Beyond Access: Why Patients Should Care About Laboratory Quality in Rare Disease Genomic Testing

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The aim of this study is to synthesize published evidence on how laboratory quality influences diagnostic accuracy, equity, and patient outcomes in rare disease exome and genome sequencing.

BACKGROUND

- Rare disease families, payors, and clinicians often view exome and genome sequencing (ES/GS) as a uniform, interchangeable service; however, laboratories vary significantly in the evidence and datasets they use to interpret variants.
- "Lab quality" includes the depth of the laboratory's rare disease knowledge base and its ability to maintain accurate, ancestry-aware classifications.
- Variation in these factors may influence whether a family receives a timely molecular diagnosis or remains on a prolonged diagnostic odyssey.
- Recognition of these quality signals empowers patients, families, and clinicians to advocate for the most rigorous and equitable testing available.

METHODS

- We conducted a rapid narrative review on July 7, 2026 searching PubMed (2015–2026) for studies involving ES/GS in rare or undiagnosed indications addressing laboratory-specific factors: interpretation rigor, classification variability, and reference dataset representativeness.
- Abstracts were screened and coded into pre-specified impact themes.

Figure 1. LABORATORY-SPECIFIC FACTORS INFLUENCE GENETIC TEST RESULTS

Same test. Different lab. Could that affect your results?

Laboratory A Limited rare disease experience, expertise, and support.	QUALITY FACTOR	Laboratory B Extensive rare disease experience, expertise, and support.
Limited rare disease experience Some labs do not specialize at all, while others focus on one or many disease areas such as cancer. As a result, they have limited experience testing families impacted by rare disease.	**RARE DISEASE EXPERIENCE** The extent of a laboratory's experience testing families with rare disease.	**Extensive rare disease experience** Other labs focus entirely on rare disease. These labs routinely evaluate complex cases and genetic changes, giving them more experience finding answers for families.
Less diverse population data Labs with limited experience may rely on public databases, which historically underrepresent much of the U.S. population. This limitation can lead to more uncertainty.	**DATASET DIVERSITY** How well the laboratory's data reflect people from different ancestries and backgrounds	**More diverse, representative data** Broader representation supports more accurate, confident, and equitable interpretation across patient populations.
Limited expertise and support Less access to rare disease experts may make complex results more difficult to interpret and act on.	**SPECIALIZED EXPERTS & SUPPORT** The rare disease expertise involved in interpreting results and supporting families and clinicians.	**Human experts, personalized support** Across rare disease areas, in-house experts help interpret complex findings and support families and clinicians in understanding what results may mean for care.

CLINICAL IMPLICATIONS Differences in laboratory experience, data, and expertise may impact the likelihood of receiving definitive answers that end the diagnostic odyssey.

Greater Diagnostic Uncertainty	IMPACT FOR ALL FAMILIES	Greater Diagnostic Clarity & Support
• Uncertain or inconclusive results • Prolonged diagnostic odyssey • Additional testing or re-evaluation • Lost opportunity for personalized care • Reactive care and higher costs • Limited post-test support		• More accurate, certain results • Greater potential to end the diagnostic journey • Avoidance of unnecessary tests • Clearer next steps and personalized care • Proactive, targeted care management • Post-test support for families

RESULTS

From 32,872 unique returns, we performed a detailed review of 18 key publications with evidence that mapped to three laboratory-driven themes.

1. **RIGOR IN INTERPRETATION AND ACCURACY OF CLINICAL RESULTS**
   Studies suggest that a laboratory's interpretive framework directly influences the accuracy and confidence of clinical results in rare disease ES/GS. Inconsistent rigor may contribute to uncertain or discordant findings, which can prolong the diagnostic odyssey, increase costs, and complicate downstream care.
2. **INTER-LABORATORY CLASSIFICATION VARIABILITY**
   Evidence documented clinically meaningful differences in how different laboratories classify the same variant. These discrepancies stem from varying evidence thresholds and access to internal data, which can directly influence clinical decision-making and medical management for a rare disease family.
3. **DATASET DIVERSITY AS A QUALITY PILLAR**
   Multiple sources identified that the representativeness of a laboratory's reference evidence is a direct driver of interpretability. Laboratories relying on limited or non-diverse rare disease datasets may have reduced diagnostic confidence for underrepresented populations, making dataset diversity a laboratory quality issue with important implications for diagnostic equity.

CONCLUSIONS

- Laboratory quality is an important but often overlooked factor that may affect diagnostic accuracy, uncertainty, and equity in rare disease genomic testing.
- As access to exome and genome sequencing expands, the next frontier is not only ensuring access to testing, but also ensuring access to high-quality testing.
- Patient, advocate, and provider education can empower families to better understand laboratory differences and make informed decisions about testing.
- Improving awareness and selection of high-quality testing may help reduce diagnostic delays, improve outcomes, and lower downstream healthcare costs, particularly in rare disease where small differences in interpretation can have meaningful consequences.

Figure 2. QUESTIONS FOR FAMILIES TO ASK

1. **Is rare disease the laboratory's primary area of expertise?**
   Some laboratories focus specifically on rare disease, while others test for many different types of conditions.
2. **How long has the laboratory performed rare disease genetic testing, and how many rare disease families has it tested?**
   The more rare disease experience a laboratory has, the more likely it is to have encountered similar conditions, genetic findings, and ancestral backgrounds that may help them find answers for your family.
3. **If my child's results are complex, does the laboratory have the right experts to interpret them?**
   Specialized expertise can help labs understand difficult genetic findings and what they may mean for your family.
4. **Will we have access to the laboratory's experts if we have questions before or after testing?**
   Some labs provide access to genetics experts before and after testing, while others may offer more limited support. For example, experts can help explain variants of unknown significance and appropriate next steps.