
One test.
Endless insights.
Whole-genome sequencing puts thousands of rare diseases in plain sight
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Neonatologist
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Shorten the diagnostic

There are many ways to investigate the genetic cause of disease, yielding varying results. The current standard of care is far from optimal and can:

- Involve multiple tests
- Include average of or up to 8 physicians[1,2]
- Take 5-7 years[1,2]
- Result in 2-3 misdiagnoses[1]

During this time, patients and their families may experience a long, expensive, emotional diagnostic odyssey.

up to

80%

of rare disease are genetic or have a genetic subtype[1,3-5]

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[6]

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.

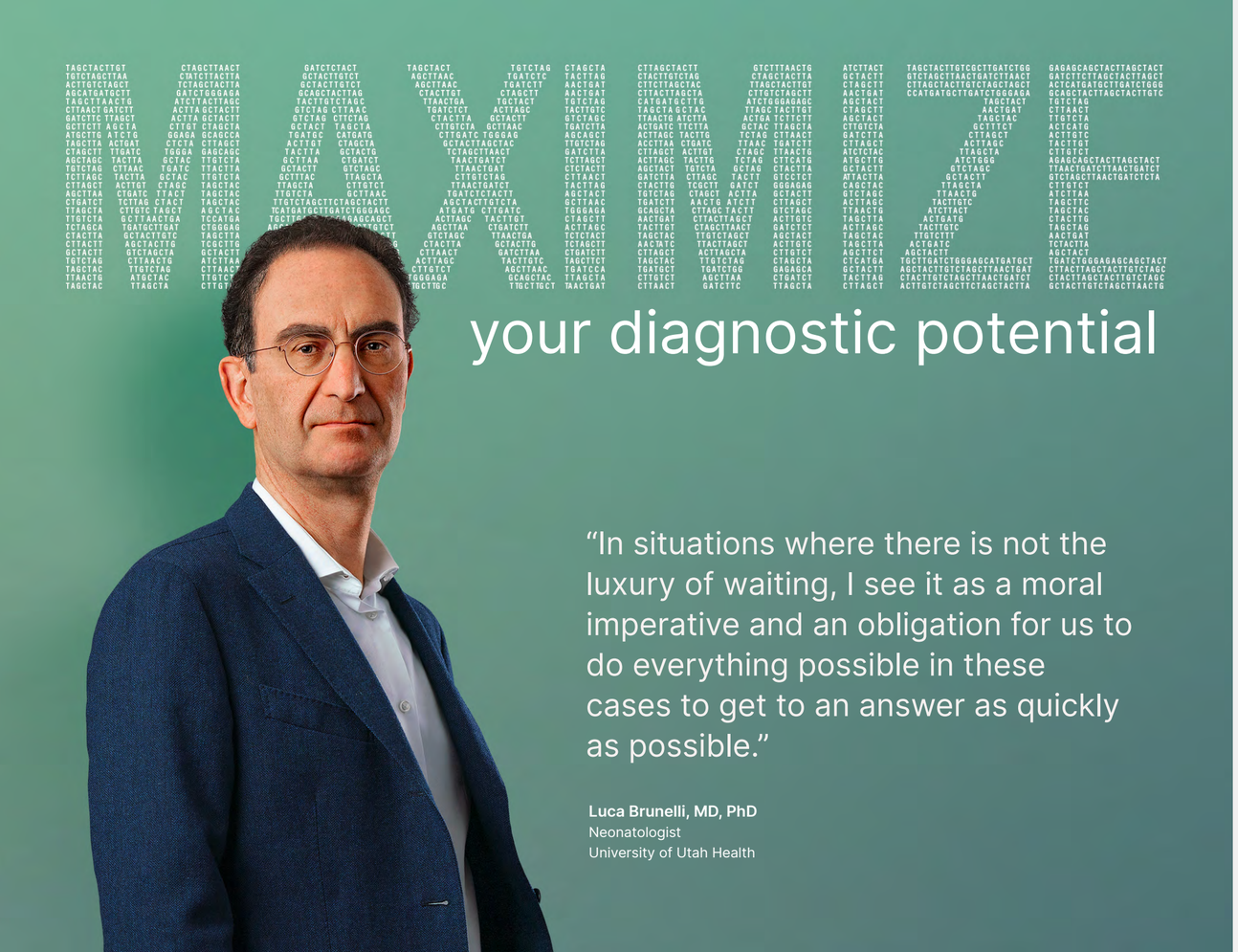
Whole-genome sequencing (WGS) provides the most comprehensive analysis of geneomic variants among all clinical genomic testing methods[7-9]

It is clear WGS is contributing significantly to end diagnostic odysseys in rare disease. With guidelines advocating use as a first–tier test,[10] inclusion in national health care systems,[11] and increasing evidence of economic value when used as a first–tier test,[12] 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



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.[13,14] In a large randomized-controlled trial, WGS demonstrated the greatest success in finding a diagnosis in rare disease.[15]

Advantages of WGS:

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

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.[27]

Advances in genomic testing are leading to answers faster than ever before.

