Abstract

Introduction: First permanent molars (FPM) of poor prognosis are routinely extracted in children throughout the UK. National guidelines suggest that to achieve spontaneous closure, for the lower arch, the FPM should be extracted at 8 to 10 years, during bifurcation formation of the second molar. The literature is of limited quality and has suggested alternative variables that may be associated with successful space closure. Aim: To investigate the radiographic prognostic factors associated with space closure following extraction of FPM. Objectives: 1. To determine factors that may predict space closure of the second molar after extraction of the FPM. 2. Development of a toolkit to aid clinical decision-making. Methods: 148 upper and 153 lower FPM extractions from 81 participants were assessed retrospectively. Dental age, second molar developmental stage molar, second premolar and second molar angulation and the presence/absence of the third molar were assessed on pre-extraction orthopantomograms. Outcome was assessed via visual examination, study models or radiographs. Results: Closure occurred in 89.9% of upper and 49.0% of lower quadrants. Dental age was statistically, but not clinically, significant within the upper arch ($p<0.05$). For the lower arch, presence/absence of the third molar and second molar angulation were found to be statistically and clinically significant ($p<0.01$ and $p<0.05$ respectively). A toolkit was developed in relation to the lower arch variables. Conclusions: These findings are contradictory to the RCS Guidelines and suggest the presence of the third molar and a mesially angulated second molar are favourable for space closure. The developed toolkit requires further validity testing.

Keywords: Interceptive orthodontics, first molar, space closure

Introduction

The first permanent molar (FPM) is one of the first adult teeth to erupt into the mouth at around six to seven years of age[1]. This early eruption, along with the position towards the back of the mouth, can make this tooth more susceptible to diseases such as dental caries. Recent UK Dental Health Surveys also show an increase in incidence of decay associated with the first molars[2,3]. This, along with, developmental disorders of enamel such as molar incisal hypomineralisation results in a significant level of poor prognosis first molars that may be incorporated into orthodontic extraction patterns[4]. In malocclusions, where space in not required to reduce an overjet or relieve crowding, it may be beneficial to extract the first molar in circumstances that favour the mesial eruption of the second molar into this extraction space. This would eliminate, or at the very least, reduce the need for fixed appliance treatment with its associated risks, particularly in patients who may already be susceptible to dental caries[5]. Attempting to close this extraction space can also lead to undesirable orthodontic effects[6,7,8] such as excessive retraction of the lower labial segment.

The majority of research assessing factors which could affect this spontaneous space closure of the first molar space has been undertaken in the 1960's and 1970's[9-15]. Positive associations had been found between space closure and chronological age[13,14,15], the angulations of the developing second molar and second premolar[11], the presence of the third molar[9], crowding[9,11,13] and skeletal relations including retrognathic maxillae and prognathic mandibles[14]. However, these studies relied on subjective measures of outcome, a lack of statistical analyses and incomplete reporting of results.

Current UK guidelines[16], developed by the Royal College of Surgeons of England state that space closure occurs relatively easily in the upper arch due the root morphology of the second molar and mesial tipping of the second molar during eruption. In the lower arch, the guidelines suggest that interceptive extractions should be undertaken between 8 to 10 years of age. Previous guidelines[17] suggested that extraction of the first molar when the bifurcation of the second molar is forming could be considered a predictor of successful space closure however the more recent work guidelines have recognised that the response of the second molar can be variable[18] and "acceptable positions are also possible in association with extraction at earlier and later stages of development". However, the quality of literature on which this is based is not robust as there are no studies that would be validated by Cochrane standards[19].

The aim of this study was to investigate whether the following radiographic prognostic factors associated with space closure following extraction of FPM:

1. Dental Age (DA) at the time of extraction
2. Bifurcation development stage of the second molar (2^{nd}MStage) at time of extraction
3. Angulation of the second premolar (2^{nd}PM) at the time of extraction
4. Angulation of the second molar (2^{nd}M) at the time of extraction
5. Presence of absence of the third molar at time of extraction (3^{rd}M+/-)

The null hypothesis for the study is that the above factors have no influence on successful spontaneous space closure following extraction of the first permanent molar.

