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Title:
Taming concerns regarding the accuracy of laboratory clinical data: a detailed comparative analysis

Abstract:

Purpose: Genetic testing laboratories accumulate large amounts of clinical data from clinicians via test requisition forms (TRFs) and other clinical documents such as pedigrees and/or detailed clinic notes ('clinicals'). When curated, phenotype data can be used in variant assessment, genetic disease characterization, and clinical research; however, the completeness and accuracy of phenotype data from laboratory-based cohorts is often questioned. The purpose of this study is to evaluate the completeness and accuracy of TRF data for patients undergoing hereditary cancer multigene panel testing (MGPT).

Methods: Ten percent of MGPT cases were randomly selected and reviewed from a cohort tested between January and June 2015 at a single clinical laboratory. For cases where clinicals were submitted *after* the test order date, TRF-reported cancer types and ages at diagnosis (dx) for probands and relatives were evaluated for accuracy and completeness using clinicals as the comparison standard.

Results: Of 2,893 MGPT cases reviewed, 43.7% (n=1,263) submitted a pedigree and/or clinic note. For 31.3% (n=395) of cases, clinicals were submitted *after* the test order date and thus further evaluated. Cancer type and age at dx (+/- 2 years) were accurately reported for 99.4% and 97.8% of proband cancers, respectively. Proband cancer type was incomplete for 5.1% of cases and age at dx was incomplete for 7.4% of cases. Compared to probands, cancer type and age at dx for relatives were also highly accurate (type: 98.9%, p=0.553; age at dx: 95.8%, p=0.130) but significantly more likely to be incomplete (type: 29.7%; p=3E-28; age at dx: 26.4%; p=3E-16). When compared to 1st and 2nd degree relatives, incomplete data was more frequently observed among 3rd degree relatives and beyond (p=6E-8 and p=3E-5 for cancer types and ages, respectively). No significant differences were observed between maternal and paternal family history data.

Conclusions: In this laboratory cohort, cancer type and age provided on the TRF is highly accurate for probands and relatives. Proband cancer histories exhibited a high level of completeness; however, this diminishes somewhat among relatives, particularly as relationship to the proband becomes more distant. It is imperative for clinicians to provide complete data not only on probands but also on relatives to aid in accurate molecular results interpretation, disease characterization and interpreting the overall health implications of genomic data.

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