- A single, comprehensive WGS test can provide more information and be completed more quickly than multiple, iterative tests[28]
- WGS can save years on the time to diagnosis compared to standard genetic testing[29,30]

WGS can help provide answers more quickly in patients with immature phenotypes or those with heterogenous symptoms.[31]

WGS can provide answers faster than standard testing*

Acutely ill NICU infants:

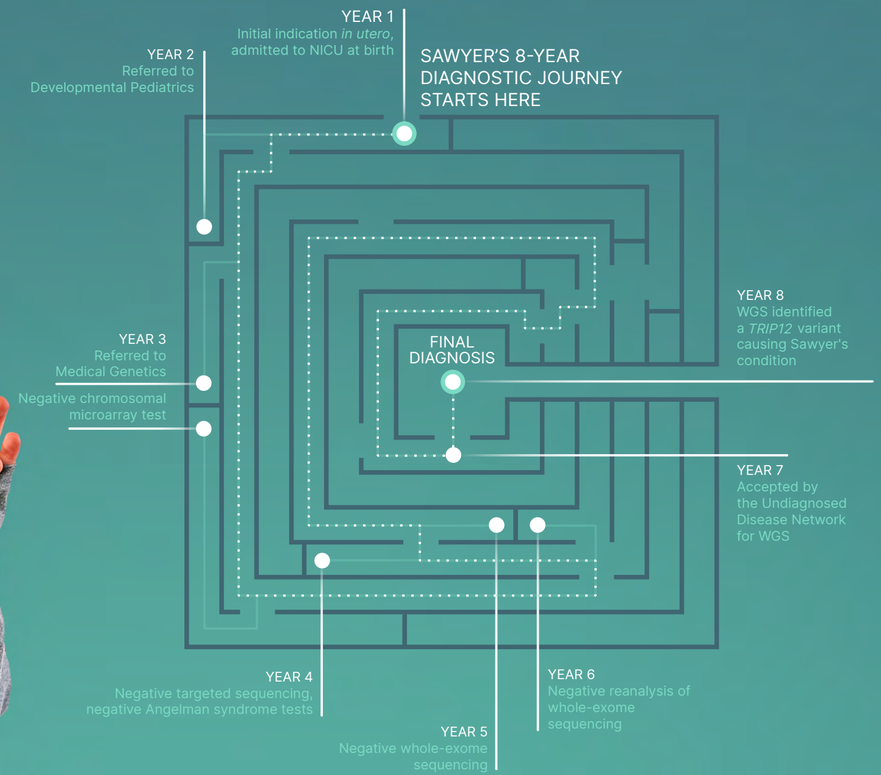
Time to diagnosis using WGS vs standard genetic tests in the NICU

Pediatric patients:

Average time to diagnosis using WGS vs standard genetic tests in pediatric patients

* Standard tests include: CMA, fluorescence *in situ* hybridization (FISH), karyotype, targeted gene panels, methylation studies, and gene detection or duplication assays.

Sawyer was on an 8-year diagnostic odyssey before his family found an answer with WGS.[32]



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

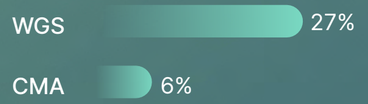
> 20% > 40% > 60% > 70%

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[27]

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



*95% CI: 0.17-0.40 P<0.0001

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

A promising future for all

WGS and WES are already in use and showing positive results in several neonatal intensive care units (NICU)[15,40] and is recommended by the ACMG as a first or second-tier test.
With its improved diagnostic performance and faster time to answer, WGS holds the promise of helping patients and their families end a diagnostic odyssey—or prevent one altogether—and focus on care management.

→ Click here to learn how patients have benefited from WGS

Request WGS for your patients from your preferred laboratory

Anxhela Gustafson, PhD
Scientist
Genomics Institute at Shriners Children's

Now recommended by the ACMG

In 2021, the American College of Medical Genetics and Genomics (ACMG) released guidance recommending the use of WES or WGS as first- or second-tier tests in patients with one or more congenital anomalies prior to one year of age or intellectual disabilities/ developmental delay prior to eighteen years of age.[18]

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