The American Thyroid Association recently classified all MEN2A-associated codons into increasing risk levels A-C and stated that some patients may delay prophylactic thyroidectomy if certain criteria are met. One criterion is a less aggressive family history of MTC but whether families with the same mutated codon have variable MTC aggressiveness is not well described. We developed several novel measures of MTC aggressiveness and compared families with the same mutated codon to determine if there is significant inter-familial variability. Pedigrees of families with MEN2A were reviewed for codon mutated and proportion of \textit{RET} mutation carriers with MTC. Individuals with MTC were classified as having local or distant MTC and whether they had progressive MTC. MTC status and age were assessed at diagnosis and most advanced MTC stage. For those without MTC, age was recorded at prophylactic thyroidectomy or last follow-up if the patient did not have a thyroidectomy. For each pedigree, the mean age of members without MTC, with MTC, and the proportion of \textit{RET} mutation carriers with local or distant and progressive MTC were calculated. We assessed differences in these variables using ANOVA and the Fisher’s exact test. Sufficient data for analysis were available for families with mutated codons 609 (92 patients from 13 families), 618 (41 patients from 7 families), and 634 (152 patients from 13 families). The only significant differences found were the mean age of patients without MTC between families with codon 609 and 618 mutations even after accounting for prophylactic thyroidectomy ($p=0.006$ and 0.001, respectively), and in the mean age of MTC diagnosis between families with codon 618 and 634 mutations even after accounting for symptomatic presentation ($p=0.023$ and 0.014, respectively). However, pedigree analysis suggests these differences may be explained by generational differences in ascertainment of \textit{RET} carriers and the availability of genetic testing when the proband initially presented. Much of our analyses were restricted by insufficient numbers and further research on this topic is needed.

\textbf{Advisory Committee:}  
Thereasa Rich, M.S., C.G.C., Chair  
Stephen Daiger, Ph.D.  
Carol Etzel, Ph.D.  
Craig Hanis, Ph.D.  
Elizabeth Grubbs, M.D.