

All in the family: a first look at outcomes when multiple relatives undergo multi-gene panel testing

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In the hereditary cancer setting, single site analysis has proven to be a fast and cost-effective testing strategy for relatives once a genetic mutation has been identified in a family. However, more comprehensive testing of family members is sometimes indicated, such as in the presence of bilineal family history of cancer or when a patient's clinical presentation is not consistent with the previously identified familial mutation. With the widespread adoption of next-generation sequencing, testing costs have decreased while efficiency has improved. While many family members still pursue targeted familial mutation testing, others are opting for multi-gene panel testing (MGPT) even in the presence of a known familial mutation. The aim of this study was to assess the results of testing in families who had multiple individuals pursue MGPT for hereditary cancer risk at the same laboratory. In total, 727 families were identified in which multiple relatives pursued MGPT, including 663 families with two individuals undergoing MGPT and 64 families with three or more relatives undergoing MGPT. In 76 families, MGPT was ordered on the same date for all relatives. In 39 families, testing for relatives was ordered before the proband's results were reported, and in 612 families relatives were tested after the proband's result was reported. Of 357 families where relatives pursued MGPT following identification of a mutation in the proband, additional alterations were detected on relatives' MGPT in 68 families (19.0%), including 12 families (3.4%) where relatives carried mutations not identified in the proband, 53 families (14.8%) where relatives carried variants of unknown significance (VUS) not in the proband, and three families (0.8%) where relatives carried both mutations and VUS not in the proband. Results from this exploratory study demonstrate that, in a subset of cases, clinicians are ordering MGPT for relatives of mutation-positive probands. Further studies are needed to help identify characteristics of families who are most likely to benefit from multiple MGPTs.