

2024 Global Rare Disease Diagnostics Report

Key Challenges

Emerging Opportunities

Expert Insights

3billion

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Introduction

The 2024 Global Rare Disease Diagnostics Report by 3billion offers a comprehensive overview of key insights from an in-depth survey of physicians, geneticists, and researchers specializing in genetic testing and rare disease diagnostics. Drawing responses from over 30 countries and prestigious institutions—including Johns Hopkins, Stellenbosch University, Semmelweis University, and King Saud University—the report explores the current challenges, emerging trends, and transformative opportunities shaping rare disease diagnosis and care on a global scale.

With advancements in next-generation sequencing (NGS), the growth of genetic databases, and innovations in diagnostic technology, the medical community is seeing a major shift in the approach to identifying and treating rare diseases. **This report captures the perspectives of experts leading the field, highlighting their insights on diagnostic challenges, the expanding role of genetic reanalysis, and the importance of interdisciplinary collaboration in improving patient outcomes.**

Whether you are a clinician, researcher, or industry professional, this report provides critical insights that will guide your understanding of the challenges and possibilities within rare disease diagnostics in 2024 and beyond.

Key Insights at a Glance

- 1 **Whole Exome Sequencing (WES)** is recognized as the leading genetic testing method for diagnosing rare diseases, with 70.8% of physicians reporting it as **the most commonly used technique in their countries**.
- 2 An equal 70.8% of physicians recommend **Whole Exome Sequencing (WES)** as their **first-choice genetic test for patients** showing symptoms of rare diseases.
- 3 **Neurodevelopmental disorders** are the most frequently encountered category of rare diseases, noted by 59.7% of surveyed physicians in their practice or research.
- 4 For physicians, **financial barriers** are a significant obstacle, with 77.8% of surveyed participants identifying it as the primary challenge to providing access to genetic testing.
- 5 For patients, **the high cost** of testing remains a critical issue, with 84.7% of physicians reporting it as a major barrier when diagnosing suspected rare diseases.

1

Current Landscape of Genetic Testing for Rare Diseases

Current Landscape of Genetic Testing for Rare Diseases

Genetic testing for rare diseases has made significant improvements in recent years, allowing for earlier and more accurate diagnoses. This section highlights the most commonly seen rare diseases according to surveyed physicians, offering a clear picture of the challenges faced across different fields of medicine.

The survey collected responses from participants regarding the rare diseases they most frequently encounter in their practice or research. The results revealed that **neurodevelopmental disorders** top the list, followed closely by other complex and difficult-to-diagnose conditions. The data highlights the critical need for continued advancements in genetic testing to address the diagnostic challenges presented by these disorders.

Top Rare Diseases Encountered by Physicians

The following table summarizes the top 5 rare disease categories most commonly reported by physicians:

Rare Disease Category	Percentage of Physicians Encountering Them
Neurodevelopmental Disorders	59.7%
Metabolic Disorders	50.5%
Neuromuscular Disorders	51.4%
Movement Disorders	37.5%
Retinal Disorders	20.8%

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Diagnostic Workflows for Rare Disease Patients

The diagnosis of rare diseases typically involves a multi-step process, integrating patient history, physical examinations, biochemical tests, and advanced genetic testing. Based on survey responses from physicians worldwide, we have identified several common stages in the diagnostic workflow. While the precise steps can vary depending on the physician's specialty and the patient's condition, the general process includes:

1. Initial Suspicion:

Physicians suspect a rare disease based on clinical symptoms, medical history, or alarm signs (e.g., unusual developmental delays, dysmorphology, or unexplained neurological symptoms).

2. History Taking and Physical Examination:

The next step is gathering detailed medical and family history, followed by a comprehensive physical and/or neurological examination. Some physicians also conduct biochemical tests early in this phase, depending on the suspected disorder.

3. Preliminary Diagnostic Testing:

Following history and physical examination, physicians often perform biochemical tests or other laboratory investigations to rule out more common conditions or provide initial clues for diagnosis. This stage may include neuroimaging (e.g., MRI, EEG) or metabolic screenings in certain cases.

4. Referral to a Geneticist:

If initial evaluations indicate a possible genetic condition, physicians can request genetic testing directly. However, if needed, a medical geneticist or specialized genetic service may be involved at this stage to support the diagnostic process. The geneticist can conduct a detailed assessment, including family pedigree analysis, to help clarify the genetic basis of the condition.

5. Genetic Testing:

Based on the geneticist's evaluation, genetic testing—such as Whole Exome Sequencing (WES) or other advanced molecular techniques—may be recommended to confirm the diagnosis and guide further treatment decisions.

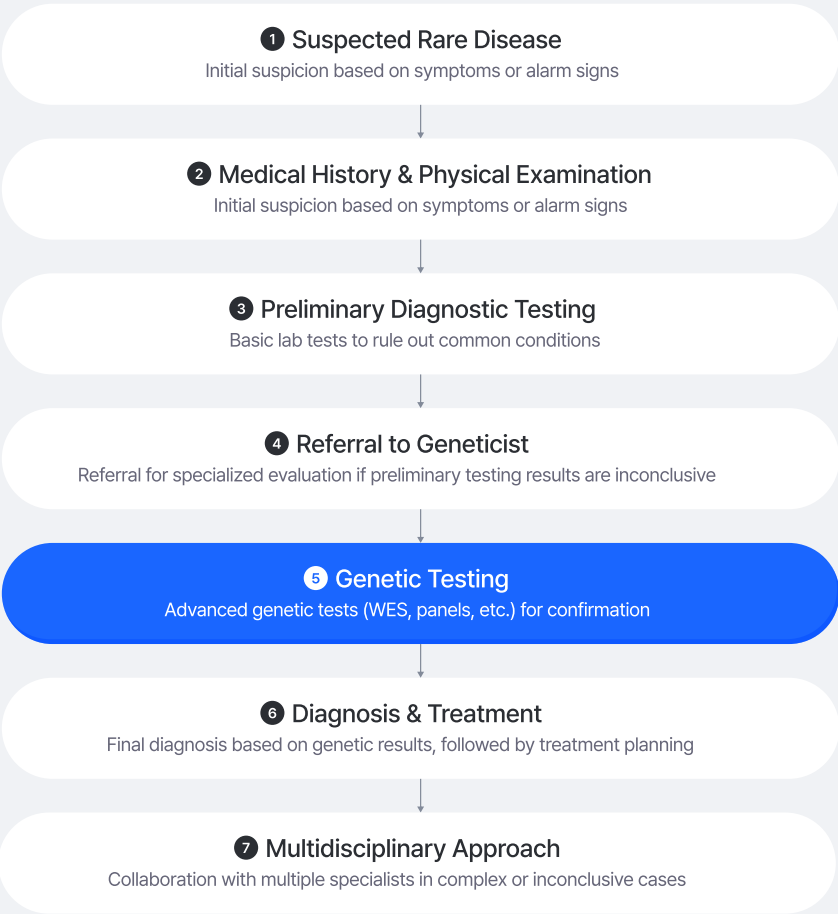
6. Diagnosis and Follow-up:

After receiving genetic results, a diagnosis is made if possible, and relevant medications or treatments are prescribed. Even if a precise treatment is not available, interventions may be initiated to manage or delay symptom progression. If a diagnosis cannot be made, further steps may include testing family members, conducting Whole Genome Sequencing (WGS), re-analyzing existing genomic data, or exploring participation in research studies.

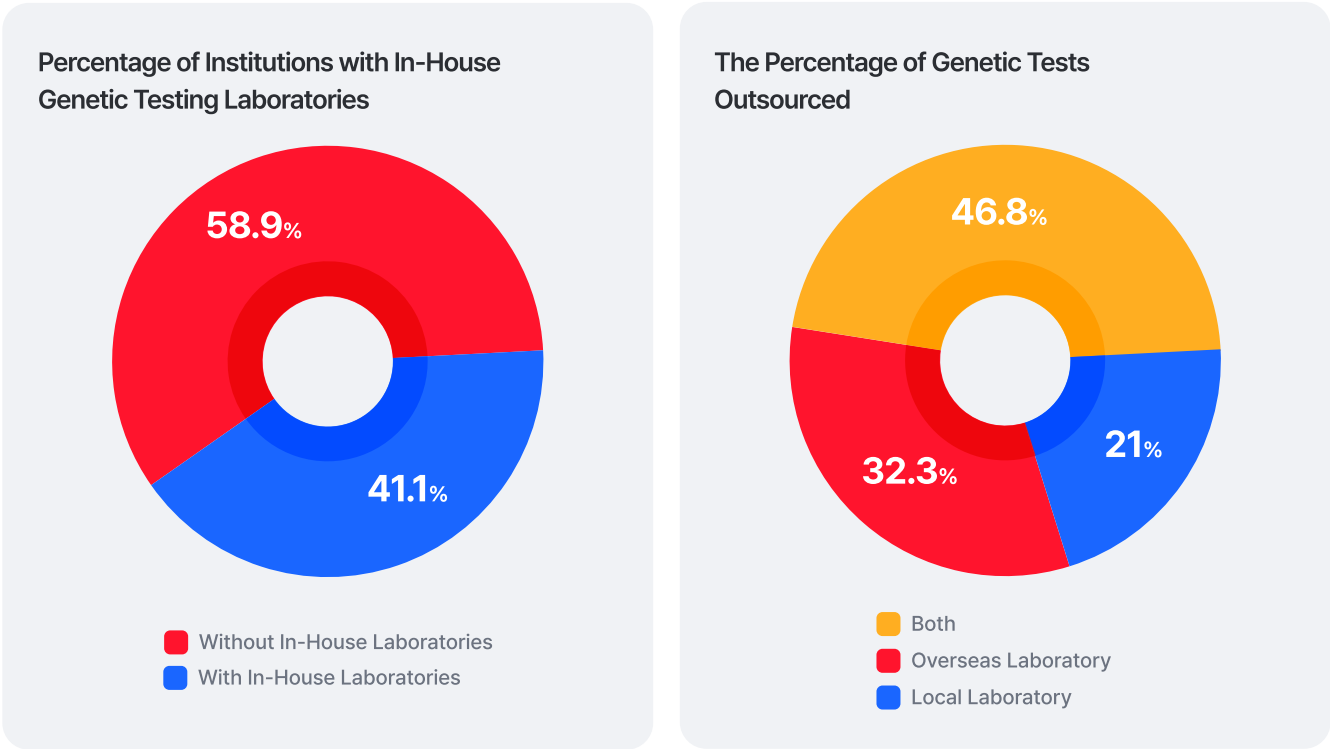
7. Multidisciplinary Involvement (if necessary):

In more complex cases, a multidisciplinary approach is required. Physicians may collaborate with experts from various fields (e.g., neurology, metabolic specialists, geneticists) to discuss the patient's condition and tailor the diagnostic and treatment pathway.

Summary of Diagnostic Workflow (Common Steps)