Main Study

<u>Method</u>

Study Design: This was a retrospective longitudinal study.

Sample size calculation: Due to the quality of the previous research, the only potential variable that could be used for sample size calculation was the developmental stage of the second permanent molar. The study with the largest sample size[13] was used. For a power of 0.80 with a significance level of $p<0.05$ showing a clinically significant difference of 30% between the groups, a sample size of 49 molars were required per group (early, ideal and late) for a total of 147 molars. It has been recognised that upper and lower second molars behave differently and, therefore, these were analysed as separate samples requiring 147 upper molars and 147 lower molars; 294 in total.

Data Collection: Subjects were recruited from four sources. A previous audit within the Paediatric department identified children who had had interceptive extractions of first molars using hospital general anaesthetic theatre lists (Source 1). Outcome data in relation to space closure was used from this audit from patients who had attended an invitation for review (Source 1A)[19]. This audit had a significant failure to attend rate and therefore, those patients who did not attend the review, and were no longer under the care of the hospital, were recalled for the purpose of this study (Source 1B). Some patients within this source were still under the care of the Paedatric Dentistry or Orthodontic departments and these patients were invited to participate in the study at their next appropriate review (Source 1C). Patients were also recruited from Paediatric Dentistry and Orthodontic clinics on an ad hoc basis (Source 2). As this study involved patient recall and use of patient information from those who had not been discharged, ethical approval was required and granted (REC Number 13/WM/0398; IRAS Project ID 125278).

Explanatory Variables:

All radiographs were taken at the EDH using PM 2002 EC Proline [Planmeca; Helsinki, Finland]. If more than one orthopantomogram was present, the radiograph made closest to the extraction date was used.

Calculation of the Dental Age

Calculation of DA followed the "weighted average method" derived from the Demirjian classification[20] and a previously established reference data set[21]. The reference data set determined the mean age of attainment of each stage of development for each tooth. For each participant, all the upper and lower teeth present on the left side of the orthopantomogram and all four third molars were assessed for development according to the 8 stage system (Figure 1) described by Demirjian's classification (Demirjian *et al.,* 1973). Each development stage for each tooth was associated with a mean age of attainment and standard error derived from the reference data set. The data was then copied into STATA (version 12) statistical software and the weighted average was calculated using meta-analysis commands. This method not only factors the mean and standard error but also the size of each subset of data (each tooth at each developmental stage). The meta-analysis then produced a mean age for each patient.

Calculation of the Developmental Stage of the Second Molar

2ndMStage was assessed with the orthopantomogram placed on a light box in a darkened room. This was assessed against Demirjian's 8-stage model. Stage E corresponds to bifurcation development and this was recorded as "ideal" timing. Extraction of the FPM at second molar development stages A to D were termed "early" and F to H. "late".

Angulation of the Second Premolar and Second Molar

2^{nd}PM and 2^{nd}M was assessed using a modification of Shiller's method[22]. This was developed to assess the angulation of third molars. For the first permanent molar in question, a line was traced along the occlusal plane (White Line). As showing in Figure 2, a line was also traced through the body of the second premolar or second molar (Dotted Line) and the distal angle formed by the intersect of this line with the occlusal plane was recorded as the angulation of the tooth (X). This means that the smaller the angle, the more mesial the angulation.

As there was no previously published data available regarding the distribution of 2^{nd}PM and 2^{nd}M, the data from within the study was used to determine the distribution of the angles.

For each data set, the data were divided into three groups; "mesially angulated", "upright" and "distally angulated". If required, data were transformed to achieve a normal distribution. The limits of the upright group were the mean ± one standard deviation. This meant that the upright group consisted of the central 68%, the distally angulated group, 16% and the mesially angulated group, 16%.

