

Practical aspects and implications of variant interpretation in the clinical setting

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Next-generation sequencing (NGS) technology has resulted in the generation of massive amounts of variant data. Despite efforts to standardize variant interpretation, recent data sharing efforts have revealed a significant number of discordant classifications between labs. This current paradigm underlines the need for additional review prior to disclosing results to patients. Many clinical genetic counselors have naturally assumed this responsibility as they are in the unique position to contextualize variant classification with clinical circumstances, as well as bridge the gap between clinical sites and laboratories. Current studies are investigating the application of variant review and classification in cardiology clinics, subsequently leaving a gap in knowledge for other specialties. The purpose of this study was to analyze current trends and perceived barriers to variant review and secondary interpretation in pediatric and oncology settings. A survey was sent out through the NSGC Special Interest Groups (SIGS) to cancer and pediatric genetic counselors. Study results indicate that the majority of genetic counselors in both cancer and pediatric settings will review test results, primarily for variants of uncertain significance. Half of respondents indicate that they would perform a complete secondary variant interpretation. In circumstances in which discordant classifications arise, genetic counselors typically report the laboratory's interpretation to the patients. Most genetic counselors would not notify laboratories of noted discrepancies. Primary concerns of genetic counselors that do not perform secondary variant classification are training, liability, and time management. In addition to the need for more systematic and consistent variant classification across laboratories, these findings suggest that there is a need to more specifically define a clinical genetic counselor's role regarding variant review and classification.