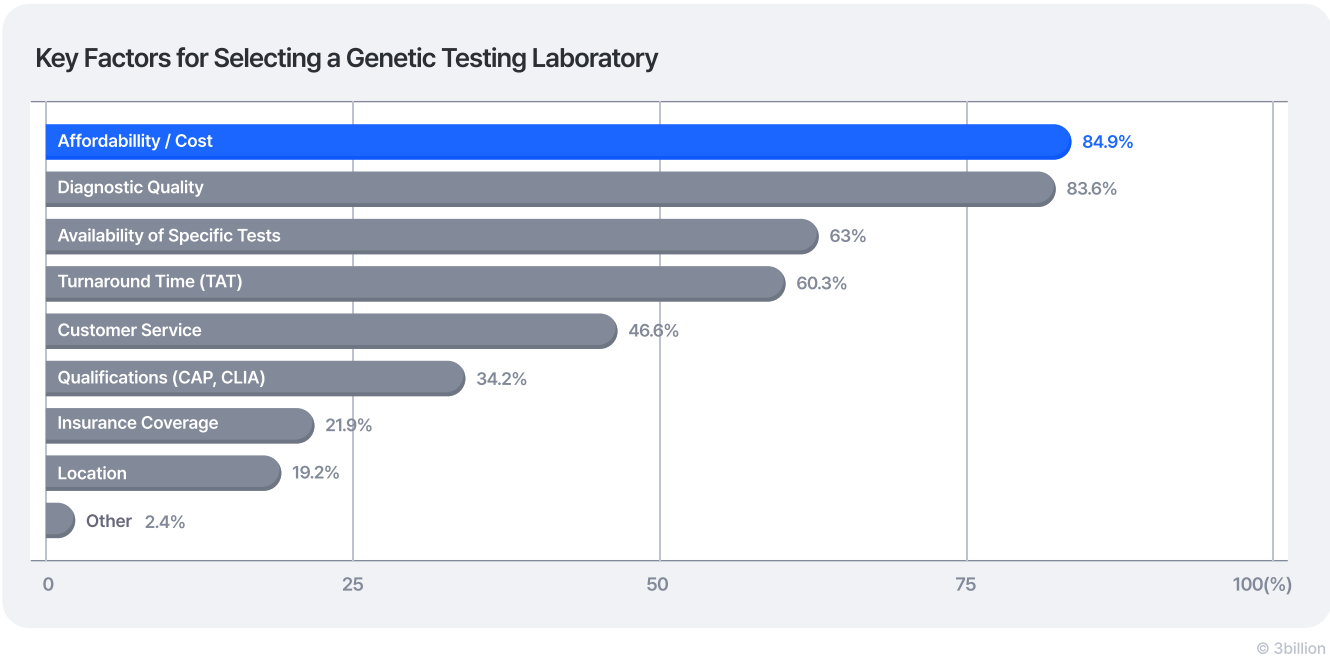


■ Infrastructure and Resources for Genetic Testing



According to our survey, 58.9% of respondents do not have access to an in-house laboratory for genetic testing, while 41.1% do. This reflects the significant reliance on external laboratories to conduct genetic tests for rare diseases. Among those without in-house facilities, a majority (46.8%) reported that they send samples to both local and overseas laboratories, suggesting that institutions often need to partner with multiple facilities to fulfill testing needs. Additionally, 32.3% of respondents send their samples exclusively to overseas laboratories, while 21% rely solely on local laboratories.

This outsourcing highlights potential gaps in regional infrastructure for advanced genetic testing, particularly in countries where local resources may be limited. The reliance on overseas laboratories may also indicate a need for specialized testing services that are unavailable locally or a preference for established international expertise.



When it comes to selecting a laboratory for genetic testing, several factors weigh heavily on decision-makers. According to our survey, the top priority for respondents was **Affordability / Cost**, with 84.9% identifying this as a critical consideration. This reflects the financial burden that genetic testing can pose, especially for rare disease patients, and emphasizes the importance of finding cost-effective solutions.

Following closely, **Diagnostic Quality** was ranked as the second most important factor by 83.6% of respondents. This demonstrates that while cost is a significant concern, ensuring accurate and reliable diagnostic outcomes remains essential. For many healthcare providers, selecting a laboratory with recognized diagnostic qualifications, such as CAP and CLIA certifications, is crucial to delivering effective patient care.

The **Availability of Specific Tests** ranked third, with 63% of respondents citing it as a key criterion. As rare diseases often require highly specialized and sometimes obscure genetic tests, the ability of a laboratory to provide the right test can make a significant difference in diagnosis and treatment options.

Turnaround Time (TAT) was also a notable consideration for 60.3% of respondents. Quick results are often necessary, especially in time-sensitive cases where a delayed diagnosis can impact patient care. Laboratories that offer expedited testing processes can therefore be a vital resource for practitioners.

Lastly, **Customer Service** was identified by 46.6% of respondents as an important factor. This underscores the role of effective communication and support when navigating the complexities of genetic testing, from ordering tests to interpreting results.

■ Insurance Coverage for Genetic Testing

Despite the importance of genetic testing in diagnosing and managing rare diseases, the survey revealed significant gaps in insurance coverage, with many patients unable to fully access or afford these essential services.

- 21.9% of respondents reported that insurance partially covers gene panels, though many rare disease patients are excluded from this coverage. This partial coverage often leaves families with considerable out-of-pocket expenses.
- 15.1% indicated that insurance only covers microarray, MLPA, or single-gene testing, which is often insufficient for patients who present with a wide range of symptoms requiring broader testing methods like Whole Exome Sequencing (WES) or Whole Genome Sequencing (WGS).
- A similar 12.3% echoed this sentiment, citing that microarray and single-gene testing are inadequate for patients with complex or undiagnosed conditions.
- Only 9.6% of respondents reported that insurance fully covers Whole Exome Sequencing (WES), benefiting rare disease patients who require comprehensive genetic analysis. This small percentage highlights the need for more inclusive insurance policies to ensure broader access to advanced testing methods.

The survey data points to critical factors that influence the selection of genetic testing laboratories, with affordability, diagnostic quality, and test availability emerging as top considerations. However, the lack of comprehensive insurance coverage for many rare disease patients remains a significant barrier. More inclusive insurance policies and greater access to a wider range of genetic tests are necessary to support rare disease diagnosis and treatment, ensuring that all patients receive the care they need.

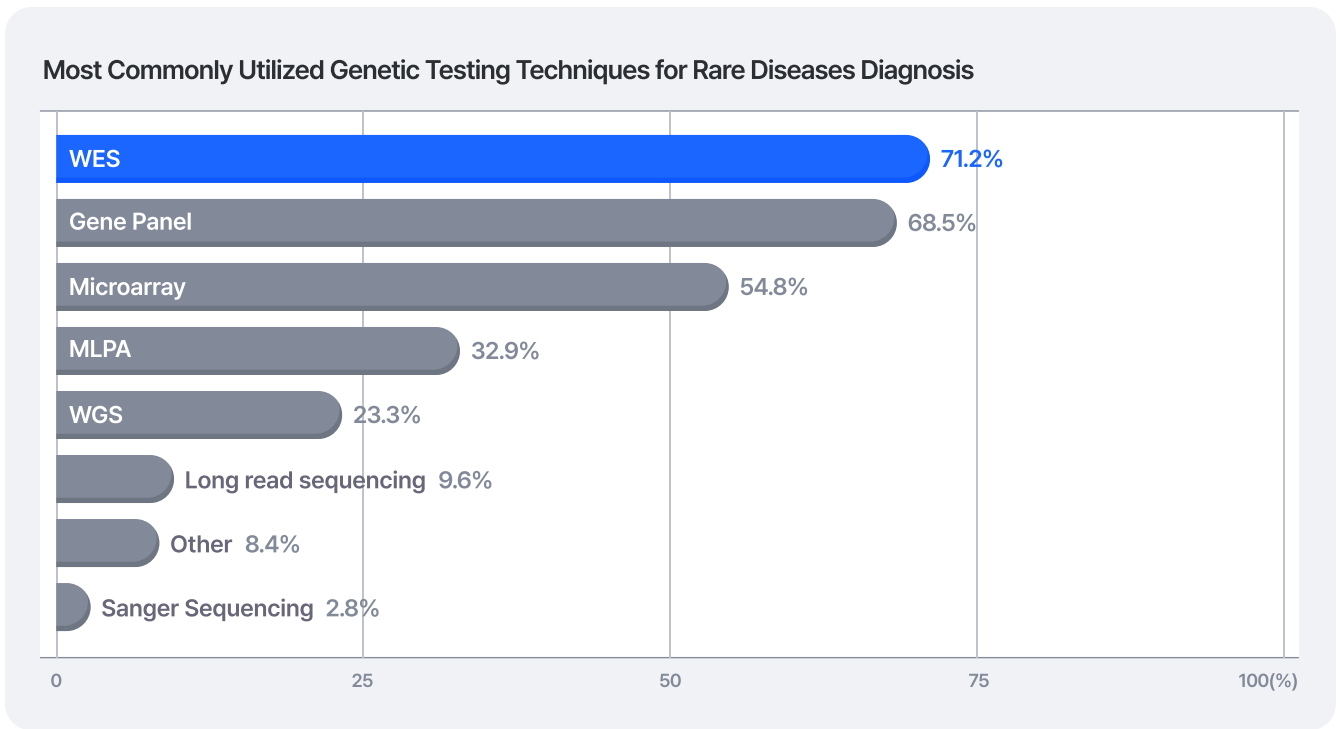
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Trends in Genetic Testing for Rare Diseases



