)(65,84)(65,83)
α25	Q6Q7	(61,73)(61,74)(61,75)(62,73) (62,74)(62,75)(63,73)(63,74) (63,75)(64,73)(64,74)(64,75) (65,73)(65,74)(65,75)
α26	Q8Q7lag5	(83,73)
α27	Q8Q7lag6	(84,73)(83,74)
α28	Q8Q7lag7	(85,73)(84,74)(83,75)
α29	Q8Q7lag8	(85,74)(84,75)
α30	Q8Q7lag9	(85,75)

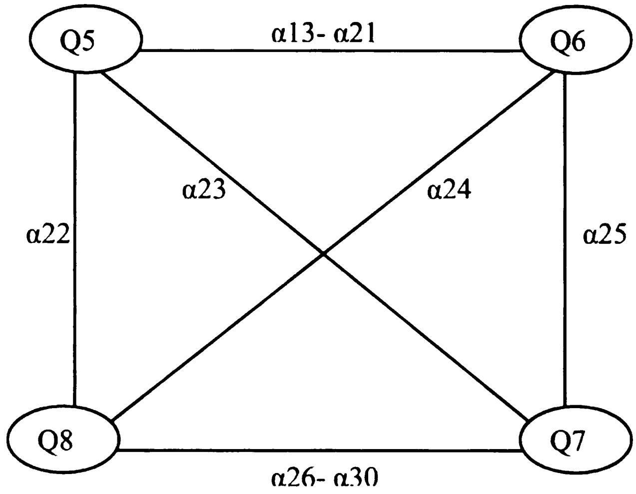

Figure 2. 2 Parameters representing the quadrant-level association

In Figure 2.2, we present the parameters used to assess the spatial association of caries outcomes at the quadrant level. As an example, the set of parameters α_{13} to α_{21} denoted $\alpha_{13} - \alpha_{21}$ captures the left right association for the upper jaw and the parameters $\alpha_{26} - \alpha_{30}$ that of the lower jaw. Our model assumes that "across" and the up-down associations are captured by a single parameter. As an example, the association between quadrant 5 and quadrant 8 is captured by α_{22}. This model assumes that the log odds ratio of dental caries of any tooth in quadrant 5 relative to any tooth in quadrant 8 is constant. Similar assumptions are made for quadrant 5 and quadrant 7, quadrant 6 and quadrant 7, quadrant 6 and quadrant 8. This structured odds ratio model was necessary to achieve model convergence. Any attempt to leave these association terms unstructured, lead to computational challenges.

Hence, to assess the left-right quadrant-level association as compared to other quadrant-level association, we consider the following null hypothesis,

$$\frac{\alpha_{13:21}+\alpha_{26:30}}{14}=\frac{\alpha_{22}+\alpha_{25}+\alpha_{23}+\alpha_{24}}{4}.$$

In the formula above, we define $\alpha_{u:u*}=\alpha_u+\alpha_{u+1}+\Lambda+\alpha_{u*-1}+\alpha_{u*}$ for $u<u^{*}$. To evaluate whether the association between quadrants 5 and 6 is the same as that of quadrants 7 and 8, we consider the following null hypothesis,

$$\frac{\alpha_{13:21}}{9}=\frac{\alpha_{26:30}}{5}.$$

Other hypotheses tests about model parameters, which are not of primary importance, can be evaluated to reduce the number of parameters in the working model. This will be discussed in the results section. These hypotheses can be evaluated using the classical Wald test statistic with its chi-squared limiting distribution. For the specific null hypotheses examples above, a 1 degree of freedom Wald test can be used to conduct the test.

CHAPTER 3

Analysis and Results

Descriptive analysis

From table 3.1, it can be seen that the highest prevalence of dental caries is found in the molars of the mandible (lower jaw). This is consistent with the findings of previous studies (see for example Zhang et al., 2009). There is also as expected, an extremely low prevalence of dental caries in the incisors of the lower jaw teeth (82, 81, 71, 72).

