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Prediction of periodontal pathology around third molars using linear mixed effects modeling

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Objective To compare the random intercept multilevel model with other linear mixed effects models in an assessment of the effect of quadrant-, jaw-, and person level covariates on probing depth of asymptomatic third molars. ***Basic Research Design*** Five different covariance models were considered: 1) the random intercept multilevel 2) multi-level with unequal jaw variance 3) multi-level with unequal tooth variance 4) multi-level with unequal jaw and side variance and 5) the general linear model for correlated data with unstructured covariance matrix. ***Participants*** 235 subjects with all four third molars erupted were included. Fifty-one percent were female and 75% Caucasian. The average age was 29.1 years (sd = 7.0). ***Results*** The extended multi-level with unequal residual variance was the best fit to the data. Likelihood ratio tests in a stepdown selection approach resulted in a final model for mean probing depth that included one statistically significant three-way interaction (age x gingival inflammation x gender), two statistically significant two-way interactions (jaw x gingival inflammation and jaw x gender) and one significant main effect (ethnicity). ***Conclusions*** Linear mixed effects modeling is a powerful tool for the analysis of correlated dental data. However, no one covariance structure is appropriate for all purposes.

Key words: Linear mixed effects model, periodontal pathology, third molar

Introduction

Third molars are usually not included in full mouth clinical or epidemiological assessments of periodontal health. The inclusion of third molars may substantially impact the interpretation of the findings. For example, a recent clinical study of 329 patients with four asymptomatic third molars indicated that the percentage of patients with periodontal pathology using the Third National Health and Nutrition Examination Survey (NHANES III, NCHS, 1996) criterion of at least one probing depth of 5mm or greater was substantially higher when third molars were included in the examination : 9% vs. 1% for subjects < 25 years old; 17% vs. 3% for those 25 or older (Blakey *et al*., 2002). This suggests that the United States population may be less healthy periodontally than is commonly reported.

The visible presence of a third molar in the quadrant was associated with twice the odds of a probing depth (PD) of at least five mm on the adjacent second molar in the NHANES III data, while controlling for other subject level factors associated with a visible third molar and periodontal disease.(Elter *et al*., 2004). The increased risk of a PD of clinical concern on a second molar, given a visible third molar in the quadrant, was confirmed in a cohort of 7,000 men and women aged 52-64 being studied prospectively for cardiovascular disease (Elter *et al*., 2005). In addition, re-evaluation of data available from the Oral Conditions and Pregnancy Clinical Trial suggests that third molar PD ≥ 4mm is associated with preterm birth and elevated serum CRP levels (Moss *et al*., 2005). These findings illustrate the importance of including visible third molars in epidemiologic studies of periodontal health and in future studies assessing the association of oral and systemic health.

Usually pocket depth is measured by periodontal probing at multiple sites per tooth and multiple teeth are examined in each subject. These multiple values are frequently then aggregated to a single value for each subject by setting a subject level criterion as in NHANES III. Subject level aggregation frequently satisfies the purpose of epidemiological and health services research and has the advantage of simplifying a complex set of values. However, for clinically based studies, particularly those focused on the longitudinal progression or treatment of periodontal disease, such aggregation results in the loss of potentially valuable detail (Sterne *et al*. 1988, DeRouen, 1989; Abandar and Goldstein 1992). For example, using the NHANES III criterion of at least one PD of 5mm or greater, two subjects may be classified in the same category but one subject may have only one while the second has five teeth that exhibit signs of periodontal pathology. In addition to the loss of detail, the possible influence of within-subject effects (for example, tooth angulation or gingival inflammation in the quadrant) cannot be examined since differences among jaws and/or quadrants and the within-subject anatomical relationships are not distinguishable when information on outcomes and explanatory variables are aggregated to the subject level. The appropriate level of aggregation is dependent on the

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purpose of the research study. For this study, the level of interest was the occurrence of periodontal pathology around a tooth – not the variation in pathology among sites per tooth or the explanation of tooth-site specific pathology by a tooth-site specific predictor.

