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Research For Your Practice

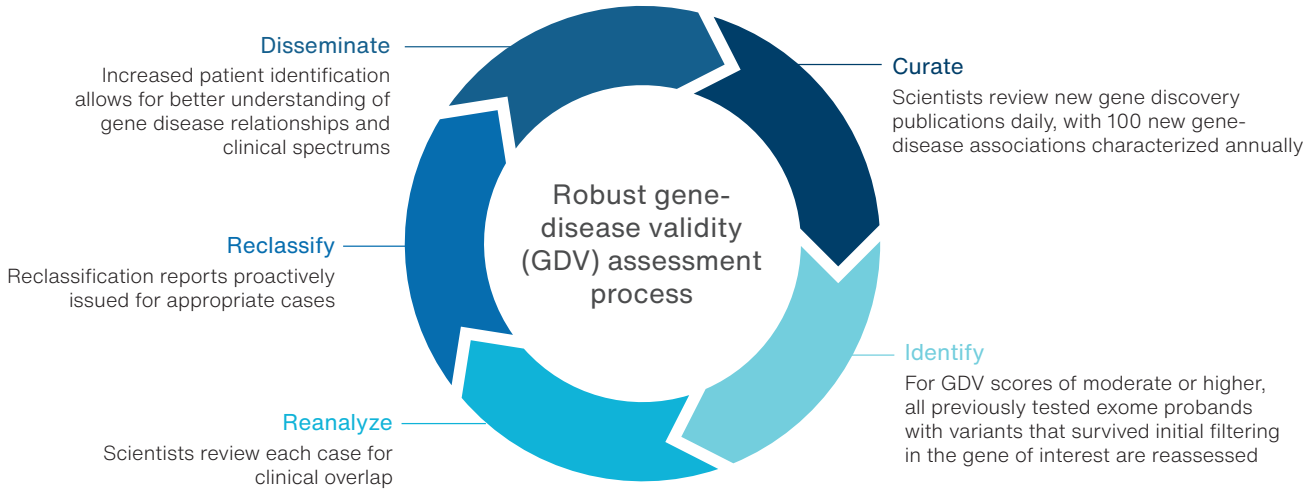
The Ambry Patient For Life™ Reanalysis Program Revolutionizes Rare Disease Diagnosis

Exome sequencing (ES) has revolutionized genetic diagnostics, but many cases remain unsolved—making ongoing reanalysis essential as new gene-disease links and variant interpretations emerge. Despite its demonstrated potential to improve diagnostic yield, there is still no consensus on the optimal timing, frequency, or methodology for ES reanalysis. In addition, the reanalysis process can place a significant workload on clinicians and laboratories, limiting its widespread adoption.

Patient for Life—a proactive, laboratory-driven reanalysis program and a core component of Ambry's Classifi® clinical interpretation engine—systematically monitors and updates prior ES results in light of new genomic discoveries. By automating variant reclassification and case review, it reduces the burden on healthcare providers while ensuring that patients benefit from the latest scientific advances (Figure 1).

This study evaluates the clinical utility of Patient for Life by comparing its impact on diagnostic yield with that of family-based testing and clinician-initiated reanalysis, demonstrating its effectiveness in enhancing diagnostic outcomes in a large ES cohort.

Figure 1. Patient for Life Process

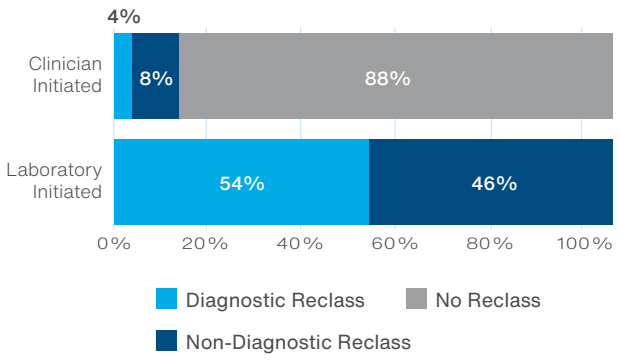


CLINICAL IMPACT AND EFFICIENCY OF THE PATIENT FOR LIFE PROGRAM

Among 10,921 individuals who underwent exome sequencing (ES), 23% (2,495 cases) received at least one reanalysis. Of these, 35% (993 cases) were reclassified, demonstrating the clinical value of reanalyzing ES data as new evidence emerges. Importantly, reanalysis increased overall diagnostic yield by 5%. The method of reanalysis initiation significantly influenced outcomes.

