The Evidence is In: Rapid Whole Genome Sequencing is the New Standard of Care for Acutely Ill Infants

Faster diagnosis. Comprehensive answers. Reduced healthcare expenses.

Introduction

Each year, up to10% of babies born in the United States are hospitalized in an intensive care unit- either neonatal (NICU), pediatric (PICU), or cardiovascular (CVICU). Approximately 15% of these hospitalizations are due to an underlying genetic disease.[1,2,4] Historically, testing for these genetic disorders has been a long, difficult process that rarely provided actionable data in time to change the patient's medical management. Rapid Whole Genome Sequencing™ (rWGS®) changes this paradigm, reducing the time from sample to report, enabling timely intervention or changes in management.[3,4] A growing body of clinical evidence demonstrates that rWGS as a first-line, standard-of-care test for acutely ill infants (Figure 1) results in improved outcomes and reduces healthcare costs.[3-13]

The value of whole genome sequencing data

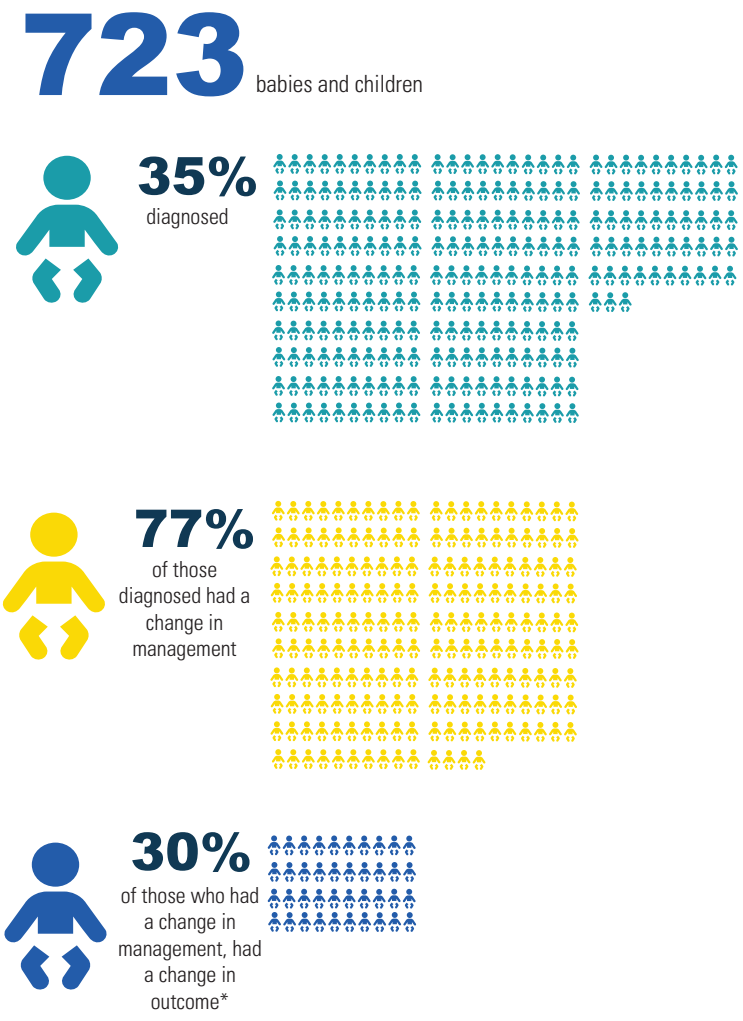
While several methods exist for genetic evaluation, whole genome sequencing singularly provides a comprehensive view of the genome. Analyses by PCR and microarray both survey a limited number of specified genes while whole-exome based sequencing covers only ~2% of the genome. While these tests have their uses, their design inherently causes them to miss potentially valuable information. In a 2020 study, whole genome sequencing revealed a genetic diagnosis missed in 14.5% of patients who had previously undergone exome sequencing tests.[14]

rWGS as a first-line test improves outcomes

Genetic diseases often have a short therapeutic window between presentation of symptoms and effective therapeutic intervention.[4] Compared to the current standard of care, rWGS reduces the time to diagnosis and increases diagnostic yield,[1] warranting its use as a front-line test.[6] rWGS has identified rare genetic variants affecting 1/1,000,000 individuals.[3]