This paper examines the use of random intercept multilevel and related expanded models for the purpose of examining the effects of multi-level factors on maximum PD of asymptomatic third molars. The risk factors associated with increased probing depth around asymptomatic third molars are presumed to be those associated with pocketing around other teeth. However, no data is available to validate this assumption. Multilevel models, or hierarchical linear models as they are sometimes called, are becoming popular in dental research (Sterne *et al*. 1988; Abandar and Goldstein 1992; Gilthorpe *et al*., 2000; 2001). Multilevel models, which are methodologically equivalent to the class of general linear mixed models (Cnaan *et al*., 1997), are useful for describing the effects of explanatory variables at different levels of data structure on a continuous outcome (Sullivan *et al*., 1999). In particular, multilevel models without explanatory variables (except for an intercept) have been called variance component models (Gilthorpe *et al*., 2000). These models have variance parameters that together provide a decomposition of the total variance of the response according to the levels of data. Multilevel models that include explanatory variables have been referred to as random intercept models (Gilthorpe *et al*. 2000). Variance parameters in these models decompose the total residual variance of the response after adjustment for explanatory variables. Disadvantages of random intercept multi-level models (in their usual formulation) are that, in some cases, they may oversimplify, or otherwise misspecify, the covariance structure of repeated measurements of the outcome variable within persons. Because the validity of maximum likelihood analyses require the correct specification of both the mean and covariance models, misspecification of the latter may cause bias in the estimation of risk factors for mean values of dental outcomes such as probing depth (Cnaan *et al*., 1997). More general covariance structures for linear mixed models may be needed to mitigate if not entirely to avoid this problem.

Several covariance structures for linear mixed effects models, that have the random intercept multilevel model as a special case are proposed and evaluated These models are nearly as parsimonious as the random intercept multilevel model and yet retain interpretations with respect to explaining different sources of variability. In particular, the proposed expanded multilevel models, unlike the random intercept multilevel model, allow variance decompositions to vary across the basic level of observational units; for example, variance across subjects for third molars in the maxilla versus the mandible. The statistical models are illustrated in the analysis of the effect of quadrant-, jaw-, and person-level covariates on PD of asymptomatic third molars from subjects that participated in a recent clinical study.

Methods

Subjects

410 subjects were enrolled in an IRB approved trial at two clinical centers, University of North Carolina and University of Kentucky, over a 30 month period. Inclusion criteria dictated that patients be healthy (ASA I, II); between the ages of 14 and 45 years; and have four asymptomatic third molars (erupted or visible on panorex if unerupted) with adjacent second molars present. Patients with the most severe form of periodontal disease (AAP IV); who were pregnant; who had taken antibiotics within the last three months or with a history of treatment for a psychiatric disorder within the past 12 months were excluded from participation. Ninety of the 410 subjects presented with all four third molars unerupted. These subjects were excluded from consideration since probing depth cannot be obtained on unerupted teeth.

Descriptive analysis prior to model selection suggested that the number of third molars erupted, the cluster size, was informative (Table 1). Specifically, subjects with fewer than four erupted third molars were more likely to have teeth with mild inflammation and to be younger than those with all four third molars erupted. Because the magnitude of the effects of potential predictors on probing depth may vary by cluster size, and because the limited number of subjects for cluster sizes 1, 2, 3 precluded an in-depth study of these, only the 235 subjects with all four third molars erupted were included in the mixed model analysis. Thus, the cluster size, or number of observations contributed to the statistical analysis by each subject, was four. Subjects studied were more likely to be Caucasian females.

Outcome

At a subject's entry into the study, a full mouth periodontal probing, six sites per tooth including third molars, was performed. Periodontal probing depth, defined as the maximum PD of a tooth, was recorded for each third molar. The tooth-level maximum PD was selected as the outcome since this measure represents the maximum disease expression for a tooth and is the standard measure used in clinical (Blakey *et al*., 2002) and epidemiological (Elter *et al*., 2004) studies on periodontal health. The mean probing depth averaged across sites probed for a given tooth is not a clinically meaningful measure of periodontal pathology. For example, person 1 has a mean 3rd molar PD of 1.7 mm resulting from specific site PDs of 2,2,1,2,1,2 while a second person has a mean 3rd molar PD of 1.5 mm resulting from specific site PDs of 0,0,0,0,5,4. Defining disease based on the mean suggests that the first molar has more disease, whereas defining disease based upon the maximum leads to the more clinically accepted conclusion that the pathology of the 3rd molar in the second person is of greater concern. Despite possibilities such as this, the correlation between mean PD and maximum PD in our data set was high (0.84).