Table 3.1 Prevalence of caries experience (% affected) in the primary dentition of 7-year-old children n=4,351.

TOOTH	55	54	53	52	51	61	62	63	64	65
Prevalence	8.92	5.20	0.74	3.72	7.81	7.06	2.23	1.86	5.20	8.55

TOOTH	85	84	83	82	81	71	72	73	74	75
Prevalence	10.78	13.75	1.12	0.74	0.37	0.37	0.37	0.37	11.15	9.67

These descriptive statistics suggest a left-right spatial symmetrical pattern in terms of caries frequencies. Specifically, paired teeth 5k-6k, k =1,2,...,5 have roughly the same caries observed frequencies. Similarly findings are observed for paired teeth 8k-7k, k =3,4,5. One, however, should be careful in interpreting these results as they only represent population averaged frequencies, which may not be relevant in understanding the spatial distribution in the mouth. Indeed, at the mouth level, molars 55 and 65, as an example, may still achieve the same caries prevalence estimates by being negatively correlated.

An appropriate method to study the spatial distribution of dental caries in the mouth needs additional parameters that capture the within-mouth associations. This is achieved by explicitly modeling the odds ratios using the ALR model. To allow this ALR model to converge reliably, we imposed some structure on the odds ratio model as described in the previous chapter. The model estimates for the ALR model are given in Tables 3.2 and 3.4.

Table 3.2 Analysis of dental caries experience: ALR model estimates of γ_{jk} (log odds of dental caries for each tooth) (standard errors) and corresponding 95% confidence intervals in 7-year-old children

TOOTH	PARAMETER γ_{jk}	ESTIMATES	95% CI
55	γ_{55}	-1.1149 (0.0523)	(-1.2173, -1.0124)
54	γ_{54}	-1.3094 (0.0551)	(-1.4174, -1.2015)
53	γ_{53}	-3.5345 (0.1368)	(-3.8027, -3.2663)
52	γ_{52}	-3.0670 (0.1282)	(-3.3182, -2.8158)
51	γ_{51}	-1.9837 (0.1167)	(-2.2125, -1.7550)
61	γ_{61}	-2.0377 (0.1212)	(-2.2753, -1.8001)
62	γ_{62}	-3.2256 (0.1400)	(-3.4999, -2.9512)
63	γ_{63}	-3.7970 (0.1538)	(-4.0985, -3.4955)
64	γ_{64}	-1.2136 (0.0537)	(-1.3188, -1.1084)
65	γ_{65}	-1.0238 (0.0512)	(-1.1242, -0.9234)
85	γ_{85}	-0.9002 (0.0499)	(-0.9979, -0.8024)
84	γ_{84}	-0.7349 (0.0483)	(-0.8296, -0.6401)
83	γ_{83}	-3.2840 (0.1205)	(-3.5201, -3.0479)
73	γ_{73}	-3.5176 (0.1345)	(-3.7812, -3.2540)
74	γ_{74}	-0.8005 (0.0490)	(0.0490, -0.8966)
75	γ_{75}	-0.9603 (0.0504)	(-1.0592, -0.8615)

Table 3.3 Analysis of dental caries experience: results of comparison of prevalence of dental caries in upper and lower jaws in 7-year-old children.

TEETH INVOLVED	WALD STATISTIC (P-VALUE)
Molars in upper jaw tooth 55 = tooth 65 tooth 54 = tooth 64	6.005 (0.0497)
Molars in lower jaw tooth 85 = tooth 75 tooth 84 = tooth 74	3.857 (0.1454)
Canines in upper jaw tooth 53 = tooth 63	2.536 (0.1113)
Canines in lower jaw tooth 83 = tooth 73	3.752 (0.0527)
Incisors in upper jaw tooth 4= tooth 7 tooth 5= tooth 6	1.237 (0.5387)

We used parameters γ_{jk} from the ALR logistic regression model to assess whether the frequencies of caries for each type of teeth in the left quadrants are the same as those of the corresponding teeth in the right quadrants. Results of these analyses are presented in Table 3.3. All teeth, except for the left and right molars in the upper jaw, have the same caries prevalence with the corresponding teeth across the midline. Even the result for the left and right molars in the upper jaw was marginally significant at 5% level (p-value=0.0497).