Development of the Third Molar

The presence of a crypt or initial calcification of the third molar was taken as presence of development. If none of these signs were present, it was determined that there was no third molar development at this stage.

Outcome Variables:

Assessment of space closure was binary i.e. space closed or space present (unsuccessful space closure) between the mesial aspect of the second molar and the distal aspect of the second premolar. The presence of a visible contact between the second molar and second premolar with no significant vertical or transverse discrepancies at the contact was considered a success. This was determined clinically through patient call back and recruitment from outpatient clinics or from study models and radiographic records if orthodontic treatment had commenced. If there was any significant chipping or distortion of the study models or radiographic distortion, these data were excluded from the study.

Repeatability:

For DA, SMStage, 2^{nd}PM, 2^{nd}M and 3^{rd}M+/-, all four quadrants of the same ten orthopantomograms were assessed two weeks apart. For DA, acceptable reliability for SMStage was taken as a proxy, as the method used for both of these variables was the same. For the dependent variable (space closure), data was only used from subjects who had study models, photographs or radiographs to prevent the need for repeat visits.

Reliability Testing

For numerical variables (2^{nd}PM and 2^{nd}M), paired t-tests and Lin's Concordance Correlation Coefficients were used and for categorical variables (2^{nd}MStage, 3^{rd}M+/- and space closure) kappa and weighted kappa scores were used as appropriate[23].

Calibration

Measurements of angles and detecting the presence of a developing third molar is considered within the scope of the day to day practice of the primary researcher and therefore calibration to a gold standard is not required. SMStage was calibrated to a gold standard clinician. As this was a categorical variable, Cohen's weighted kappa test was used.

Statistical Analyses

SPSS21 and STATA statistical packages were used for initial data analysis. All patient identifiable data were removed. Each participant was allocated a study number known only to the primary researcher and this number was used throughout the study.

Comparison of the Sources of Data

In this study, as data were collected from up to four different sources, it is important to ensure that there are no significant differences between these groups. The chi-squared test was used to ensure that the outcome frequencies are not different to allow the data to be combined.

Transformative Statistics

The distributions of upper and lower 2^{nd}PM and 2^{nd}M were assessed for normality based on skewness and kurtosis. Previous literature has described a skewness of near-zero and kurtosis less than one are acceptable for accepting normality[24].

Model Construction

As data were being collected from up to four quadrants within each participant, multilevel analysis was undertaken to account for any clustering effects using MLwiN version 2.1. The analysis worked at two levels; the level of the patients (DA) and the level of the quadrants (2^{nd}MStage, 2^{nd}PM, 2^{nd}M and 3^{rd}M+/-).

A generalised mixed model construction was used including all variables and data was entered into MLwiN. Any non-significant variables ($p>0.05$) were removed from the model and the model re-run. The resultant model was then tested against the data set to determine the goodness-of-fit. Given the nature of *in vivo* models, a goodness-of-fit of ≥80% was considered a good fit.

Results

A total of 94 patients were included in the initial part of the study however, 13 patients were excluded (orthodontic treatment = 4; non-interceptive extraction = 3; medical conditions = 2; no pre-extraction orthopantomogram = 2; primary failure of eruption = 1). Seven quadrants within the remaining 81 patients were also excluded (ankylosis of primary teeth; impacted second premolars; developmental absence of second premolars = 2 each; delayed eruption of the second molar = 1). This left a total of 148 upper and 153 lower teeth.

Reliability testing for the explanatory and dependent variables showed substantial agreement (Table 2). The results for the numerical data are outlined in Table 3. For categorical variables, intraoperator reliability ranged from 0.8337 to 1.000 (almost perfect to perfect).

Calibration for SMStage achieved a kappa of 0.8529 and 1.000 for the lower and upper arches respectively.