Although the selection of the maximum PD per tooth rather than the average as the outcome has a valid clinical basis, the distribution of the maximum PD may not meet the assumption of a normally distributed outcome. While the empirical moments of three random

Table 1. Demographic and clinical characteristics of subjects enrolled in a longitudinal study to monitor the health of aymptomatic third molars comparing those subjects who had one to three erupted 3rd molars and those who had all four erupted third molars

	One to Three		*All four*	
	n	*%*	*n*	*(%)*
Gender				
Female	46	54	121	51
Male	39	46	114	49
Ethnicity				
Caucasian	64	75	176	75
Non-Caucasian	21	25	59	25
Regular Dentist				
No	50	60	124	53
Yes	33	40	109	47
% Teeth in Quadrant >= mild inflammation				
<=25%	47	55	145	62
>25%	38	45	90	38
	Mean	*Std*	*Mean*	*Std*
Age	25.3	6.7	29.2	7.0

Table 2. Explanatory variables considered for inclusion in the multi-level model.

Patient Level	*Values*	
Age	Continuous – centered prior to modeling	
Gender	Male	Female
Ethnicity	Caucasian	Non-Caucasian
Jaw Level		
Jaw	Maxillary	Mandibular
Quadrant Level		
Gingival Inflammation	<=25% of teeth	>25% of teeth

variables (the individual site PD values, the mean PD per tooth, and the maximum PD per tooth) indicate a similar amount of skewness (0.98, 1.03, and 1.28 respectively), the pertinent assumption of a linear mixed model analysis is not that the response (unadjusted for covariates) is normally distributed but that the variance components of the model are normally distributed. In particular, if the individual-specific random effects and random within-subject or "pure" error terms are statistically independent (a standard assumption of linear mixed models), then assuming the 'total' error is normally distributed implies both the random effects and random "pure" error terms are normally distributed (Gurka *et al*. 2006, Lemma 1). The implication is that it is sufficient to assess for normality of the total residual, that is the residual about the fitted population-averaged regression mean model.

Explanatory Variables

The data set consisted of information from three different levels (subject, jaw, and quadrant) and the explanatory variables for each level are presented in Table 2. The level of quadrant (or jaw and side level) is synonymous with tooth level since one tooth, the third molar, was studied per quadrant. *Subject-level Covariates.* Demographic data (age, gender, ethnicity) were recorded for each subject. Age was centered on the mean value of 29.13 years of age in order to aid model estimation. *Jaw-level Covariate.* A previous report (Blakey *et al*., 2002) suggested that periodontal pathology occurs more frequently in the mandible. An indicator variable was created to differentiate mandibular from maxillary third molars. *Quadrant-level Covariate.* Gingival Index (GI) was scored from 0 to 3 for each tooth including third molars: 0 = absence of inflammation; 1 = mild inflammation; 2 = moderate inflammation with moderate glazing, redness, edema and hypertrophy of soft tissue; 3 = severe inflammation with bleeding on probing(Loe, 1967). An indicator variable was created to indicate the level of gingival inflammation in each quadrant. Each quadrant was categorized as having 0 to 25 % of the teeth in the quadrant with moderate or severe inflammation (2 or 3) or greater than 25% of the teeth with scores of 2 or 3. Panoramic radiographs were obtained to assess the

inclination of the third molar compared to the long axis of the adjacent second molar and the position relative to the occlusal plane of each of the third molars. During the descriptive analysis phase the sparseness of third molars in the mesio/horizontal angulation and below the occlusal plane categories (3% vs 97% for both variables) was noted. In addition, angulation and occlusal plane position were statistically associated (Chi-square, $p < 0.0001$). The collinearity of the two measures and the sparseness in one of the two categories for each of the measures led to the removal of these measures as potential explanatory variables prior to model development.

Model Specification

The purpose of this investigation was to examine the effects of multi-level factors (patient, jaw, and side level) on the maximum pocket PD of asymptomatic erupted third molars. The basic linear mixed effects model of interest is

$$Y_{ijk} = \beta_0 + b_i + b_{ij} + \beta^T x_{ijk} + e_{ijk}$$

where Y_{ijk} = the PD for the k^{th} third molar of the j^{th} jaw from the i^{th} person, j = 1 (mandible) or j = 2 (maxilla); k = 1 (left) or k = 2 (right). The notation x_{ijk} corresponds to a vector of fixed effect covariates at the quadrant, jaw or person level, β_0 is an intercept term, b_i is a random subject-specific effect, b_{ij} is the random effect for jaw within a person and e_{ijk} is a random error term at the tooth level. The total error is defined as $u_{ijk} = b_i + b_{ij} + e_{ijk.}$

