ACMG Secondary Findings: A Review of Patient Choices in Reporting

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BACKGROUND

Reporting secondary findings on whole exome sequencing (WES) and whole genome sequencing (WGS) tests is guided by recommendations from the American College of Medical Genetics and Genomics (ACMG). ACMG first issued guidance in 2013 on reporting pathogenic/likely pathogenic variants considered medically actionable in a specific list of genes regardless of proband phenotype. The initial guidance did not favor offering individuals the choice to opt out of receiving these findings, however, a revised statement was issued in 2014 that supported offering the choice to receive or not receive secondary findings to individuals being tested. We evaluated internal data to assess patient choices for secondary findings and reviewed the ordering and reporting practices for secondary findings from 15 US-based laboratories offering WES/WGS tests.

METHODS

Internal data was pulled for reported duo/trio WES and WGS cases pertaining to indication, phenotype, results reported, and decision by each family member of duos/trios to opt into reporting of secondary findings.

A search of the Genetic Testing Registry (GTR) was performed in April 2023 using the terms "exome" or "genome" with "Laboratories" selected and lab location set to "United States". The website for each laboratory was reviewed to confirm that they performed clinical duo or trio WES/WGS. Information regarding mechanism for patient consent to report secondary findings, whether individual reports were issued for proband and family members, and if separate (independent) reporting of secondary findings were available for proband and family members. Where necessary, laboratories were contacted directly by email or phone call to obtain or clarify information. All commercial laboratories where sufficient information was obtained were included. Several academic laboratories were also selected to be included in this review based on available information. The data from each of these labs were anonymized.

TABLE 1

Baylor Genetics	GeneDx	Perkin Elmer	Prevention Genetics	Variantyx
Rady Children's	ARUP	LabCorp	Blueprint	Quest
Mayo Clinic	Centogene	Ambry	Knight Diagnostics	Greenwood

Table 1: Laboratories included for this review on practices.

RESULTS

Internal data from >1900 individuals indicated that 9% of the time there was a discrepant choice to opt-in or opt-out among family members as part of a duo or trio WES/WGS test (Figure 1). Additionally, 2.3% of individuals did not indicate any choice on the requisition form and thus opted out by default. Finally, of the 686 families tested, 10 families (1.5%) were positive for parental secondary finding(s) not identified in the proband. Two families (0.3%) were positive for secondary finding(s) only in the proband (Figure 2). In both reporting scenarios, all members of all families had opted into SF reporting.

Data from 15 laboratories were obtained (Table 1). Among the reviewed laboratories, consenting and reporting practices vary significantly. 12/15 utilize either a default opt-in or opt-out approach to report secondary findings if the patient does not choose whether these should be reported (Figure 3). Two determine if secondary findings should be reported based on the WES/WGS test code alone and one has no default option. 8/15 allow for proband and comparators to have independent secondary finding analysis performed, of which 6 do so by default.

FIGURE 1

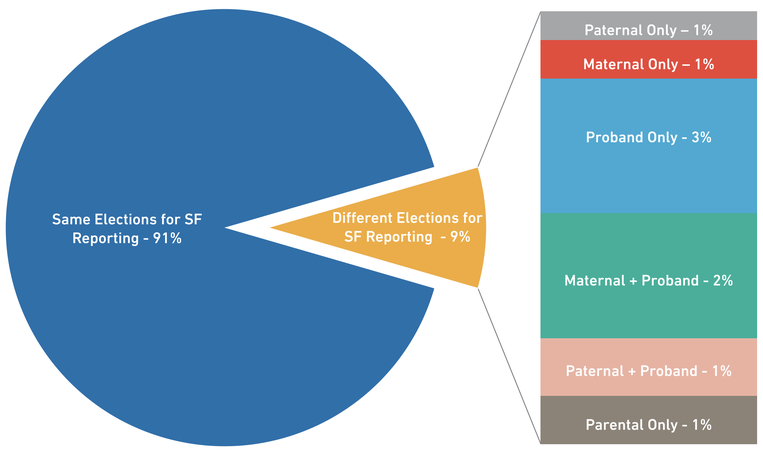


Figure 1: Ordering patterns of family members at Baylor Genetics.

FIGURE 2

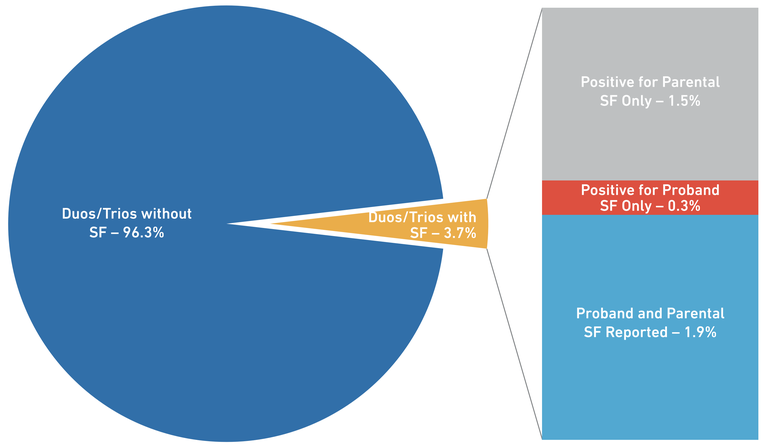
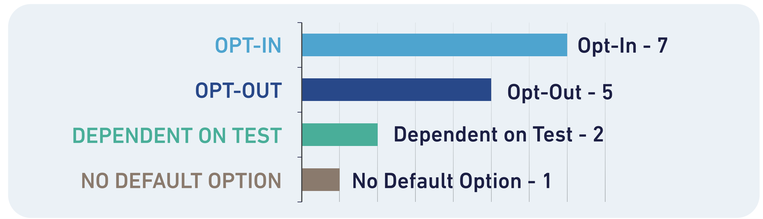


Figure 2: Breakdown of cases where secondary findings were reported.

FIGURE 3



CONCLUSIONS

While ACMG has continued to update both the reporting guidance and the list of reportable medically actionable findings, there is no clear consensus by laboratories on how to implement this guidance. Internal patient data supports offering independent opt-in for secondary findings for all family members given that many families do not uniformly want these findings. Inconsistent industry practices highlights the incongruencies and potential counseling issues that these differences create. Standardizing reporting and other practices would be beneficial to ensure providers and patients are best informed of these practices and can make appropriate decisions prior to testing.