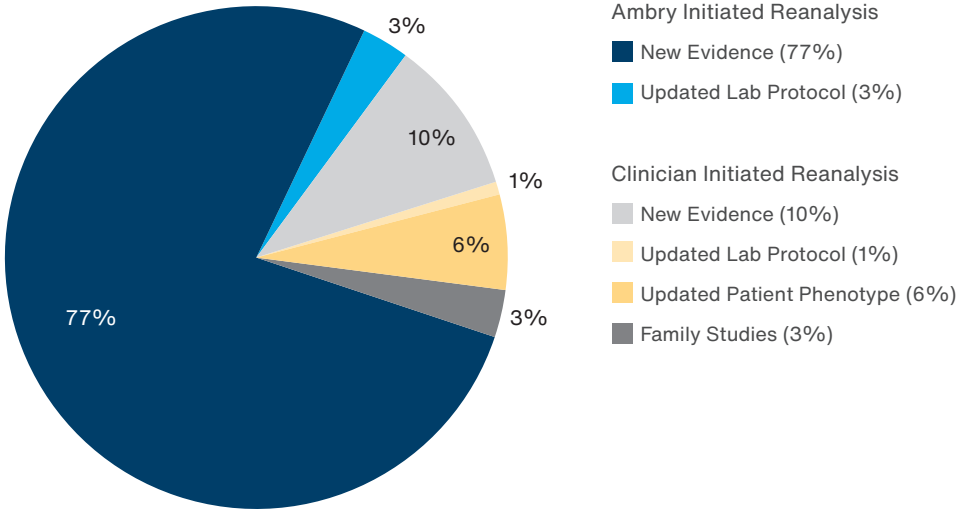
Ambry's Patient for Life program, a laboratory-driven approach, achieved a 54% diagnostic reclassification rate ($p < 0.0001$), compared to just 4% for clinician-initiated reanalysis (Figure 2). Most clinician-initiated requests did not lead to any reclassification. These findings highlight the advantages of a proactive, lab-led model in identifying and applying emerging gene-disease associations to improve patient outcomes.

Figure 2. Outcomes of Reanalysis



The majority of impactful "new evidence" identified by Ambry stemmed from newly established gene-disease relationships, underscoring the value of continuous literature curation and database updates (Figure 3). Collectively, these results support widespread adoption of proactive reanalysis to maximize the diagnostic utility of ES.

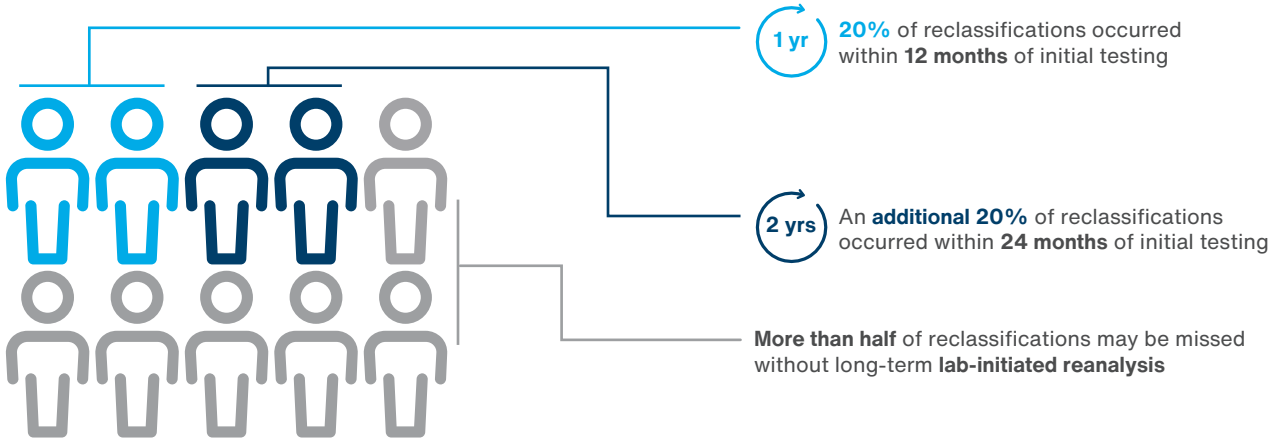
Figure 3. Factors Contributing to Reclassifications



OUTDATED REANALYSIS TIMELINES RISK MISSED DIAGNOSES

Many laboratories restrict reanalysis to a single request, typically performed two years after initial testing. The Patient for Life program removes these limitations by enabling continuous, proactive reanalysis. Our findings show that only 20% of reclassifications occurred within just one year, suggesting that limited opportunities for reanalysis may unnecessarily delay important diagnoses (Figure 4). In contrast, when reanalysis is limited to the two-year mark, more than half of potential reclassifications are missed.

Figure 4. Proportion of Reclassifications Completed Over Time



CONCLUSION

Our results show that proactive, laboratory-initiated reanalysis is a critical component of a comprehensive genomic diagnostics strategy. Ambry's Patient for Life approach maximizes patient benefit by continuously integrating emerging evidence and expanding opportunities for diagnosis—without relying on patient return visits or clinician requests.

Reference
Towne MC, Huang J, Saliganan S, et al. Impact of laboratory-driven proactive reanalysis: reclassification to positive in 5% of initially negative or uncertain exome sequencing cases. *Genet Med*. 2025;101464. doi:10.1016/j.gim.2025.101464.

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