Five different covariance models for PD were considered. Model specification was completed with assumptions regarding variances of the random effects b_i, b_{ij} and e_{ijk}. The five models in increasing order of complexity are: (1) the random intercept multi-level model; (2) a multi-level model with unequal jaw (Maxillary vs Mandibular) variances; (3) a multi-level model with unequal jaw and side (Right vs Left) variances; (4) a multi-level model with unequal tooth (quadrant) variances; and (5) the general linear model for correlated data with unstructured covariance matrix. All five models assume that random effects are mutually independent and normally distributed. Additionally, Model (1) assumes $b_i \sim N(0, \sigma^2_S)$, $b_{ij} \sim N(0, \sigma^2_J)$, $e_{ijk} \sim N(0, \sigma^2_e)$; Model (2) is like Model (1) except that the variance term for jaw may be different for the mandible versus the maxilla, eg, $b_{i1} \sim N(0, \sigma^2_M)$ and $b_{i2} \sim N(0, \sigma^2_X)$; the two models are nested since $\sigma^2_X = \sigma^2_M$ implies Model (1). The 3rd and 4th models are like models (1) and (2), respectively, with respect to assumptions about b_i and b_{ij} but they generalize the restrictive assumption that all third molars within a person have a common random error term σ^2_e; instead, the relaxed assumption is e_{ijk} is normally distributed with mean 0 and tooth-level variances σ^2_{eML}, σ^2_{eMR}, σ^2_{eXL}, and σ^2_{eXR}, corresponding to the mandibular left (j=1, k=1), mandibular right j=1, k=2), maxillary left (j=2, k=1), and maxillary right (j=2, k=2) third molars, respectively. Finally, Model (5) specifies a saturated or unstructured covariance matrix for the vector of a person's four tooth level responses by setting $\sigma^2_s = \sigma^2_J = 0$, and $Var(e_i) = V$ where V is an unstructured 4 by 4 covariance matrix of $e_i = (e_{i11}, e_{i12}, e_{i21}, e_{i22})^T$. The Appendix provides more detail of the five covariance structures. Appendix material is available from Dr. Phillips. Requests should be sent to ceib_phillips@dentistry.unc.edu

Model Selection

The first step of the analysis used restricted maximum likelihood estimation (McCulloch and Searle, 2001) to fit the "full" predictor model that includes 3 subject, 1 jaw, and 1 quadrant level main effects (Table 2), and all possible two and three-way interactions among the main effects. With the full model specified, REML was used to estimate the five covariance models. Akaike's Information Criterion (AIC) and Schwarz's Bayesian Criterion (BIC) were used to identify the best covariance model; the best fitting model under each criterion is the one with the smallest value (Littell *et al*., 1996). Once the appropriate covariance structure was chosen, maximum likelihood estimation was used to fit a series of nested models. These were compared using likelihood ratio tests based upon asymptotic chi-square distributional assumptions in a stepdown model selection approach, similar in strategy to the partial F test used in multiple regression, to eliminate sets of variables (Cnaan *et al*, 1997). The ordering of the sets of variables considered for elimination is given in Table 3. The number of degrees of freedom at each step was equal to the number of terms subtracted from the model. Proc Mixed in SAS (Littell *et al*., 1996) was used for estimation and model selection. The level of significance was set at 0.05. The normality assumptions of the final model were assessed with a quantile-quantile plot (Gurka *et al*. 2006) of the total residuals, :

$$\hat{u}_{ijk} = y_{ijk} - (\hat{\beta}_0 + \hat{\beta}^T x_{ijk}).$$

Results

The estimated variance/covariance matrices of PD for the five covariance models under the full predictor model are provided in the Appendix. Using the AIC criterion, the extended multi-level with unequal jaw and side variances (AIC = 2224.7 with range of AIC from 2224.7 to 2283.0 for the standard multi-level) provided the best fit to the data. Under the BIC criterion, two models, the multi-level model with unequal quadrant variances (BIC = 2248.6) and the multi-level with unequal jaw and side variances (BIC = 2248.8) provided better fit to the data than the other three models (BIC ranged from 2248.6 to 2293.4 for the standard multi-level). Considering the AIC and BIC criteria together, the multi-level model with unequal jaw and side variances was chosen as the best one to represent the covariance structure of PD.

