Washington State Health Care Authority

Health Technology Clinical Committee
DRAFT Findings and Decision

Topic: Whole genome sequencing
Meeting date: June 14, 2024
Final adoption: Pending

Number and coverage topic:
20240614A – Whole genome sequencing

HTCC coverage determination:
Whole genome sequencing is a **covered benefit with conditions.**

HTCC reimbursement determination:
Limitations of coverage:
Whole genome sequencing (WGS) is a covered benefit with conditions for the evaluation of unexplained congenital or neurodevelopmental or neurodegenerative disorders in a phenotypically affected individual when **ALL of the following** criteria are met:

1. A board-certified or board-eligible Medical Geneticist, or an Advanced Practice Nurse in Genetics (APGN) credentialed by either the Genetic Nursing Credentialing Commission (GNCC) or the American Nurses Credentialing Center (ANCC), who is not employed by a commercial genetic testing laboratory, has evaluated the patient and family history, and recommends and/or orders the test; and

2. A genetic etiology is considered the most likely explanation for the phenotype, based on **EITHER of the following**;

   - Multiple abnormalities affecting unrelated organ systems, (e.g. multiple congenital anomalies); or

   - **TWO of the following criteria are met:**

     — Significant abnormality affecting at minimum, a single organ system,
     — Unexplained cognitive changes in adulthood,
     — Profound global developmental delay[1], or intellectual disability[2] as defined below,
     — Family history strongly suggestive of a genetic etiology, including consanguinity,
     — Period of unexplained developmental regression (unrelated to autism or epilepsy),
     — Biochemical findings suggestive of an inborn error of metabolism where targeted testing is not available; and

3. Other circumstances (e.g. environmental exposures, injury, infection) do not reasonably explain the constellation of symptoms; and

4. Clinical presentation does not fit a well-described syndrome for which single-gene or targeted panel testing (e.g., comparative genomic hybridization [CGH]/chromosomal microarray analysis [CMA]) is available; and

5. The differential diagnosis list and/or phenotype warrant testing of multiple genes and **ONE of the following**:

- WGS is more efficient and economical than the separate single-gene tests or panels that would be recommended based on the differential diagnosis (e.g., genetic conditions that demonstrate a high degree of genetic heterogeneity); or
- WGS results may preclude the need for invasive procedures or screening that would be recommended in the absence of testing (e.g. muscle biopsy); and

6. A standard clinical work-up has been conducted and did not lead to a diagnosis; and
7. Results will impact clinical decision-making for the individual being tested; and
8. Pre- and post-test counseling is performed by an American Board of Medical Genetics or American Board of Genetic Counseling certified genetic counselor.

Non-covered indicators:

WGS is not covered for:

- Carrier testing for "at risk" relatives.
- Prenatal or pre-implantation testing.

Definitions:

[1] **Global developmental delay (GDD)** is used to categorize children who are younger than five years of age.

GDD is defined as a significant delay[2] in two or more developmental domains, including gross or fine motor, speech/language, cognitive, social/personal, and activities of daily living and is thought to predict a future diagnosis of ID. Such delays require accurate documentation by using norm-referenced and age appropriate standardized measures of development administered by experienced developmental specialists, or documentation of profound delays based on age appropriate developmental milestones are present.

Reference: *Comprehensive Evaluation of the Child With Intellectual Disability or Global Developmental Delays Pediatrics 2014;134:e903–e918. Page e905*

Significant delay is typically defined as performance two standard deviations or more below the mean on age-appropriate, standardized, normal-referenced testing.

[2] **Intellectual disability (ID)** is a life-long disability diagnosed at or after age five when intelligence quotient (IQ) testing is considered valid and reliable. The Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-V), defines patients with ID as having an IQ less than 70, onset during childhood, and dysfunction or impairment in more than two areas of adaptive behavior or systems of support.

Related documents:

- Final key questions
- Final evidence report
- Meeting materials and transcript

Agency contact information:

Agency	Phone Number

Labor and Industries	1-800-547-8367
Public and School Employees Health Plan	1-800-200-1004
Washington State Medicaid	1-800-562-3022

HTCC coverage vote and formal action:

Committee decision

Based on the deliberations of key health outcomes, the committee decided that it had the most complete information: a comprehensive and current evidence report, public comments, and state agency utilization information. The committee discussed and voted on the evidence for the use of whole genome sequencing. The committee decided that the current evidence on whole genome sequencing is sufficient to determine coverage with conditions. The committee considered the evidence, public comment and expert input, and gave greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

Based on these findings, the committee voted to cover with conditions whole genome sequencing.

	Not covered	Covered under certain conditions	Covered unconditionally
Whole genome sequencing	0	9	0

Discussion

The committee reviewed and discussed the available studies for use of whole genome sequencing. Conditions for coverage were discussed, drafted, and voted on. All committee members present supported the conditions of coverage of whole genome sequencing. Details of study design, inclusion criteria, outcomes, cost, cost-effectiveness, and other factors affecting study quality were discussed as well as clinical application.