Forty-eight of the 81 participants were female with an ethnic breakdown of 65% Caucasian, 20% South Asian, 10% Afro-Caribbean and 5% of other ethnicities. The vast majority (83% participants) had extraction of all four first molars. The descriptive statistics are outlined in Table 3.

The majority (55.6%) of patients had the extraction of the first permanent molar at the "Ideal range" of eight to ten years of age with 9.9% having earlier extractions and 34.6% later. For the upper arch, 58.8% of extractions were undertaken at the ideal time, 18.2% early and 23.0% late. For the lower arch, this was 54.9%, 20.3% and 24.8% respectively.

Analyses of the distribution of the angulation 2^{nd}PM and 2^{nd}M revealed that three of the four quadrants required simple transformations to achieve normality. This data was then converted into boundaries for distal, upright and mesial angulation for each of the quadrants independently.

At the time of radiographic exposure, 62.2% of upper quadrants and 74.5% of lower quadrants showed evidence of third molar formation.

At review, 89.9% of upper quadrants and 49% of lower quadrants exhibited successful space closure.

Data was analysed for upper and lower arches independently as shown in Table 4. In the upper arch, the only statistically significant variable was DA (p=0.022). A scatter diagram (Figure 3) shows the relationship between success rate and dental age. The line of best fit (success = 0.98 – 0.0083 x DA) shows a close relation to the scatter plot with R^2 of 0.994.

For the lower arch, the 2^{nd}M and 3^{rd}M+/- were statistically significant in the prediction of successful space closure (p=0.002 and p=0.023 respectively). The predicted probabilities of the chances of successful space closure for the combination of each of the variables are outlined in Table 5. The resultant models for the upper and lower arches showed a high level of specificity (1.00 and 0.949 respectively) and sensitivity (0.978 and 0.948 respectively).

Toolkit

<u>Method</u>

Determination of the angulation of a second molar radiographically can be difficult. To make this more reliable, a toolkit was developed. The developed toolkit (Figure 4) consists of a clear sheet of acetate 5cm x 21cm. Two protractors are included within the toolkit with the boundaries between mesial, upright and distal clearly demarcated. The table indicates the predicted success of space closure for each combination of the two variables. The toolkit underwent validity testing via intraoperator and interoperator testing, clinical validity, simplicity of use and acceptability.

<u>Results</u>

Intraoperator reliability for the toolkit was assessed on twelve DPTs two weeks apart. Kappa and weighted kappa tests were undertaken for 3^{rd}M+/- and 2^{nd}M respectively. Intraoperator reliability was undertaken by SMP with kappa values of 0.857 for angulation and 1.000 for third molar suggesting very good to perfect agreement. Interoperator agreement was undertaken using two orthodontic specialty trainees, one orthodontic post CCST, one orthodontic specialist practitioner and one orthodontic consultant, none of whom were involved in the study. Participants were given brief instructions and a demonstration on the use of the ruler and the time taken was recorded. The interoperator agreement ranged from 0.680 to 0.857 for 2^{nd}M (good to very good agreement) and 0.700 to 0.924 for presence/absence of 3^{rd}M+/- (good to very good agreement). It took the participants 14 to 18 seconds to determine the predicted chances of success of space closure for each quadrant, suggesting that the toolkit is easy to use. Use of the toolkit requires no further examination or diagnostic tests for the patient that would not otherwise be taken and therefore can be considered acceptable to patient and parent. The participants in the interoperator tests also reported that the toolkit is acceptable to use. Clinical validity would require the use of second sample of data on which to assess the validity of the toolkit. No second source of data was available to the research team and therefore bootstrapping was undertaken to assess the internal validity of the overall success rate. This confirmed the internal validity of the data. This toolkit requires further external validity testing.

Discussion

This study suggests that the angulation of the developing second molar could be predictive of spontaneous space closure with a more mesial angulation related to a higher success rate. These results are supported by previous studies[11]. The study also suggests that the presence of the third molar also contributes to successful space closure supporting previous authors of prospective studies[9,13].