The next step addressed model selection with respect to the predictors of maximum third molar PD. Seven nested models were fitted and compared with likelihood ratio tests (Table 3). An analysis of deviance of selected models resulted in a final model (Model 2 in Table 3) that included one statistically significant three-way interaction (age x gender x gingival inflammation), five two-way interactions, and all main effects. Two of the two-way interactions (jaw x gingival inflammation and jaw x gender) were statistically significant predictors as was the main effect of ethnicity. The other three two-way interactions and main effects were maintained

Table 3. Analysis of Deviance for Selection of the Final Mixed Model based on a Stepdown Selection Approach using Nested Models*

Model	*Stepdown Selection*	*-2logL*	*difference*	*Df*	*p-value*
7	Full Model	2110.8			
			7.4	3	0.06
6	Removal of threeway interactions containing jaw*GI	2118.2			
			7.2	6	0.30
5	Removal of remaining threeway interactions except gender*GI*age(centered)	2125.4			
			5.3	3	0.15
4	Removal of jaw*race; gender*race; race*GI	2130.7			
			3.4	1	0.07
3	Removal of race*age(centered)	2134.1			
			3.6	1	0.06
2	Removal of jaw*age(centered)	2137.7			
			10.8	1	0.001
1	Removal of jaw*GI	2148.5			

The full predictor model (Model 7) includes the fixed effects, age, gender, and ethnicity, and the random effects of jaw and gingival inflammation. All two and three-way interactions among age, gender, race, jaw, and quadrant gingival inflammation were included.

* For all models, the covariance structure is specified as extended multi-level with unequal residual variances. Results are based upon maximum likelihood estimation.

Table 4. Regression parameter estimates and 95% confidence intervals from two variance components models

	Random Intercept Multi-Level		*Multi-Level with Unequal Jaw and Side Variances*	
Effect	*Estimate*	*95% CI*	*Estimate*	*95% CI*
Intercept	2.74	2.57, 2.90	2.74	2.59, 2.88
Between Subject Effects				
Age(Centered)	0.02	0.003, 0.04	0.03	0.01, 0.04
Gender(Male)	-0.02	-0.24, 0.19	-0.004	-0.19, 0.18
Ethnicity(Non-Caucasian)	0.65	0.44, 0.86	0.68	0.48, 0.88
Within-subject Effects				
Jaw - level				
Jaw(Mandible)	0.84	0.67, 1.00	0.84	0.68, 1.00
Quadrant – level				
G.I. (>25% of teeth)	0.46	0.16, 0.75	0.38	0.13, 0.64
Interactions				
Jaw*Gender	0.33	0.10, 0.56	0.28	0.06 ,0.50
Jaw*G.I.	-0.48	-0.78,-0.17	-0.50	-0.79,-0.21
Age* Gender	-0.01	-0.03, 0.02	-0.01	-0.03, 0.02
G.I. * Gender	0.08	-0.29, 0.44	0.17	-0.18, 0.52
Age*G.I.	-0.07	-0.10,-0.03	-0.06	-0.09, 0.02
Age*G.I.*Gender	0.13	0.07, 0.18	0.12	0.07, 0.17
Variance Components				
Person, σ_S^2	0.27	0.17,0.36	0.26	0.17,0.35
Jaw, σ_J^2	0.24	0.16,0.31	---	
Jaw, σ_M^2	---		0.33	0.20,0.46
Jaw, σ_X^2	---		0.13	0.04,0.22
Jaw and Side, σ_{JK}^2	0.32	0.28,0.36	---	
Tooth, σ_{XR}^2	---		0.12	0.07,0.18
Tooth, σ_{XL}^2	---		0.27	0.20,0.34
Tooth, σ_{MR}^2	---		0.57	0.43,0.71
Tooth, σ_{ML}^2	---		0.32	0.20,0.43

• based upon maximum likelihood estimation

in the final model even if not statistically significant because of the inclusion of the effects in the significant three way interaction. Figure 1(a) shows some deviation from normality in the q-q plot of the total residual in the final model. Figure 1(b) gives the q-q plot after 11 observations (1.2% of the observations) with total residual > 3.0 were removed (there were no observations with residual < -3). Normality appears well justified in this case. Because parameter estimates for the fixed effects (not shown) were little affected by the presence of these 11 "outliers" they were kept in the model.