Table 3.4 ALR Results: log odds ratio estimates (standard errors), 95% confidence interval and Z statistic values for dental caries for all teeth in 7-year-old children

PARAMETERS	LOG ODDS RATIO ESTIMATES (STD ER.)	95% CI	Z STATISTIC
α1	2.5716 (0.1139)	2.3483-2.7949	22.57
α2	2.0906 (0.1902)	1.7178-2.4634	10.99
α3	2.0510 (0.1468)	1.7633-2.3387	13.97
α4	2.0141 (0.1596)	1.7013-2.3269	12.62
α5	2.3822 (0.0869)	2.2118-2.5526	27.40
α6	1.8365 (0.1026)	1.6354-2.0375	17.90
α7	1.9646 (0.1364)	1.6972-2.2320	14.40
α8	1.7960 (0.2167)	1.3712-2.2208	8.29
α9	2.2510 (0.1397)	1.9771-2.5249	16.11
α10	2.8227 (0.4282)	1.9834-3.6620	6.59
α11	2.1807 (0.2174)	1.7546-2.6068	10.03
α12	0.4988 (0.5913)	-0.6601-1.6577	0.84
α13	2.8487 (0.1873)	2.4815-3.2159	15.21
α14	1.9026 (0.1608)	1.5875-2.2178	11.83
α15	1.9292 (0.1592)	1.6257-2.2328	12.46
α16	1.8720 (0.1207)	1.6354-2.1085	15.51
α17	2.1789 (0.0993)	1.9843-2.3735	21.95
α18	2.1477 (0.0967)	1.9581-2.3373	22.20
α19	2.1708 (0.1014)	1.9721-2.3694	21.42
α20	2.0753 (0.1090)	1.8617-2.2890	19.04
α21	2.1450 (0.1464)	1.8580-2.4320	14.65
α22	1.9406 (0.0827)	1.7786-2.1027	23.48
α23	2.0953 (0.1094)	1.8807-2.3098	19.14
α24	2.1764 (0.0732)	2.0330-2.3197	29.75
α25	2.2554 (0.1013)	2.0567-2.4540	22.25
α26	2.7768 (0.2313)	2.3234-3.2302	12.00
α27	2.1216 (0.4104)	1.3172-2.925	5.17
α28	2.6272 (0.2066)	2.2223-3.0321	12.72
α29	1.8707 (0.1828)	1.5124-2.2291	10.23
α30	2.7120 (0.2726)	2.1777-3.2464	9.95

For meaning of **α** values, please refer to Table 2.2.

Table 3.5 Hypothesis test results on odds ratio parameters

HYPOTHESIS	PARAMETERS UNDER NULL HYPOTHESIS	WALD STATISTIC (P-VALUE)
(Q5lag1) = (Q6lag1) (Q5lag2) = (Q6lag2) (Q5lag3) = (Q6lag3) (Q5lag4) = (Q6lag4)	$\alpha 1 = \alpha 5$ $\alpha 2 = \alpha 6$ $\alpha 3 = \alpha 7$ $\alpha 4 = \alpha 8$	3.313 (0.507)
(Q8lag1) = (Q7lag1) (Q8lag2) = (Q7lag2)	$\alpha 9 = \alpha 11$ $\alpha 10 = \alpha 12$	11.935 (0.003)
(Q8lag1) = (Q7lag1)	$\alpha 9 = \alpha 11$	0.092 (0.762)
(Q8lag2) = (Q7lag2)	$\alpha 10 = \alpha 12$	11.809 (0.001)
Overall horizontal left-right quadrant compared with all other quadrant associations	$\frac{\alpha_{13:21} + \alpha_{26:30}}{14} = \frac{\alpha_{22} + \alpha_{25} + \alpha_{23} + \alpha_{24}}{4}$	4.835 (0.028)
Left-right in Lower and Upper Jaw	$\frac{\alpha_{13:21}}{9} = \frac{\alpha_{26:30}}{5}$	3.092 (0.079)
(Q5Q8) = (Q5Q7) = (Q6Q8) =(Q6Q7)	$\alpha 22 = \alpha 23 = \alpha 24 = \alpha 25$	13.370 (0.004)
(Q5Q8) = (Q6Q7)	$\alpha 22 = \alpha 25$	7.295 (0.007)
(Q5Q7) = (Q6Q8)	$\alpha 23 = \alpha 24$	0.461 (0.497)