Trends in Genetic Testing for Rare Diseases

Most Commonly Utilized Genetic Testing Techniques for Rare Diseases



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As the field of genetic testing evolves, several key technologies have become widely adopted for diagnosing rare diseases. In our survey, respondents identified **Whole Exome Sequencing (WES)** as the most commonly utilized technique, with **71.2%** indicating it as their preferred method. WES has gained prominence due to its ability to provide comprehensive analysis by sequencing the protein-coding regions of genes, where most known disease-causing mutations are found.

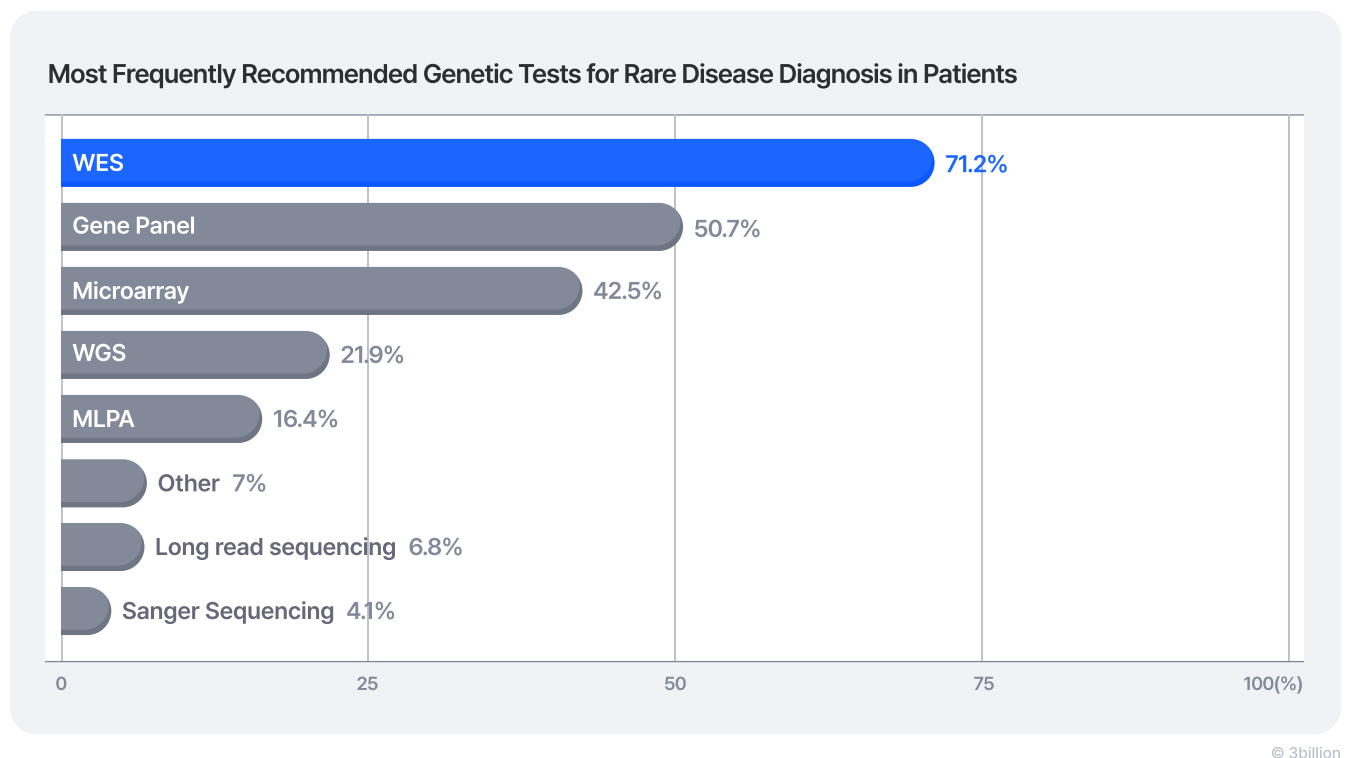
Gene Panel Testing, which targets a specific set of genes related to particular conditions, was the second most commonly used technology, cited by **68.5%** of respondents. Gene panels offer a focused approach, making them an effective and more cost-efficient option for conditions where a particular set of genes is known to be involved.

Chromosomal Microarray Analysis (CMA), a technique that detects chromosomal abnormalities such as copy number variations, ranked third, with **54.8%** of respondents using it. While CMA is not as comprehensive as sequencing, it remains a critical tool for detecting structural changes in the genome.

Multiplex Ligation-dependent Probe Amplification (MLPA) was also commonly used by **32.9%** of respondents. This technique is useful for detecting deletions or duplications of specific genomic regions, especially in cases where more common methods might not provide sufficient resolution.

Finally, **Whole Genome Sequencing (WGS)**, which sequences the entire genome rather than just exons, was utilized by **23.3%** of respondents. While WGS offers the most comprehensive genetic analysis available, its lower usage may be due to its higher cost compared to other methods.

Most Frequently Recommended Genetic Tests for Rare Disease Diagnosis



When asked which types of genetic tests they most frequently recommend to their patients for rare disease diagnosis, healthcare professionals demonstrated a similar preference for **WES**, with **71.2%** selecting it as their top recommendation. The popularity of WES highlights its diagnostic power, offering clinicians a broad view of a patient's genetic makeup.