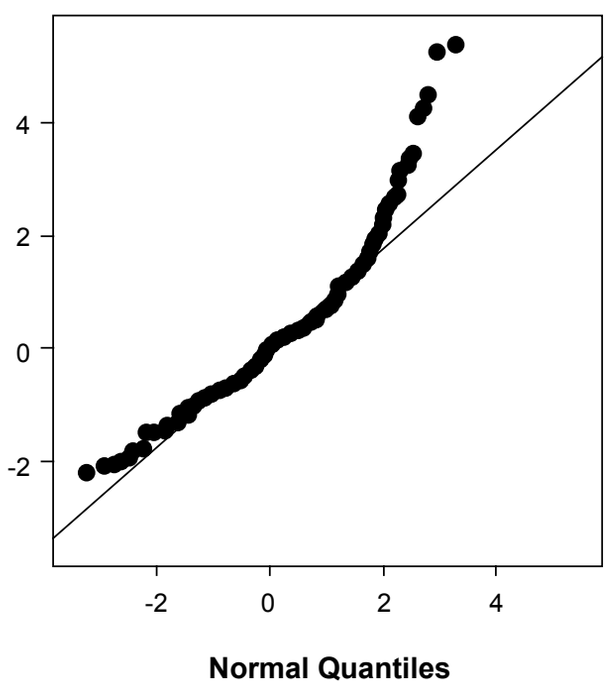
The variance component estimates for the multi-level model with unequal jaw variances (Table 4) quantify certain aspects regarding variation of probing depth for 3rd molars in our sample. First, the variability in the mandible is about 2.5 (i.e., .33/.13 times higher than in the maxilla. Second, the variability among right (and to a smaller degree left) 3rd molars in the mandible is greater than in the maxilla. On the other hand, the estimates of the three variance components from the random intercept multilevel model (also provided in Table 4) do not indicate the effect of location (jaw) on the variability in PD. Similar conclusions are also reached if the 11 "outliers" are removed from the analyis; however, certain variance estimates are reduced.

The parameter estimates from the final predictor model are given in Table 4. Estimates for gingival inflammation and its interaction with gender appear sensitive to specification of the covariance structure, underlining the importance, in this case, of basing inference on the multilevel model with unequal jaw and side variances. Because of the presence of the statistically significant three and two-way interaction terms in the model, the quadrant, jaw and subject level covariates must be interpreted within certain subgroups. For younger subjects, females with more than 25% of the teeth in a quadrant with moderate gingival inflammation have the highest average probing depth (Figure 2). In older subjects, males with gingival inflammation in the quadrant had the deepest average probing depth. This was approximately 1mm deeper than for males with fewer than 25% of teeth in the quadrant with gingival inflammation and for females regardless of gingival inflammation level.

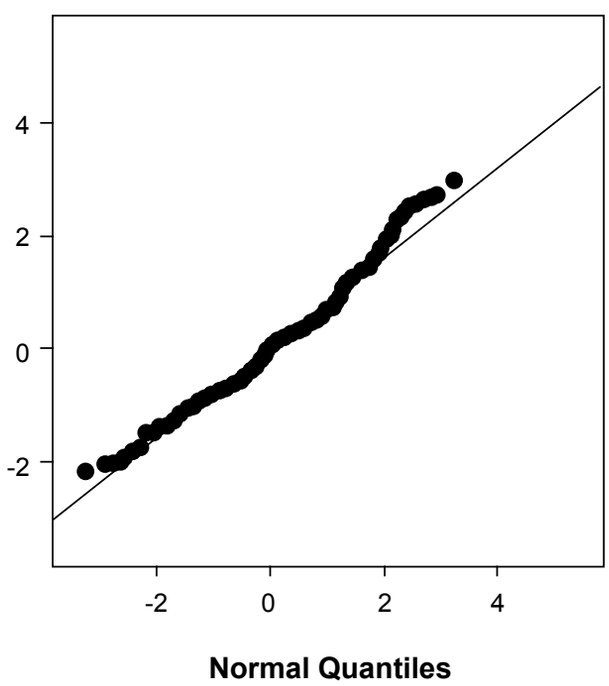
For both males and females, the predicted average PD is deeper around the mandibular third molars than the maxillary (1.1mm for males and 0.8mm for females) (Figure 3). Although statistically significant, the differential effect of gingival inflammation on PD in the mandible and maxilla was small (Figure 4). Non-Caucasians had, on average, a 3.4 mm PD (s.e.= 0.10) while Caucasians had a 2.7 mm PD (s.e. = .07).