The Royal College of Surgeons Guidelines regarding the Extraction of the First Permanent Molars in Children (2014)[16] suggests that in order to achieve spontaneous closure of the extraction space, for the lower arch, the FPM should be extracted at 8 to 10 years old but recognises that high success rates can be achieved with earlier and later extractions[16]. Previous work in relation to the other variables within this study was not discussed, likely due to the quality of these studies.

The nature of this study meant that multiple operators were assessing outcome with no opportunity for calibration. Complete closure of space was considered a success in this study to accommodate for the fact that multiple uncalibrated operators were used. In reality, a small interdental space may be acceptable and therefore it is likely that the overall success rates for an acceptable result would be higher in both arches.

This study has found that there is a high success rate of space closure in the upper arch supporting previous studies which have exhibited similar success rates[12,13]. Dental age was found to be statistically significant for predicted space closure in the upper arch, however, the clinical significance of this is doubtful. This suggests that for every increasing year of dental age, there is a 0.83% reduction is the rate of success. This, along with the complex calculations required, would mean that this is unlikely to impact on clinical decision making. No other studies have previously assessed possible predictive factors in the upper arch.

For the lower arch, less than 50% of the quadrants exhibited successful space closure supporting previous findings of success rates of 38.5-50%[12,13]. Unsuccessful space closure can lead to significant consequences in relation to orthodontic treatment including extended treatment time, more complex mechanics, and risks of iatrogenic orthodontic effects[6-8].

There were a number of limitations within this study. Due to the retrospective nature of this study, it was difficult to ensure that there were equal numbers within each group (distal/present, upright/present, mesial/present, distal/absent, upright/absent, mesial/absent). Groups containing few data may make any inferences about the chances of space closure within this group less reliable. It has been previously recognised that positioning errors while taking an orthopantomogram and differing orthopantomogram machines can alter the apparent angulation of the dentition, however the differences were in order on 3 degrees which is unlikely to impact on the reliability of these findings[25,26].

The lower third molar has been found to begin initial crypt formation at 9.81±2.35 years in females and 9.79±1.63 years in males[21]. The average age at radiographic exposure was 9.2 years. Therefore, the absence of third molar formation at this age does not mean that a third molar will not develop, particularly in relation to the lower arch. Any conclusions relating to the third molar may, therefore, be attributed to *early* third molar formation rather than the *presence* of the third molar. This may reduce the applicability of the toolkit for older children.

Other studies have also suggested that skeletal relations[14] and crowding[9,11,13] may be potential predictive factors but, due to the retrospective nature of the study, these were not tested.

Conclusions

- Dental age shows a statistically significant relationship to the success of space closure in the upper arch, however, this is not clinically significant.
- The angulation of the developing second molar and the presence of the third molar have both a statistically and clinically significant relationship with space closure in the lower arch.
- The stage of development of the second molar and dental age have no relationship with the success of spontaneous space closure in the lower arch
- The developed toolkit exhibits sufficient validity for further testing

Further Research

Further research needs to be undertaken to assess the predictive value of non-radiographic factors such as skeletal relation and crowding on the chances of successful space closure. External validity testing is also required in relation to the developed toolkit.

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Figures

Figure 1: Schematic representation of Demirjian stages of dental development (Roberts *et al.*, 2008)