Since 2012, numerous published studies have demonstrated the clinical utility of rWGS or urWGS® (ultra-rapid Whole Genome Sequencing™) in diagnosing patients with diseases of unknown etiology (Table 1). Overall, use of rWGS or urWGS led to a 35% diagnosis rate, with 17%* of patients seeing a positive change in outcome (Table 1). Notably, the Project Baby Bear study, concluded in 2020, demonstrated that rWGS provided a diagnosis for 43% of infants and led to a change in management that resulted in fewer days for the initial hospital stay, fewer therapies, and fewer procedures for 33% of the infants.[3]

Figure 1. rWGS/urWGS implementation leads to improved management and outcomes



Aggregated data based on the 12 studies presented in Table 1. [1,3,5-9,11,13,15,16]
Does not include percentage change in management due to negative result.

A survey of physicians who received rWGS data reported utility in 75% of cases, with change of management occurring in 25% of cases.[1] In 40% of cases, communication improved with families and 15% of infants experienced a change in outcome.[2]

rWGS saves time and reduces costs

Actionable rWGS reports are available in as little as 2-3 days. This enables physicians and families to make quick, informed decisions that can alter the course of an infant's treatment, reduce the length of a hospital stay, and avoid additional costly procedures. Improved diag-

* Only 5 of the 12 studies cited reported patient outcome.

nostic rates and increased clinical utility afforded by rWGS are associated with reduced overall healthcare costs that exceed the cost of testing (Figures 2 and 3). Based on the US annual estimated births resulting in NICU admissions due to a genetic disease, sequencing all projected 60,000 infants born annually would result in an annual savings of more than ~$0.8 billon.† Currently, Blue Shield of California, Florida Blue, Blue Cross Blue Shield Hawaii, Blue Cross of Idaho, Priority Health in Michigan and Horizon Blue New Jersey deem rWGS a medical necessity for the most critically ill infants and children.[17-22] Additional pathways to reimbursement through some state and other private insurers are available as well.[22,23]

Table 1. Use of rWGS and urWGS to diagnose genetic disorders

Study Name	Sequencing Type	NICU/PICU enrollment criteria	Study size	Rate of diagnosis	Rate of change in mgmt	Rate in change of outcome
Willig, Children's Mercy, Kansas City	rWGS	<4 mo of age; suspected actionable genetic disease[13]	35	57%	31%	29%
Petrikin, RCIGM	rWGS	<4 mo of age; suspected genetic disease[6]	32	41%	31%	N/D
Farnaes, RCIGM	rWGS	Infants; suspected genetic disease[15]	42	43%	31%	26%
Mestek, UCL Great Ormond Street Institute of Child Health (GOSgene UK)	rWGS	Children; PICU and cardiovascular ICU[9]	24	42%	13%	N/D
Sanford, UCSD, RCIGM	rWGS	4 mo- to 18 yr; PICU; suspected genetic disease[8]	38	48%	39%	8%
French, School of Clinical Medicine, University of Cambridge	rWGS	Suspected genetic disease[7]	195	21%	13%	N/D
Dimmock, RCIGM	rWGS	Infants; disease of unknown etiology; within 96 hr of admission[1]	94	19%	24%	10%
Project Baby Bear, RCIGM	rWGS	Medical infants; <1 wk admission[3]	178	43%	31%	N/D
PBM, Nicklaus Children's Hospital	rWGS, urWGS	Inpatient children <18 yr, 90% in ICUs, primarily PICU[16]	50	40%	38%	N/D
Saunders, Children's Mercy, Kansas City	urWGS	NICU infants; suspected genetic disease[11]	4	75%	N/D	N/D
Clark, RCIGM	urWGS	Infants; suspected genetic disease[5]	7	43%	43%	N/D
Dimmock, RCIGM	urWGS	Infants; disease of unknown etiology; within 96 hr of admission[1]	24	46%	63%	25%
WEIGHTED AVERAGE, rWGS + urWGS			**723**	**35%**	**27%**	**17%**