Discussion

Multilevel hierarchical linear modeling, or linear mixed effects modeling, is a general analytical approach that accounts for the problems of clustered data so commonly found in dentistry and allows an examination of the relationship between covariates at multiple levels of the data structure and a continuous outcome such as periodontal probing depth (Sterne *et al*. 1988; Abandar and Goldstein 1992; Gilthorpe *et al*.,2000, 2001). Application of this approach without an examination of the within-subject correlation structure may result in a miss-specified covariance model causing the estimates in the predictor model to be biased (Littell *et al*., 1996). Nevertheless, parameter estimates for the fixed effects in Table 4 were robust to fitting a simpler covariance model. In this study, five covariance structures for mixed effects linear models were examined. The random intercept multilevel model, which assumed variances to be equal across the four third molars was not the best



A. Final model with all observations



B. After removal of 11 observations with total residual > 3.0.

Figure 1 A and B. *Q-Q plots of the total residuals.*

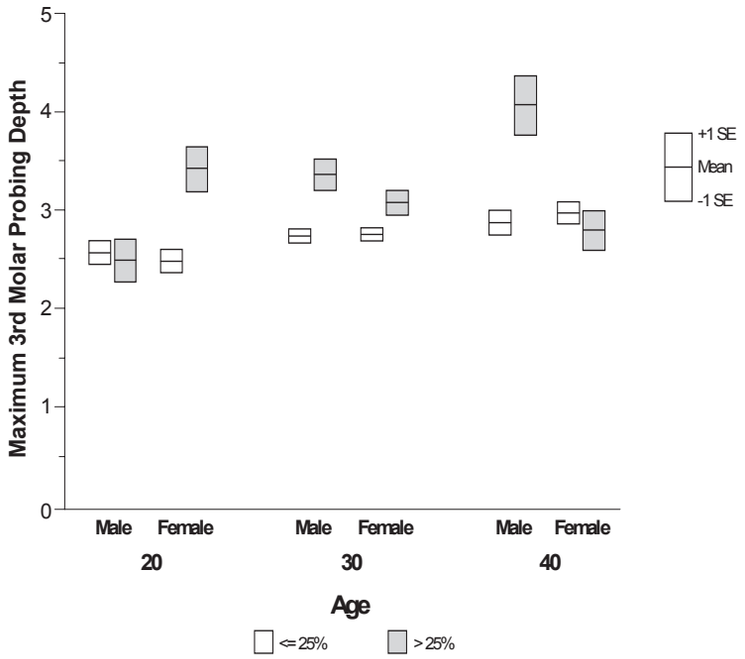


Figure 2. *Illustration of the predicted maximum periodontal probing depth of asymptomatic third molars for males and females from age 20 to age 40. PD in quadrants with less that 25% of the teeth with gingival inflammation differs very little between males and females regardless of age group. However, the difference in the PD in quadrants with more than 25% of teeth with gingival inflammation for males and females is dependent on the age at evaluation.*

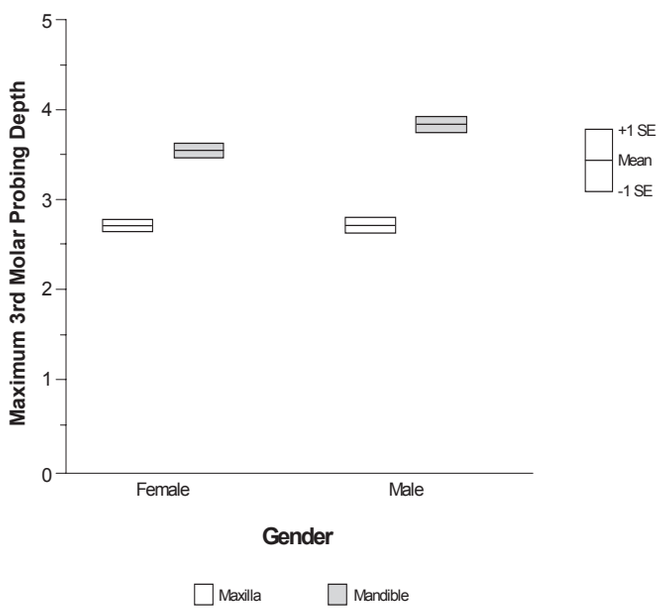


Figure 3. *Illustration of the predicted maximum periodontal probing depth of maxillary and mandibular third molars for females and males. On average, probing depths are deeper around the mandibular third molars.*

fit to the data. At the other extreme, with a cluster size of only four teeth per mouth, an unstructured covariance matrix would provide valid inference on probing depth and requires estimating only 10 covariance parameters. Such an approach, however, while justified for these data, does not provide interpretations based upon variance partitioning, a desirable feature of hierarchical modeling. This paper proposed three alternative covariance structures that are more parsimonious than the fully unstructured model, richer than the potentially overly restrictive random intercept multilevel model, and yet provide the desired interpretations. The covariance structures studied were tailored to our application, but the basic principle of generalizing the random intercept multi-level model may apply to other dental studies including those examining varying numbers of teeth per subject with perhaps additional levels (eg.,multiple visits). Random coefficient models where covariates

