Title: Validation of patient-facing digital tool risk stratification of those at risk for hereditary cancer syndrome: The CARE program™ accurately identifies high risk individuals

Authors: Haley Keller MS, CGC, Deepika Nathan, MS, LCGC, Sarah Siddiqui, MS, CGC, Heather Fecteau, MS, CGC, Carrie Horton MS, CGC, Carrie Milliard MS, CGC, Robert Pilarski, MS, CGC, MSW, Devon Thrush, MS, CGC, Lukas Lyon, BSPH, BS, Shannon Kieran, MS, CGC, MBA

The National Comprehensive Cancer Network (NCCN®) publishes curated genetic testing criteria based on personal and family cancer history (P/FHx); however, clinicians may not have a consistent, systematic way to collect and evaluate this information. A HIPPA-compliant digital tool (CARE) was developed to collect patient information and risk stratify those who meet NCCN® criteria for hereditary breast, ovarian, pancreatic, and prostate cancer (HBOP); and Lynch syndrome and familial adenomatous polyposis. The purpose of this study was to assess the analytic validity by determining the accuracy of the digital tool's execution and interpretation of NCCN guidelines® as compared to genetic counselor (GC) interpretation of the same guidelines.

To determine testing criteria eligibility, the outcome of individuals who met versus did not meet criteria was compared against a control group consisting of board-certified GCs. The GCs participating in the study had at least 3 years of recent clinical oncology experience; reviewer A works in a clinical setting, and reviewer B is an employee of Ambry Genetics. Each GC reviewed 200 unique, de-identified patient cases and evaluated whether the reported P/FHx of each case met the assessed testing criteria. Of the 400 cases, 200 did not meet and 200 did meet criteria; of the cases that met criteria, based on CARE interpretation, 150 met HBOP V2.2022 and 50 met colorectal (CRC) V1.2021 guidelines.

Out of 400 cases reviewed, CARE accurately assessed 395 (98.8%) cases. Themes for discordance included: GC interpretation correct and tool incorrect due to known gap in tool's algorithm, such as not assessing for limited family history (n=2); and matter of difference in interpretation (n=3) in which GC reviewer and/or tool made assumptions about cases' clinical histories to assess criteria, such as assuming any reported gastric cancer as diffuse type. There were 14 cases in which the tool interpretation was correct versus GC interpretation. Percent agreement for reviewer A for HBOP and CRC equaled 95.5% (Cohen's Kappa(κ)=0.91 (0.84, 0.97)) and 98.0% (κ=0.91 (0.82, 1.0) respectively. Percent agreement for reviewer B equaled 98.6% (κ=0.97 (0.94, 1.0)) and 98.6% (κ=0.96 (0.91, 1.0).

CARE accurately identifies individuals who meet NCCN® testing criteria to aid in risk stratification. Digital tools such as this may be helpful in clinical practice to collect P/FHx, identify individuals who would benefit from genetic counseling and testing and improve identification of those who are at risk for hereditary cancer syndromes.