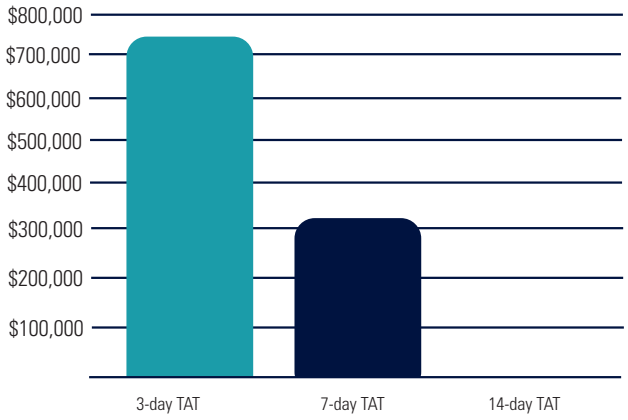
Figure 2. Healthcare savings achieved using rWGS

$2.5M in healthcare savings

- 513 fewer hospital days
- 11 fewer major surgeries
- 16 fewer invasive diagnostic tests
- Reduction in suffering and unnecessary surgeries and tests

Combined savings based on care of 29 children across the 5 hospitals that participated in Project Baby Bear.[3]

Figure 3. Reduced time to diagnosis by rWGS leads to increased cost savings.



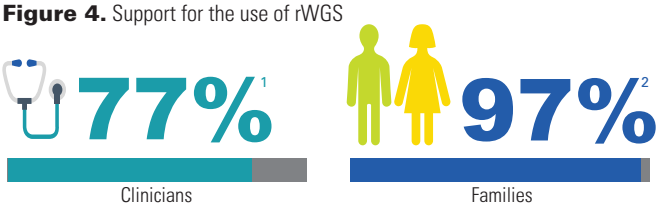
> $700K Amount saved employing a 3-day TAT test compared to a 14-day TAT test

Employing a rWGS test with a 3-day turnaround time (TAT) has the potential to reduce the length of hospital stays and minimize additional procedures, saving on total healthcare costs.[3]

Physicians and families value rWGS

In a 2020 survey, 77% of clinicians and 97% of families felt rWGS was beneficial,[1] despite a diagnostic rate of 23%, demonstrating that even a negative genome result provides useful clinical information (Figure 4).[2] Families reported that given another opportunity, they would make the same decision and move forward with genome sequencing for their child.[2]

Figure 4. Support for the use of rWGS



Partner with RCIGM for rWGS

Rady Childrens Institute for Genomic Medicine® (RCIGM) pioneered the clinical use of rWGS and urWGS for babies and children in the NICU and PICU. RCIGM is committed to advancing Rapid Precision Medicine to be the standard of care in all cases.

Physicians that partner with RCIGM for rWGS have access to:

- Fast turnaround times with preliminary results in as little as 2-3 days
- Comprehensive, actionable reports
- Expert genetic support, training and access to Genetic Counselors and MD's

Rady genomic medicine specialists consult directly with ordering physisicans to provide case-specific insights that enable personalized patient care.

† Based on Project Baby Bear, the total cost of sequencing 178 genomes was $1.737 million and saved $2.489 million in unnecessary healthcare costs. This amounted to $1.43 savings for every $1 spent. Extrapolating data out to 60,000 genomes, total cost savings is ~$0.8 billion.

Get started today

Making rWGS and urWGS a first-line standard-of-care test in the NICU and PICU provides accurate, actionable information quickly, improving patient outcomes and reducing overall healthcare expenses. When an acutely ill baby or child is struggling to survive, every minute matters.

Order a test
Urgent request rWGS
RCIGM_rWGS@rchsd.org
Call: 858.966.8127

Questions about rWGS and urWGS
ask@RadyGenomics.org

Visit our website
www.RadyGenomics.org

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