Log odds ratios estimates with associated 95% confidence intervals (CI) are presented in Table 3.2. These estimates and the associated variance covariance matrix are used to evaluate hypotheses related to odds ratios. A Wald statistic with its chi-squared limiting distribution is used to conduct the test. Following the results from the logistic regression model of caries prevalence, we evaluate whether the left and right quadrant have the same second moments. We found that the association of any lag in quadrant 5 is the same as the corresponding association in quadrant 6 (p-value=0.507). For quadrants 7 and 8, only the lag 1 association is found to be the same (p-value=0.762). The lag 2 association for these quadrants was found to be different at 5% level (p-value=0.001).

The hypotheses comparing the left-right association compared to other associations at the quadrant level were also evaluated using a traditional Wald test. The left-right quadrant-level association was significantly higher than to other quadrant-level associations (across, up and down) (p-value=0.028). This finding is consistent with that of Zhang et al. (2009) in their work on modeling spatially correlated tooth-level binary in caries research. Moreover this finding suggests that caries experience might show approximately a symmetric pattern across the midline in the deciduous dentition. Dentists believe there is a stronger left right association at the quadrant level, but it has never been evaluated using modern statistical tools. From a public health perspective, this finding suggests that if a 7-year-old presents with caries in any tooth in quadrant 5, he or she has an increased chance of presenting caries experience in quadrant 6 compared to other quadrants within the mouth. This also applies when a 7-year-old presents with caries in any tooth in quadrant 8, they have an increased chance of presenting caries experience in quadrant 7 compared to other quadrants within the mouth.

Further tests were to evaluate whether the left right association at the quadrant level was the same for both the upper and the lower jaw. There was no statistical difference between these jaws in terms of left-right association at the quadrant level (p-value=0.079). Therefore, a 7-year-old who presents with caries in any tooth in quadrant 5 has the same chance of presenting with caries experience in any tooth in quadrant 6, as a 7-year-old with caries in quadrant 8 has in presenting caries experience in quadrant 7.

Other quadrant level associations were also evaluated to better understand the spatial distribution of dental caries in the population of 7 year old school children. We tested the hypothesis (Q5Q8) = (Q5Q7) = (Q6Q8) = (Q6Q7) of whether the association between quadrants 5 and 8, was the same as that of quadrants 5 and 7, quadrants 6 and 8 and quadrants 6 and 7. The result of the test was significant at 5% level (p-value=0.004). Further analysis test was performed to identify the difference. The "across" associations represented by the odds ratio between quadrants 5 and 7 and odds ratio between quadrants 6 and 8 were found to be the same (p-value=0.497). The "up and down" associations represented by the odds ratio between quadrants 5 and 8 and odds ratio between quadrants 6 and 7 were not the same (p-value=0.007).

CHAPTER 4

Discussion

4.1 Research Study

The purpose of this study was to investigate the spatial distribution of dental caries on tooth surfaces in the primary dentition of 7 year olds, using statistical models for correlated data. The main objective was to determine which tooth surfaces are more susceptible to caries experience, and with respect to dental caries, if any spatial association of dental caries exists at the quadrant level in the mouth. This study demonstrates an application of a statistical model, where the association structure between teeth is the scientific focus of research. It further extends that done of Hujoel *et al.* (1994), and that of Vanobbergen *et al.* (2007) by using data from the entire mouth (all 20 teeth found in 7 year old children), and not just selected teeth.