Decision

Whole genome sequencing is covered with conditions for the following:

Whole genome sequencing (WGS) is a covered benefit with conditions for the evaluation of unexplained congenital or neurodevelopmental or neurodegenerative disorders in a phenotypically affected individual when **ALL of the following** criteria are met:

1. A board-certified or board-eligible Medical Geneticist, or an Advanced Practice Nurse in Genetics (APGN) credentialed by either the Genetic Nursing Credentialing Commission (GNCC) or the American Nurses Credentialing Center (ANCC), who is not employed by a commercial genetic testing laboratory, has evaluated the patient and family history, and recommends and/or orders the test; and

2. A genetic etiology is considered the most likely explanation for the phenotype, based on **EITHER of the following**; and

    - Multiple abnormalities affecting unrelated organ systems, (e.g. multiple congenital anomalies); or

- **TWO of the following criteria are met:**
  - Significant abnormality affecting at minimum, a single organ system,
  - Unexplained cognitive changes in adulthood,
  - Profound global developmental delay[1], or intellectual disability[2] as defined below,
  - Family history strongly suggestive of a genetic etiology, including consanguinity,
  - Period of unexplained developmental regression (unrelated to autism or epilepsy),
  - Biochemical findings suggestive of an inborn error of metabolism where targeted testing is not available;

3. Other circumstances (e.g. environmental exposures, injury, infection) do not reasonably explain the constellation of symptoms; and
4. Clinical presentation does not fit a well-described syndrome for which single-gene or targeted panel testing (e.g., comparative genomic hybridization [CGH]/chromosomal microarray analysis [CMA]) is available; and
5. The differential diagnosis list and/or phenotype warrant testing of multiple genes and **ONE of the following**:
   - WGS is more efficient and economical than the separate single-gene tests or panels that would be recommended based on the differential diagnosis (e.g., genetic conditions that demonstrate a high degree of genetic heterogeneity); or
   - WGS results may preclude the need for invasive procedures or screening that would be recommended in the absence of testing (e.g. muscle biopsy); and
6. A standard clinical work-up has been conducted and did not lead to a diagnosis; and
7. Results will impact clinical decision-making for the individual being tested; and
8. Pre- and post-test counseling is performed by an American Board of Medical Genetics or American Board of Genetic Counseling certified genetic counselor.

WGS is not a covered benefit for carrier testing for 'at risk' relatives and prenatal or pre-implantation testing.

Definitions:

[1] **Global developmental delay (GDD)** is used to categorize children who are younger than five years of age.

GDD is defined as a significant delay[2] in two or more developmental domains, including gross or fine motor, speech/language, cognitive, social/personal, and activities of daily living and is thought to predict a future diagnosis of ID. Such delays require accurate documentation by using norm-referenced and age appropriate standardized measures of development administered by experienced developmental specialists, or documentation of profound delays based on age appropriate developmental milestones are present.

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Action

The committee checked for availability of a Centers for Medicare and Medicaid Services (CMS) national coverage decision (NCD). Based on the information provided in the systematic review, there is no NCD for whole genome sequencing.

The committee discussed clinical guidelines identified from the following organizations:

- Medical Genome Initiative (MGI), 2024, Evidence review and consideration for use of first-line genome sequencing to diagnose rare genetic disorders
- National Society of Genetic Counselors (NSGC), 2023, Genetic testing and counseling for the unexplained epilepsies: an evidence-based practice guideline
- National Institute of Health and Care Excellence (NICE), 2022, Epilepsies in children, young people, and adults
- EuroGentest, 2022, Recommendations for WGS in diagnostics for rare diseases
- American College of Medical Genetics and Genomics (ACMG), 2021, Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability evidence-based guideline
- Canadian College of Medical Geneticists, 2015, The clinical application of genome-wide sequencing for monogenic diseases in Canada

The recommendations of the guidelines vary. The committee's determination is consistent with the noted guidelines.

HTA staff will prepare a findings and decision document on use of stereotactic body radiation therapy for the treatment of selected conditions for public comment to be followed by consideration for final approval at the next committee meeting.

Health Technology Clinical Committee Authority:

Washington State's legislature believes it is important to use a science-based, clinician-centered approach for difficult and important health care benefit decisions. Pursuant to chapter 70.14 RCW, the legislature has directed the Washington State Health Care Authority (HCA), through its Health Technology Assessment (HTA) program, to engage in an evaluation process that gathers and assesses the quality of the latest medical evidence using a scientific research company that takes public input at all stages.

Pursuant to RCW 70.14.110, a Health Technology Clinical Committee (HTCC) composed of eleven independent health care professionals reviews all the information and renders a decision at an open public meeting. The Washington State HTCC determines how selected health technologies are covered by several state agencies (RCW 70.14.080-140). These technologies may include medical or surgical devices and procedures, medical equipment, and diagnostic tests. HTCC bases its decisions on evidence of the technology's safety, efficacy, and cost effectiveness. Participating state agencies are required to

comply with the decisions of the HTCC. HTCC decisions may be re-reviewed at the determination of the HCA Director.