Advances in carrier screening: Making the case for APBD

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Counsyl is a DNA testing and genetic counseling service that runs a fully automated lab, providing the capability to screen for many rare genetic diseases at scale. Counsyl's *Family Prep Screen*, an expanded carrier screen panel, was first made available in 2009. While professional societies currently recommend testing for a limited number of single gene conditions based on self-reported ethnicity and family history, more than 80% of children born with rare genetic diseases have no such family history. Using technological advances in molecular genetics, Counsyl has made it both possible and affordable to screen for a large number of conditions independent of ethnicity or family history. Carrier screening recommendations by the ACOG and ACMG even differ in terms of recommended diseases to screen for, highlighting the ongoing challenge of determining what conditions to include in prenatal screening guidelines and expanded carrier screening panels.

Counsyl recently published data in JAMA pointing to limitations in the current screening guidelines. The study was a retrospective modeling analysis of expanded carrier screening results from 346,790 individuals spanning 15 self-reported ethnic categories. Results showed that when analyzed and compared to current carrier screening recommendations by professional organizations (ACOG and ACMG), guideline-based screening misses a significant percentage of pregnancies affected by serious conditions. We have proposed a design model for expanded carrier screening that optimizes the clinical detection of at-risk couples by accounting for disease severity, incidence, and gene-specific sensitivity. By utilizing this approach, we recently reviewed more than 650 genes of consideration for addition to our *Family Prep Screen* and elected to add 100 new conditions, including the *GBE1*-related disorders, glycogen storage disease IV (GSD IV) and adult-onset polyglucosan body disease (APBD).