Gene Panel Testing was recommended by **50.7%** of respondents. It remains a popular choice when clinicians have a clearer understanding of the specific genetic mutations to target, as it provides actionable insights while being more affordable than broader tests like WES or WGS.

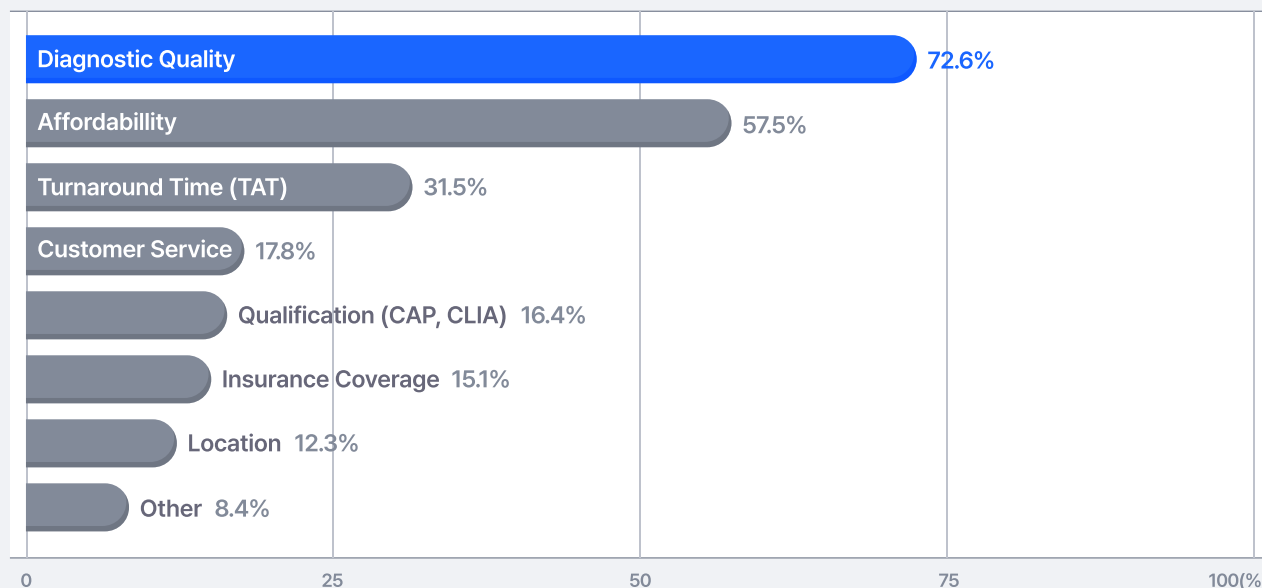
Microarray testing was the third most frequently recommended test, chosen by **42.5%** of respondents. It continues to play a crucial role in diagnosing structural variants and chromosomal abnormalities, especially in patients with developmental disorders or intellectual disabilities.

Whole Genome Sequencing (WGS) was recommended by **21.9%** of respondents. While its adoption is slower compared to WES, its comprehensive nature makes it ideal for cases where other genetic testing methods fail to yield a conclusive diagnosis.

Lastly, **MLPA** was recommended by **16.4%** of respondents, typically in cases where specific copy number variants are suspected, such as in Duchenne muscular dystrophy or certain types of cancer.

■ Key Factors Behind Test Recommendations

Reasons for Recommending Specific Genetic Tests for Rare Disease Diagnosis



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Healthcare professionals provided several reasons for their choice of genetic tests, with **Diagnostic Quality** emerging as the most important factor, cited by **72.6%** of respondents. This underscores the critical importance of accurate and reliable results in the diagnosis of rare diseases, where timely and precise information can lead to better treatment outcomes.

Affordability was the second most common reason for recommending specific tests, mentioned by **57.5%** of respondents. Given the high costs associated with some genetic tests, it is clear that cost considerations play a significant role in the decision-making process, especially in regions where insurance coverage is limited or non-existent.

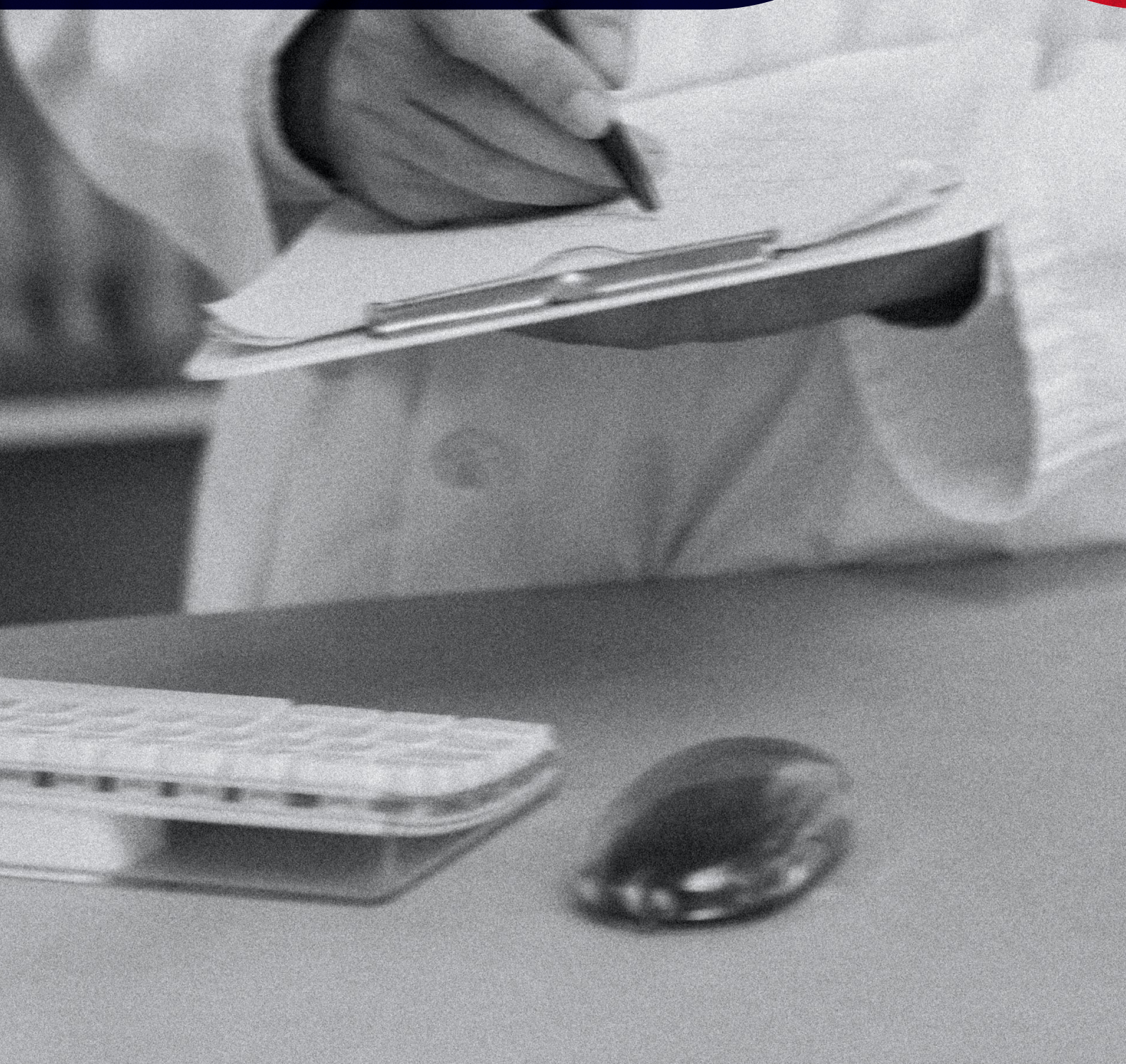
Turnaround Time (TAT) was highlighted by **31.5%** of respondents as a key factor in test selection. Faster results allow clinicians to make timely decisions regarding patient care, which is particularly important for patients with rapidly progressing conditions.

