

Health Technology Clinical Committee Findings and Decision

Topic: Whole exome sequencing
Meeting date: November 22, 2019
Final adoption: May 15, 2020

Meeting materials and transcript are available on the [HTA website](#).

Number and coverage topic:

20191122A – Whole exome sequencing

HTCC coverage determination:

Whole exome sequencing is a **covered benefit with conditions**.

HTCC reimbursement determination:

Limitations of coverage:

Whole exome sequencing (WES) is considered medically necessary for the evaluation of unexplained congenital or neurodevelopmental 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,
 - Profound global developmental delay¹ or intellectual disability² 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

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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**:
 - WES 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
 - WES results may preclude the need for multiple 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:

WES is not covered for:

- Uncomplicated autism spectrum disorder, developmental delay, mild to moderate global developmental delay.
- Other circumstances (e.g. environmental exposures, injury, infection) that reasonably explain the constellation of symptoms.
- 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 delay² 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.

Agency contact information:

Agency	Phone Number
Labor and Industries	1-800-547-8367
Public 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 decided that the current evidence on whole exome sequencing is sufficient to make a determination on this topic. The committee discussed and voted on the evidence for the use of the test, considered the evidence 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 exome sequencing for children and adults.

	Not covered	Covered under certain conditions	Covered unconditionally
Whole exome sequencing	0	10	0

Discussion

The committee reviewed and discussed the available information and limitations of the evidence base. A majority of committee members found the evidence sufficient to determine that whole exome sequencing is more effective in some scenarios and equally safe to other similar tests. In drafting the conditions for coverage, the committee recognized a need for more information and refinement of the proposed coverage criteria. Agency staff were directed to compile the information and provide the committee a draft for consideration at the next meeting scheduled for January 17, 2020.

Limitations

N/A

Action

As noted the committee chair directed agency staff to prepare additional information for the proposed conditional criteria for whole exome sequencing to be considered by the committee at the next meeting.

At the January 17, 2020 committee meeting the committee checked for availability of a Centers for Medicare and Medicaid Services (CMS) national coverage decision (NCD). There is no Medicare NCD for WES. The committee checked for availability of clinical guidelines identified for WES. No clinical practice guidelines were identified specific to diagnostic testing with WES.

The committee chair directed HTA staff to prepare a findings and decision document on use of whole exome sequencing for public comment to be followed by consideration for final approval at the next public 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

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the quality of the latest medical evidence using a scientific research company and 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.