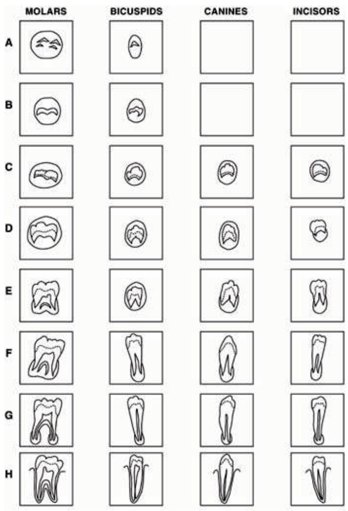


Figure 2: Dental orthopantomogram showing method for angular measurements

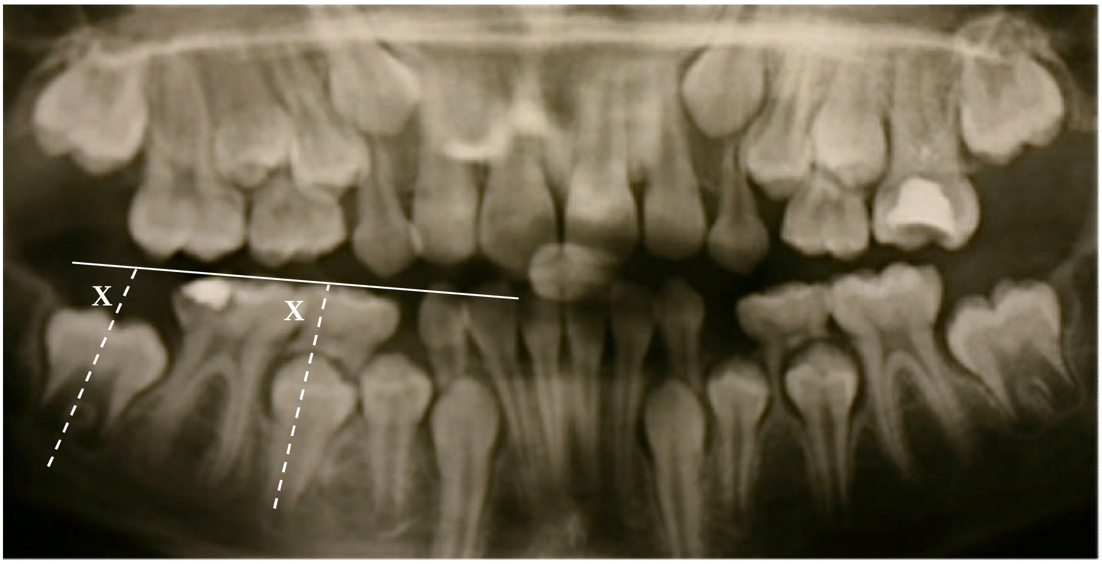


Figure 3. Scatter diagram of dental age against predicted probability of spontaneous space closure for upper quadrants

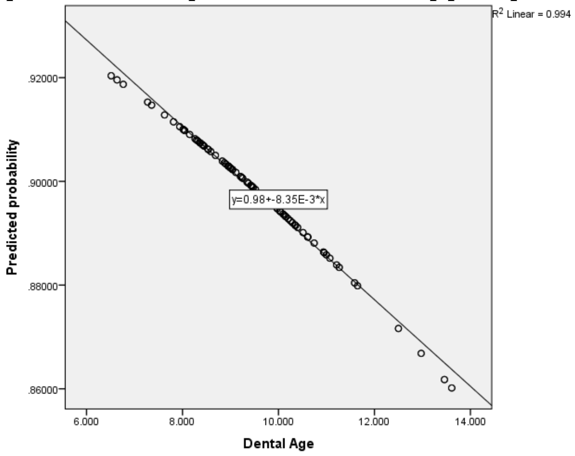
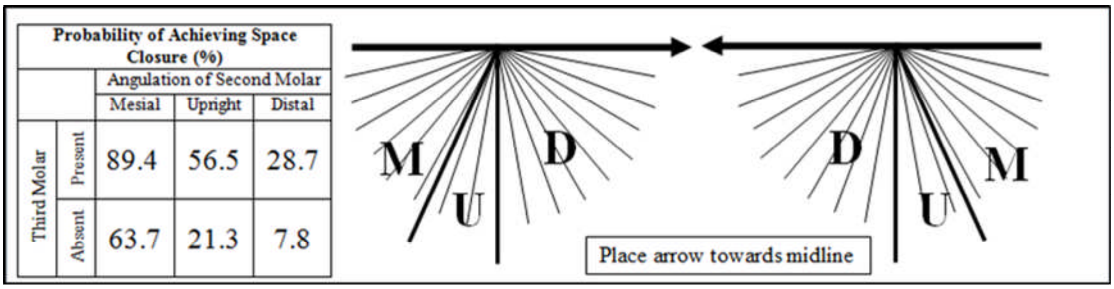


