



# One test. Endless insights.

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Whole-genome sequencing puts  
thousands of rare diseases in plain sight

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# What are you missing with current tests?

Traditional methods for genetic analysis are limited in the type of variants they detect and the amount of genome coverage they provide, reducing their potential utility.



## Single-gene tests

Provide data for only one gene, which may or may not be informative for diagnosis



## Multigene panels

Focus on a minimal selection of genes with known clinical relevance and do not allow for examination of new and emerging targets



## Chromosomal microarrays (CMA)

Analyze < 0.01% of the genome, missing opportunities to find underlying genetic causes for disease<sup>6</sup>



## Whole-exome sequencing (WES)

Sequences the protein coding regions of genes that account for around 2% of the genome leaving 98% unexplored

Iterative testing places additional burdens on an already stressed health care system, requires multiple patient samples, adds complexity to test ordering, and increases the cost and time to answer.

Whole-genome sequencing (WGS) provides the most comprehensive analysis of genomic variants among all clinical genomic testing methods<sup>7-9</sup>

It is clear WGS is contributing significantly to end diagnostic odysseys in rare disease. With guidelines advocating use as a first-tier test,<sup>10</sup> inclusion in national health care systems,<sup>11</sup> and increasing evidence of economic value when used as a first-tier test,<sup>12</sup> genome sequencing appears to be on the path toward standard of care.

	Sanger*	Targeted NGS*	PCR*	CMA*	WES*	WGS*
Single-Nucleotide Variants (SNVs)	✓	✓	✓		✓	✓
Insertions & Deletions (Indels)	✓	✓	✓	✓	✓	✓
Copy Number Variants (CNVs)		✓	✓	✓	✓	✓
Repeat Expansions			✓			✓
Structural Variants (SVs)				✓	✓	✓
Mitochondrial	✓	✓			✓	✓
Paralogs	✓		✓			✓

✓ Limited capabilities

✓ Capable

\*Variant detection may vary depending on laboratory and test offering  
NGS = next-generation sequencing, PCR = polymerase chain reaction



TAGCTACTGT CTAGCTTAAC GATCTCTACT TAGCTACT TGCTTAG CTAGCTA CTTAGCTACTT GTCTTAACTG ATCTTACT ATCTTACT  
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# your diagnostic potential

“In situations where there is not the luxury of waiting, I see it as a moral imperative and an obligation for us to do everything possible in these cases to get to an answer as quickly as possible.”

Luca Brunelli, MD, PhD  
Neonatologist  
University of Utah Health

WGS provides the broadest coverage of the human genome and includes regions NOT targeted by other methods.<sup>13,14</sup> In a large randomized-controlled trial, WGS demonstrated the greatest success in finding a diagnosis in rare disease.<sup>15</sup>

## Advantages of WGS:

-  Get to a diagnosis faster, with lower costs<sup>16,17</sup>
-  Find actionable answers, even when a negative result is returned<sup>18</sup>
-  Enable more personalized care management than other genomic tests<sup>15</sup>
-  Obtain a comprehensive view across the genome, including coding and noncoding regions<sup>16</sup>
-  Detect a diverse range of variants in a single assay<sup>16,19-26</sup>

In addition, WGS data can be stored and reanalyzed as new gene-disease associations are discovered.

Of all genomic testing methods, whole-genome sequencing has the potential to offer the highest likelihood of finding a diagnosis.<sup>27</sup>



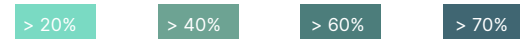




# Increased actionability

## WGS has been shown to impact clinical management

Study	Impact of clinical management driven by genetic diseases diagnosed by WGS	% Change in management
Dimmock (2021) <sup>12</sup>	Change in surgical procedures, medication, diet, and length of hospital course	61%
Lee (2021) <sup>33</sup>	Immediate changes in treatment strategies after undergoing WGS	23%
Krantz (2021) <sup>15</sup>	Clinical management modification, including change of treatment and care	75%
Wang (2021) <sup>34</sup>	Therapeutic strategy change including transplant, diet, medication change, etc	48%
Sandford (2019) <sup>35</sup>	Genome-informed changes in pharmacotherapy and transition to palliative care	76%
French (2019) <sup>17</sup>	Modification of treatments and care pathways and/or informing palliative care decisions	70%
Scocchia (2019) <sup>36</sup>	Clinical management modification including referrals to specialists, avoidance of invasive muscle biopsies, additional clinical investigations, genetic counseling, and palliative care	49%
Mestek-Boukhibar (2018) <sup>37</sup>	Enabled counseling on prognosis, avoidance of unnecessary investigations, and informed recurrence risk	30%
Petrikina (2018) <sup>29</sup>	Enable consideration of acute precision intervention in time for critically ill patients	95%
Farnaes (2018) <sup>19</sup>	Avoidance of invasive test and/or transplant, reducing patient costs by \$800,000-\$2,000,000	72%
Bick (2017) <sup>3</sup>	Supported treatment decisions and/or medical surveillance	75%
van Diemen (2018) <sup>38</sup>	Withdrawal of intensive care treatment	71%
Stravopoulos (2016) <sup>39</sup>	Increased diagnostic yield of WGS can have a significant impact on clinical care and management that goes beyond genetic counseling	79%

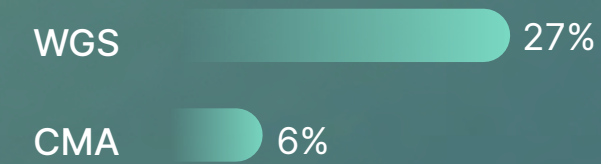


# A diagnosis can be life-changing

When WGS is implemented early in the diagnostic pathway, it has the potential to offer life-changing options to patients and their families. Identifying a disease-associated variant can lead to a diagnosis that can inform care management or future family planning.

## Difference in change of management rates with WGS vs CMA<sup>27</sup>

Rate from patients with change of management is higher with WGS than with CMA\*



## Changes to care may include:

- Pharmacotherapy
- Referral to specialists
- Avoidance of unnecessary procedures or treatments
- Access to precision medicine-based approaches
- Informed reproductive risk counseling for parents and other family members

\*95% CI: 0.17-0.40 P<0.0001







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