Customer Service, cited by **17.8%**, and **Laboratory Qualifications** such as CAP or CLIA certifications (16.4%) were also considerations. This reflects the need for healthcare providers to work with laboratories that offer not only high-quality testing but also a seamless experience and assurance of technical accuracy.

Insurance Coverage, mentioned by **15.1%** of respondents, was another factor influencing test recommendations. Limited insurance support for comprehensive genetic testing remains a barrier for many patients, which may impact a clinician's ability to recommend the most advanced diagnostic options, even when they are deemed necessary.

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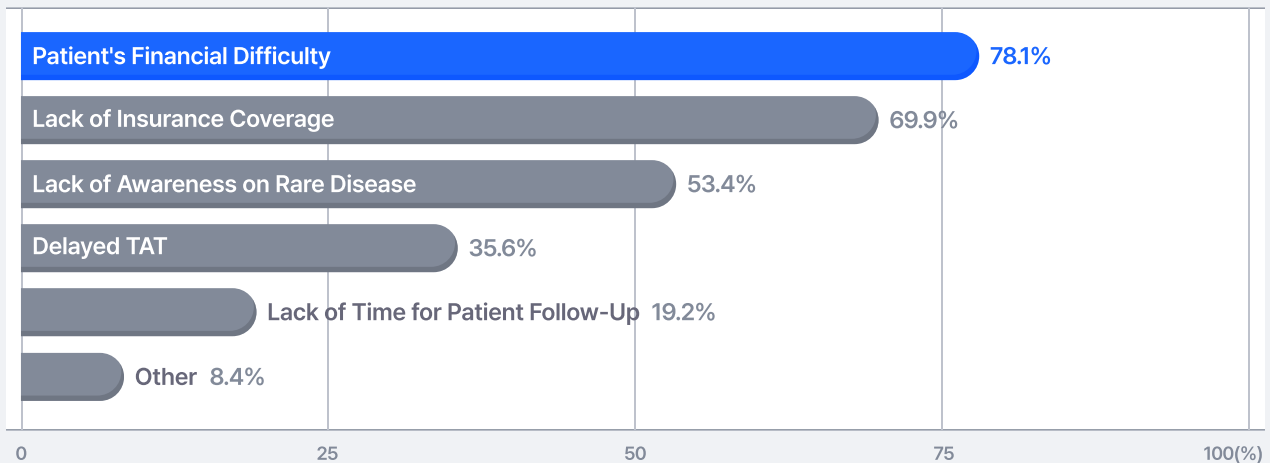
Top Challenges in Rare Disease Diagnosis



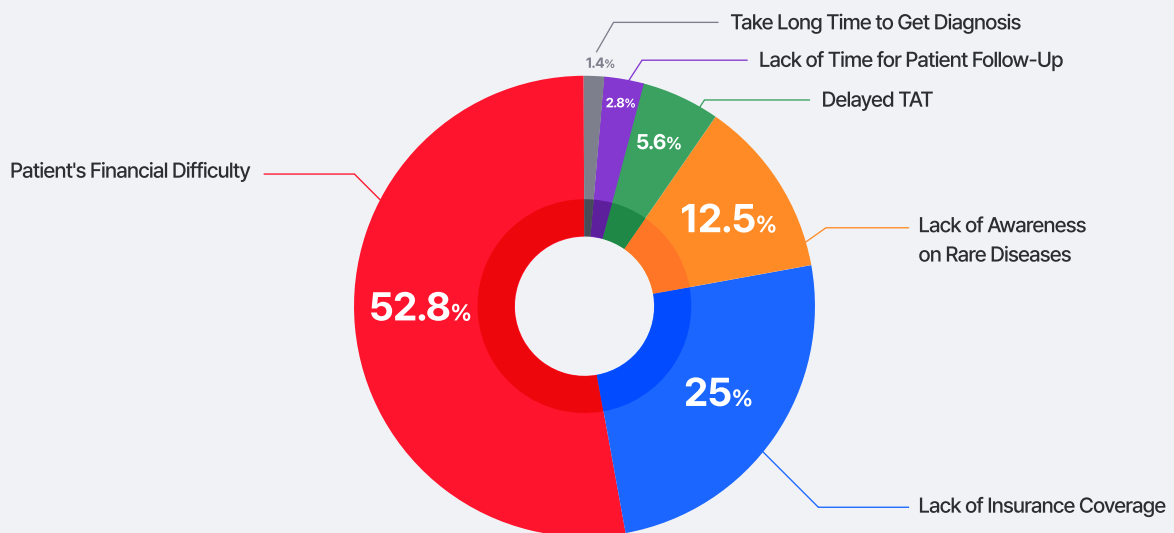
Top Challenges in Rare Disease Diagnosis

Diagnosing rare diseases comes with a unique set of challenges, from financial barriers to limitations in infrastructure and support. This section highlights the key difficulties faced by both healthcare providers and patients, along with potential solutions to improve the diagnostic journey.