Figure 4. Toolkit for prediction of spontaneous space closure for the lower arch



Tables

Table 1. Inclusion/Exclusion Criteria for Study

Inclusion Criteria	*Exclusion Criteria*
Previous removal of one or more first permanent molars with the intention of achieving spontaneous space closure	Craniofacial syndromes and anomalies of eruption
Presence of pre-extraction orthopantomogram of adequate quality within the medical records taken at the Eastman Dental Hospital	Extraction or hypodontia of other permanent teeth
Able to sign own assent (below 16 years of age) or consent forms (16 years of age or above)	Participants who have had orthodontic treatment where there is no pre-treatment record available at the Eastman Dental Hospital
Parent/Guardian agreed to give consent (for participants below 16 years of age)	No preoperative orthopantomogram

Table 2: Reliability testing for numerical data within the study

Tooth	*95% Limits of Agreement*	*p-value from paired t-test*	*Lin's CCC*	*95% CI Lin's CCC*	*Agreement*
Angulation Upper Premolar	-3.457 - 3.457	1.000	0.984	0.933 - 0.995	Substantial agreement
Angulation Lower Premolar	-3.106 – 3.506	0.7163	0.988	0.954 - 0.997	Substantial agreement
Angulation Upper Molar	-4.175 – 3.975	0.8825	0.981	0.928 - 0.995	Substantial agreement
Angulation Lower Premolar	-3.698 – 4.098	0.7577	0.971	0.891 - 0.993	Substantial agreement

Table 3: Descriptive Data in Relation to First Molar Extraction

Descriptor	*Average*	*Range*
Chronological Age at DPT (yrs)	9.2	6 - 14
Dental Age at DPT (yrs)	9.5	6-14
Chronological Age at Time of Extraction (yrs)	9.6	6-14.5
Time between DPT and Extraction (yrs)	0.41	0-0.85
Time between Extraction and Review (yrs)	4	0.9-7.5

Table 4a: Upper quadrant multilevel analysis (*p<0.05; **p<0.01; †p<0.001)

Upper	*F*	*df1*	*df2*	*Sig.*
Corrected Model	0.837	8	149	0.671
DA*	**5.339**	**1**	**149**	**0.022**
SMStage	2.233	2	149	0.111
SP°	0.008	2	149	0.992
SM°	0.242	2	149	0.785
TM+/-	1.539	1	149	0.217

Table 4b: Lower quadrant multilevel analysis (*p<0.05; **p<0.01; †p<0.001)

Lower	*F*	*df1*	*df2*	*Sig.*
Corrected Model	2.634	8	146	0.010
DA	1.750	1	146	0.188
SMStage	0.853	2	146	0.428
SP°	0.827	2	146	0.440
SM°*	**3.856**	**2**	**146**	**0.023**
TM+/-**	**9.871**	**1**	**146**	**0.002**

Table 5: Predicted probabilities of space closure in the lower arch in relation to statistically significant variables

		Angulation of Second Molar		
		Distal	Upright	Mesial
Presence/Absence of Third Molar	Present *(95% CI)*	28.7% *(14.7-39.1)*	56.5% *(43.3-66.5)*	89.4% *(78.2-97.1)*
	Absent *(95% CI)*	7.8% *(1.8-12.4)*	21.3% *(14.0-41.1)*	63.7% *(51.8-75.3)*