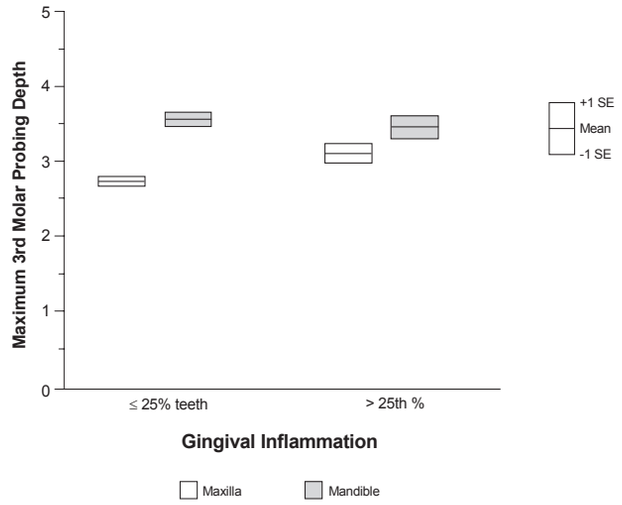


Figure 4. *Illustration of the predicted PD of maxillary and mandibular third molars with and without at least 25% of the teeth in the quadrant with gingival inflammation. The average PD of third molars in the mandible is similar regardless of GI while the average PD of maxillary molars in quadrants with ≥ 25% of teeth with gingival inflammation is deeper than those in quadrants with less than 25% of the teeth with gingival inflammation.*

exhibit variation about their mean estimates provide a related generalization of random intercept models albeit with a different parameterization particularly suitable for longitudinal data (Gilthorpe *et al*., 2001).

Inferences from this study, although supportive of clinical impressions, are limited to subjects with four erupted third molars and are limited in scope. The subjects in this sample were mostly young healthy adults without moderate or severe periodontitis and well educated, almost 60% had completed college. The non-Caucasian patients were mostly African American. Hispanic patients were under represented, less than 1% of the sample. As such, the increased risk for third molar periodontal pathology observed may not extend to other non-Caucasian ethnic groups. The results from this study should, however, benefit clinicians and patients who are assessing the risks and benefits of maintaining third molars.

Periodontal status of third molars has only been studied recently. The findings from this analysis support and extend the descriptive results published recently by Blakey (2002). In the aggregated analysis, older patients were seen as more likely to have deeper third molar probing depths than younger, males were affected more often than females, and third molars in the mandible were more often affected than those in the maxilla. This study suggests a more complicated process that involves the joint effect of subject, jaw, and quadrant level covariates in the explanation of maximum PD around asymptomatic third molars. For example, if only main effects were examined, it would appear that there was no statistically significant difference between males and females. However, the significant interaction between the location of the third molar and gender indicates that the effect of location on maximum PD is dependent on the gender of the subject. The findings from this study are cross-sectional so the effect of age and its interaction with within subject factors like gingival inflammation must be interpreted cautiously. Longitudinal data with up to five year recall will be available on the subjects in this study in the near future.

African Americans appear to be at higher risk for periodontal pathology than Caucasians. In a cross-sectional analysis Beck *et al*. (1990) found more extensive periodontal pocketing in older African American subjects as compared to Caucasians, controlling for socioeconomic status, education and dental visits. Older African Americans also had a higher incidence of periodontal attachment loss over an 18 month period. (Brown *et al*., 1994) In a younger population (ages 18 to 34), Elter *et al*. (2004) reported that being African American doubled the odds of having periodontal pathology, similar to the risk if a third molar was visible in the quadrant examined. In this study, non-Caucasians, who were predominantly African-American, had a deeper predicted PD than Caucasians regardless of age.

Blakey *et al*. (2002) have emphasized that having no symptoms does not equate to the absence of periodontal pathology. If patients retain erupted third molars, periodontal probing depths should be monitored around third molars as should be done for all retained teeth. Clinicians should consider mandibular third molars and third molars in African American patients as more at risk periodontally.

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