Challenges Faced by Physicians in Diagnosing Rare Disease Patients



Top-Ranked Challenge in Diagnosing Rare Disease Patients



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1. Patient's Financial Difficulty

The survey revealed that **78.1%** of respondents identified **patients' financial difficulty** as a major challenge, with **52.8%** marking it as the primary challenge in rare disease diagnosis. The cost of genetic testing, often necessary for diagnosing rare diseases, is prohibitively high, particularly for uninsured or underinsured patients. Limited financial resources can delay diagnosis and treatment, ultimately impacting patient outcomes.

2. Lack of Insurance Coverage

With **69.9%** of respondents highlighting **lack of insurance coverage** as a significant challenge, it's clear that coverage gaps prevent patients from accessing needed genetic tests. Insurance plans often exclude comprehensive genetic testing, such as Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS), or only partially cover certain tests. Lack of coverage places a financial burden on patients and limits the diagnostic options available to healthcare providers.

3. Limited Awareness of Rare Diseases

Over **53.4%** of survey respondents noted **lack of awareness of rare diseases** as a challenge, underscoring the need for broader education among healthcare professionals, patients, and the general public. Patients may face delayed diagnosis or misdiagnosis if primary care providers are not sufficiently aware of rare diseases or the appropriate steps to take for early detection.

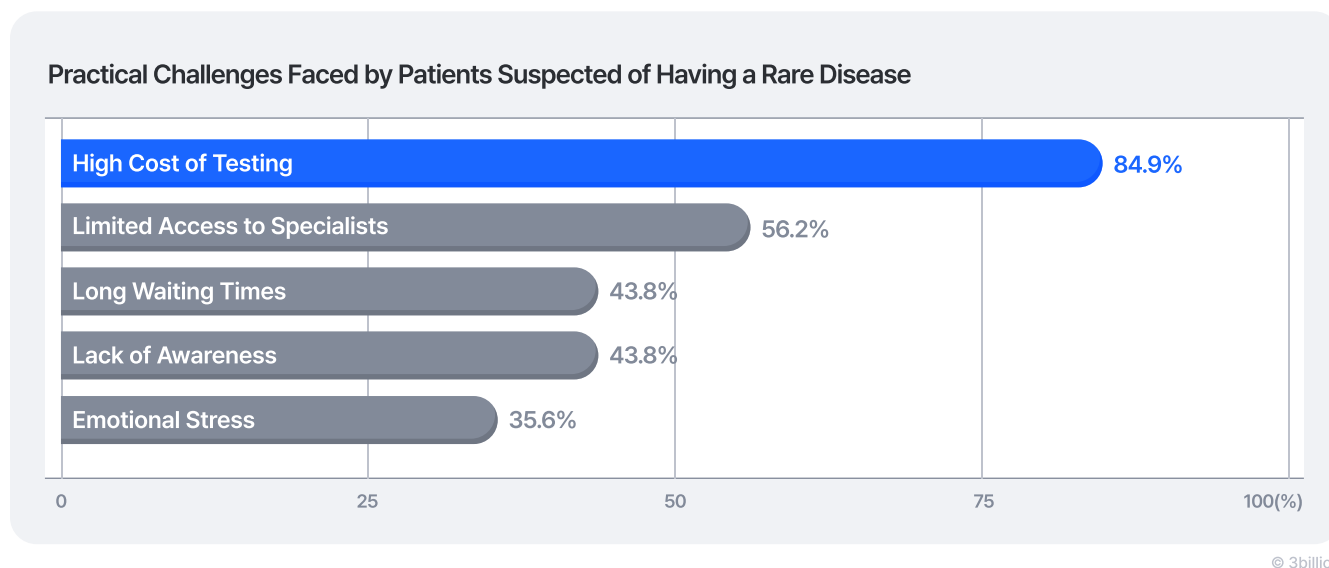
4. Delayed Turnaround Time (TAT)

Delayed TAT was reported by **35.6%** of respondents as a barrier, affecting the timely diagnosis of rare diseases. Genetic testing often requires specialized laboratories, which can result in long waiting times, especially in cases where samples are sent overseas. Faster TAT is critical, as early diagnosis allows for better disease management and care planning.

5. Lack of Time for Patient Follow-Up

Approximately **19.2%** of respondents pointed to **lack of time for following up with patients** as a challenge. Proper follow-up is crucial for managing rare disease patients, especially as new information or treatment options become available. However, limited time and resources make it challenging for providers to stay in close contact with their patients after testing.

