We conducted a likelihood analysis of parameters describing the genetic architecture of periventricular nodular heterotopia, including the relative risk ($\gamma$) and proportion of the exome related to periventricular nodular heterotopia ($\eta$). As there were substantial differences in sequenced regions across the different exome sequencing methods used in this study, we adapted our previously proposed likelihood model to incorporate trio-specific mutation rates that take into account the “callable real-estate” and observed de novo variants. This likelihood can be written as

$$L(\gamma, \eta) = \prod_i \left( \frac{\lambda_i e^{-\lambda_i} [\gamma + (1 - \gamma)(1 - C\eta)^{x_i}]}{\gamma + (1 - \gamma)e^{-\lambda_i C\eta}} \right)$$

where $x_i$ and $\lambda_i$ are the de novo variant counts and mutation rate, respectively, for the ith trio. As in previous analyses, $C$ is assumed to be a known constant, but since the de novo architecture is here restricted to nonsynonymous variation and splice sites are not considered, the value is taken to be 0.335 (estimate 30% of missence variants are deleterious and 3.5% are nonsense). Point estimates were obtained by optimizing equation 1 and likelihood ratio tests are computed by comparing the log-likelihood at this optimum to the value obtained under the null hypothesis.