

Shortening the Diagnostic Odyssey: The Impact of Genome Sequencing

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Why Genome Sequencing?

- Genome sequencing (GS) includes a comprehensive analysis across the genome which allows for the detection of diverse variant types within a single test, such as single nucleotide variants, copy number variants, short tandem repeat expansions, deep intronic and noncoding variants, and mitochondrial genome variants.
 - Due to this broad coverage, GS has a higher diagnostic yield compared to traditional genetic testing approaches such as chromosomal microarray and targeted gene panels.¹⁻³
- Benefits of establishing genetic diagnoses for individuals with rare disorders include informing treatment and medical management, future health risks and comorbidities, and genetic counseling, which can further impact patient outcomes and reduce long term healthcare costs.^{1,3}
 - In the past several years, multiple professional societies have developed genetic testing guidelines which recommend GS as a first-tier test for a variety of clinical indications.¹⁻³

Comparison of Variant Detection Capabilities Across Genetic Testing Technologies

	TARGETED GENE PANELS	CHROMOSOMAL MICROARRAY	EXOME SEQUENCING	GENOME SEQUENCING
Single Nucleotide Variants + Insertions and Deletions	Capable		Capable	Capable
Copy Number Variants	Limited	Capable	Limited	Capable
Short Tandem Repeat Expansions				Capable
Noncoding Variants				Capable
Mitochondrial Genome Variants	Capable			Capable
Structural Variants		Limited	Limited	Limited

Recommendations for GS as First-Tier Testing for Different Clinical Indications

PROFESSIONAL GUIDELINE	GENOME SEQUENCING RECOMMENDATION	PREVALENCE OF INDICATION
American College of Medical Genetics and Genomics (2021) ¹	First-tier test for children with congenital anomalies, developmental delay (DD), or intellectual disability (ID)	Major Congenital Anomaly: 2.4% ¹ DD/ID: 1-3% ²
National Society of Genetic Counselors (2022) ³ <i>Endorsed by the American Epilepsy Society</i>	First-tier test for all individuals with unexplained epilepsy, regardless of age	0.64% ³
American Academy of Pediatrics (2025) ²	First-tier test for children with intellectual disability or global developmental delay	1-3% ²