■ Practical Challenges Faced by Patients

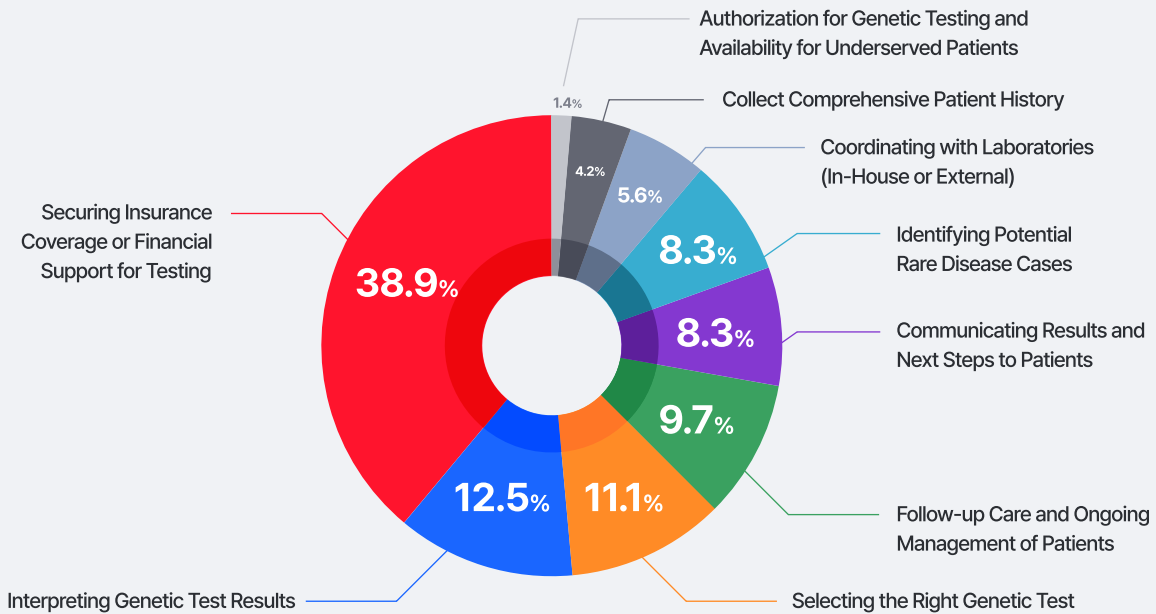


Aside from the high costs of testing, patients with suspected rare diseases face practical challenges such as **limited access to specialists** (56.2%) and **long waiting times** (43.8%), which delay timely, accurate diagnoses. The emotional toll of navigating an uncertain diagnosis, compounded by **lack of awareness** (43.8%) about rare diseases among the public and even some healthcare providers, also adds to the patient burden. Emotional stress was reported as a difficulty by 35.6% of respondents, highlighting the importance of support systems in the diagnostic journey.

Diagnostic Process Challenges for Providers

Physicians encounter several challenges throughout the rare disease diagnostic process:

Most Challenging Steps in the Rare Disease Diagnostic Process



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- **Securing Insurance Coverage or Financial Support for Testing (38.9%):** Financial constraints are a major obstacle, as securing financial support is often the most challenging part of the diagnostic process.
- **Interpreting Genetic Test Results (12.5%):** Genetic test interpretation is complex, and providers may require specialized expertise to analyze the results accurately.
- **Selecting the Right Genetic Test (11.1%):** Choosing the most appropriate genetic test for a patient requires extensive knowledge, especially given the wide variety of available tests.
- **Follow-up Care and Management (9.7%):** Providing continuous care and management for rare disease patients is a challenge due to time constraints and the complexity of these cases.
- **Communicating Results and Next Steps (8.3%):** Clear communication of complex genetic information to patients is essential yet difficult, as many patients may struggle to understand their results and the associated implications.
- **Identifying Rare Disease Cases (8.3%):** Early identification of rare diseases is challenging due to the symptoms' often ambiguous nature, which can overlap with more common conditions.

Conclusion

The findings from our survey provide a comprehensive look at the challenges, trends, and evolving needs in rare disease genetic testing. Despite significant advancements, the diagnostic journey for rare disease patients remains fraught with barriers—chiefly financial hardship, limited insurance support, and restricted access to essential testing and specialist care. While Whole Exome Sequencing (WES) and gene panels are the most widely recommended tests, diagnostic accessibility is heavily influenced by affordability and the availability of targeted insurance coverage.

Healthcare providers and patients alike highlight the high costs of testing and limited insurance coverage as the primary barriers, with diagnostic quality, turnaround time, and the need for specific tests ranking among the top considerations when selecting a lab. These insights underline the urgent need for enhanced financial assistance, expanded insurance policies, and improved laboratory infrastructure to alleviate bottlenecks and make critical diagnostic tools more accessible.

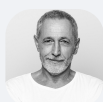
To address these complex issues, a multi-stakeholder approach is essential. Governments, insurance providers, healthcare organizations, and advocacy groups must collaborate to develop targeted programs, financial support systems, and patient education initiatives. Additionally, investment in in-house lab infrastructure and digital solutions like telemedicine can help mitigate delays, expand access to specialized care, and provide consistent follow-up support for patients on their diagnostic journey.

As we continue to navigate these challenges, this report serves as both a roadmap and a call to action. By identifying key areas for improvement and supporting targeted interventions, we can make meaningful strides toward a more inclusive and responsive healthcare system for rare disease patients worldwide.

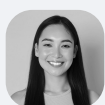
Messages of Encouragement from the Community

To foster a supportive global community, we invited healthcare professionals to share messages of encouragement for their peers who are dedicated to diagnosing and treating rare diseases. These words reflect a shared mission, resilience, and dedication to improving patients' lives. Here are some of the most inspiring messages.

“



“To all healthcare professionals dedicated to rare disease care, your work is changing lives and shaping the future of medicine. Every diagnosis and moment of care brings hope and a brighter tomorrow. Keep pushing forward!”



“It takes a mission-driven spirit to treat rare diseases. Your resilience, dedication, and compassion make a profound difference.”



“Every patient you guide, every diagnosis you reach, paves the way to hope and healing for patients and families worldwide.”



“Don't lose heart. Every challenge in rare disease care is an opportunity for growth. Keep pushing forward, knowing that your efforts are making a real impact.”



“To all in the rare disease field, remember that every test, every diagnosis, every effort is a step toward a healthier future for our patients. Together, we are making the impossible possible.”



“Awareness of rare diseases is essential. Let's continue our work, always remembering that every effort we make can change lives.”



“Keep calm and keep searching. Your commitment is the lifeline for families navigating these complex conditions.”



“Rare diseases may be complex, but remember: each patient you help holds a better future because of your dedication.”

”

A Note of Thanks

These messages are a powerful testament to the resilience, compassion, and dedication that define the rare disease community. We extend our heartfelt gratitude to all contributors for sharing their words of encouragement and for their unwavering commitment to patient care. Your insights, perseverance, and unity are inspiring, and they remind us that each step forward is taken together.

About Us

Who Are We

3billion entered the genetic testing market in 2016 to provide genetic testing for rare diseases that includes unlimited reanalysis which takes into account newly discovered diseases until diagnosis. We are committed to supporting patients and their families on their journey toward diagnosis and treatment. Our vision is a world where rare disease patients receive the attention and care they deserve.

What We Do

3billion is focused on diagnosing rare genetic diseases through NGS-based genetic testing. Our Whole Exome Sequencing(WES) and Whole Genome Sequencing(WGS) tests cover over 20,000 genes, offering a comprehensive diagnostic tool in a single test. Our life-long reanalysis technology supports undiagnosed patients until they receive a diagnosis, reanalyzing sequencing data daily with updated information at no additional cost. By integrating genetic and clinical data, our automated technology and expert medical team adhere to ACMG guidelines, ensuring that each patient receives the most accurate diagnosis for their care.

Our Mission

Many rare diseases are chronic and life-threatening, yet they suffer from limited research, medical knowledge, and public awareness. Individuals living with these conditions often struggle to obtain a clear diagnosis and access to treatment. We are dedicated to helping these patients and their families by starting with comprehensive genetic testing and diagnosis.

Stay In Touch

If you have any questions or inquiries about our services, please feel free to reach out at support@3billion.io.

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