AAO Foundation Award Final Report

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Project Title	A Genetic Epidemiology approach to Congenital Hypodontia
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Institution	Case Western Reserve University
Summary/Abstract	**Study-1.** Interest in the area of congenital hypodontia has grown in the last few years. **Objectives:** The present study was designed to evaluate patterns in congenital hypodontia (excluding third molars). **Methods:** The population consisted of patients from the Case Western Reserve University, Department of Orthodontics and a private orthodontic practice. A total of 2619 individuals, comprising 1174 males, 1445 females, 2111 Caucasians, 313 African Americans, and 195 persons of other ethnic backgrounds were examined using existing, pre-treatment panoramic radiographs. Missing teeth were denoted using the Universal numbering system and the data were entered in Excel as a dichotomous variable. The ascertained sample of 201 subjects with hypodontia consisted of 110 females, 91 males, 164 Caucasians, 26 African Americans, and 11 subjects of other ethnic origins. Pair-wise correlations were estimated for each missing tooth and other teeth using SPSS. **Results:** The analysis yielded significant (p-value < 0.01) correlations between missing # 12 and # 22 (0.579), # 15 and # 25 (0.688), and # 35 and # 45 (0.440). In addition, the Caucasian sample alone exhibited a significant (p-value < 0.05) correlation between tooth # 15 and # 35 (0.191), and tooth # 15 and # 45 (0.191). Similar overall trends were observed in males and females. **Conclusions:** These results indicate a strong association between congenital hypodontia of teeth and the corresponding contra-lateral teeth. **Study-2** **Objectives**: To estimate familial aggregation observed in congenital hypodontia and assess possible modes of inheritance. **Methods**: 283 probands affected with congenital hypodontia, previously identified and reported, were contacted along with their families for participation. Members of 88 families (N=376) were evaluated

	radiographically, clinically and/or by means of a questionnaire to characterize the phenotype. Data analyses for familial correlations included testing five patterns of congenital hypodontia observed, utilizing three different models. Recurrence risk ratios (RR) were calculated using published prevalence rates of congenital hypodontia. **Results:** 85% of the relatives were unaffected while 84% of affected relatives were missing only one or two teeth. Sibling RR ranged from 1.2 to 9.3. Parental RR ranged from 3.1 to 7.6. Resulting familial correlation estimates including: mother-daughter, mother-son, father-daughter, father-son, brother-sister, brother-brother and sister-sister relationships were not significantly different from zero for any of the five patterns. **Discussion**: Congenital hypodontia in one family member moderately increases the likelihood of another family member missing a tooth. In individuals missing second premolar, family members have a higher risk of congenital hypodontia than the general population (sibling RR=9.3, parental RR=7.6). For individuals missing maxillary lateral incisors, parents have a higher risk of missing teeth (RR=6.3) compared to siblings (RR=3.6). For individuals missing any tooth, family members had a higher risk of missing teeth compared to the general population (sibling RR=2.8, parental RR=3.1). **Conclusions**: Results indicate an increased recurrence risk of congenital hypodontia but simple Mendelian modes of inheritance were undetected by the present epidemiologic analyses. Poor familial correlations coupled with a relatively higher RR suggest that congenital hypodontia may be a complex trait with several genetic and/or environmental determinants.