Given a caries lesion on a tooth, this structured GEE-based alternating logistic regression (ALR) model enables us to determine the odds of caries lesions formation on corresponding teeth in a different quadrant. The ALR models focus on marginal expectation of the response and the second order association through pair-wise odds ratios. This class of models provides consistent estimates, and is easy to implement using commercial software. To avoid any misspecifications of the association structure at the expense of efficiency, unstructured odds ratio model, as seen in the Vanobbergen *et al.* (2007) study, are usually advocated. In caries research, a GEE-based ALR model with an unstructured design matrix for the odds ratio model requires an overwhelming number of parameters for each quadrant. For 7 year old children, it requires $190 = 20 * (20 - 1) / 2$ pair-wise odds ratios to be estimated. In this study we restricted the ALR model by adding structure to the odds ratio model, to produce fewer parameters (30 parameters for the whole mouth), and allow for convergence.

The spatial association in this analysis refers to the association of dental caries outcomes at quadrant levels. Lesaffre *et al.* (2005) and Vanobbergen *et al.* (2007) have shown that ALR can be used to evaluate the left-right association at the quadrant level. These authors with few selected teeth have shown that a tooth in the left quadrant has the strongest association with a corresponding tooth across the midline, in the right quadrant. Our analysis goes beyond those findings to investigate whether complete spatial association at the quadrant level exists when all teeth (20 teeth) are used. Also within quadrants, we observed the associations (within quadrant) seen in adjacent teeth pairs, with corresponding teeth pairs in other quadrants. In addition to the left-right quadrant level associations, we also looked at "up and down" and "across" quadrant associations, in order to fully capture the within-mouth caries associations.

The structured ALR model revealed that caries experience does follow a spatial distribution pattern. We observed that the overall left to right quadrant associations of caries experience appeared to have the strongest association. This is supported with the similar caries frequencies seen especially in the molars of quadrants 5 and 6. The molars of quadrant 5 (54 and 55) are 5.20 and 8.92, while that of quadrant 6 (64 and 65) are 5.20 and 8.55 respectively. It is also important to note the association between teeth 51 and 61, with almost identical caries frequencies of 7.81 and 7.06 respectively. Here we can see that the left-right teeth pairs have the strongest association which confirms the findings of the previous study by Vannobergen *et al.* (2007). The highest caries frequencies are seen in the molars of the lower jaw (mandible), which are consistent with previous findings (Macek *et al.*, 2003).

While the results of this study confirmed the findings of Vannobergen *et al.* (2007), it conflicted with the findings of Hujoel *et al.* (1994), which showed caries lesions tend to aggregate or cluster on one side of the mouth. In our study, clustering was only observed in the left molars in the upper jaws. Given the young age of the population, a plausible hypothesis more so than chewing patterns, would be tooth brushing style/patterns, and a change in the current oral health education might influence this left sided caries clustering. This will suggest a need for more community dental health programs for the parents and children, and within the school systems to encourage more effective ways of tooth brushing.

4.2 Implications of findings.

Dentists and dental hygienists should look towards incorporating left to right quadrant level associations to provide more effective treatment plans for patients with dental caries. If a patient presents with caries on the molars in quadrant 5, the dentist should first also look for the early development of caries on the molars in quadrant 6, as these have an increased chance of developing caries. If a patient presents with caries on any tooth in quadrant 5, firstly, care should be taken to examine the corresponding tooth in quadrant 6. They should also look towards using other association patterns such as the "across" and "up and down" quadrant level associations. Similarly, if a patient presents with caries on any tooth in quadrant 6, the dentist needs to be educated to check the teeth in quadrant 8 for caries first before looking at the other quadrants. These association methods should be implemented in dental health training. In the long term, this implementation should help decrease the prevalence of dental caries and further debilitating periodontal diseases, as well as the financial burden on dental public health, as preventive measures are undertaken. It should help encourage better quality of living, as people will be able get their teeth restored early, without the need for drastic measures such as root canals, to remove teeth.

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