Whole Exome Sequencing (WES) under Medicare

This resource has been developed to help guide clinicians requesting whole exome sequencing (WES) for patients who meet criteria under the new Medicare item number.

Key Points
- Whole exome sequencing (WES) is a diagnostic test used to identify the genetic cause of an individual’s health condition.
- WES can be performed for an individual (singleton testing) or in combination with both biological parents (trio testing).
- To be eligible for the Medicare rebate, the child must be aged <10 years and have had a non-informative chromosome microarray (CMA) test using Medicare item number 73292.
- Negative Fragile X testing and urine metabolic screening is also desirable.
- Samples (2–5 ml EDTA blood*) are ideally required from both parents and child. Stored DNA from previous diagnostic tests can also be used.

*Saliva samples are accepted by some labs

Medicare Criteria for item numbers 73358–73363

Global developmental delay OR intellectual disability of at least moderate severity
AND/OR
Dysmorphic facial features AND the presence of at least one major structural congenital anomaly

Reanalysis of genomic data at least 18 months after the initial Medicare rebated test can be requested under Medicare twice for an individual up to 16 years old. This is to capture any new information or gene discoveries that may not have been detected in the initial analysis.

The genome is comprised of both exons (regions coding proteins ~2%) and introns (non-coding regions ~98%). Genomic sequencing can detect up to 40% of causal gene variants to account for selected single gene disorders.

Eligibility for Medicare funded WES
- If the child is strongly suspected of having a single gene disorder and is less than 10 years old.
- The child has a non-informative chromosome microarray (CMA) test. Negative Fragile X testing and urine metabolic screening is also desirable.
- A clinical geneticist has been consulted about the test indications.
- The family has given informed consent using the appropriate consent forms.
- Whenever possible trio testing including child and parents is recommended.

Analysis of genomic data can include:
1) The whole genome (introns and exons)
2) The whole exome (exons only)
3) A gene panel (genes of interest only)

WES does not detect all genetic changes – it cannot detect DNA changes in the mitochondria or introns, variations in copy number, aneuploidy, polyploidy or chromosome translocations.
Consulting with clinical genetics

Clinical genetics services in each local health district will have different ways of facilitating the consultation process. Genetic counsellor support may be available for the family and requesting doctor depending on staffing resources.

Contact details for NSW metropolitan and regional genetics services can be found here: [https://www.genetics.edu.au/genetic-services/general-genetics-clinics](https://www.genetics.edu.au/genetic-services/general-genetics-clinics).

A clinical geneticist can also be consulted via the state-wide Genetics of Learning Disability (GOLD) Service ([HNELHD-GOLD@health.nsw.gov.au](mailto:HNELHD-GOLD@health.nsw.gov.au)).

Consent

NSW has a standard consent form for parents and their child, with separate consent being required from each participant i.e. three consent forms when ordering a trio exome. Copies can be obtained from the Agency for Clinical Innovation website: ([https://www.aci.health.nsw.gov.au/networks/clinical-genetics/genetic-and-genomic-testing-consent-forms](https://www.aci.health.nsw.gov.au/networks/clinical-genetics/genetic-and-genomic-testing-consent-forms)).

- To order WES, tick the ‘Diagnostic Testing’ box in the ‘Type of Genetic Test’ section on the consent form.
- For more information about the other types of tests listed on the consent form, see MedlinePlus ([https://medlineplus.gov/genetics/understanding/testing/uses/](https://medlineplus.gov/genetics/understanding/testing/uses/)).
- Further information about consent can be found at the Centre for Genetics Education website (consent for WES: [https://www.genetics.edu.au/health-professionals/genomics-1/video-3](https://www.genetics.edu.au/health-professionals/genomics-1/video-3); general consent resources: [https://www.genetics.edu.au/health-professionals/genomic-videos](https://www.genetics.edu.au/health-professionals/genomic-videos)).
Consent should include the possible outcomes of testing

1) **Genetic cause identified** – Pathogenic/likely pathogenic variant in a known gene.

2) **Uninformative result** – a genetic cause is not identified.
   This does not exclude a genetic diagnosis. This may be because –
   a. the test did not examine the gene causing the condition OR
   b. the gene causing the condition is not yet known OR
   c. the gene variant causing the condition cannot be found by the test.
   Future re-analysis is possible.

3) **Gene variant of uncertain significance (VUS)** – unclear result, may require testing in other family members, and/or may require review in the future

4) **Incidental finding** – in rare cases (<1% of reports) a gene change is found that is not related to the patient’s clinical features but may have implications for the child or relative’s current or future health

### Other points to consider

<table>
<thead>
<tr>
<th>Impact on clinical care</th>
<th>• Onward referrals may be made for screening or management based on results.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implications for insurance</td>
<td>• An incidental finding in an adult relative based on this testing may affect applications for life/income protection insurance, but not medical/private health insurance.</td>
</tr>
<tr>
<td>Impact on relatives</td>
<td>• Sometimes a genomic test result in one person has implications for another persons’ health care. NSW Health provides guidance on this (see last page).</td>
</tr>
<tr>
<td>Unexpected family relationships</td>
<td>• Trio testing could reveal non-paternity, non-maternity or unexpected family relations.</td>
</tr>
<tr>
<td>Data</td>
<td>• Data will be stored securely in databases according to Australian standards.</td>
</tr>
<tr>
<td>Limitations of testing</td>
<td>• This is not a general health test and will not identify all gene changes that could contribute to health problems</td>
</tr>
<tr>
<td>Change of mind</td>
<td>• No report will be generated if consent is withdrawn before the test is completed. If the patient withdraws consent after the test is run, the result may be captured in their health record.</td>
</tr>
<tr>
<td>Sample sharing</td>
<td>• Additional testing of the sample for further research may be requested, with consent.</td>
</tr>
</tbody>
</table>
Whole Exome Sequencing (WES) under Medicare items 73358–63

Where to order WES?

For Medicare eligibility, WES must be performed in an Australian NATA accredited lab. Labs require consent, and a request form detailing clinical information. In NSW testing is offered at:

SEALS
Fax 02 93829157 (lab) Phone 02 9382 9114
Email NSWPATH-RandwickGenomics@health.nsw.gov.au

Requirements for testing:

- Completed consent forms (x3 if trio)
- SEALS request form: see below (x3 if trio)
- Sample: 2–5 ml EDTA blood
Whole Exome Sequencing (WES) under Medicare items 73358–63

Result disclosure and the role of genetic services

Generic and disease specific resources are available at the Centre for Genetics Education (www.genetics.edu.au) to help clinicians inform families with new diagnoses as well as those who remain undiagnosed. Contact your local genetics service for assistance.

Links and resources

<table>
<thead>
<tr>
<th>Website</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><a href="https://elearning.racp.edu.au/">https://elearning.racp.edu.au/</a></td>
</tr>
<tr>
<td></td>
<td><a href="https://dontforgetthebubbles.com/?s=genomic+testing">https://dontforgetthebubbles.com/?s=genomic+testing</a></td>
</tr>
<tr>
<td>Genomic testing consent resources for Medical Specialists</td>
<td><a href="https://www.genetics.edu.au/health-professionals/genomic-videos">https://www.genetics.edu.au/health-professionals/genomic-videos</a></td>
</tr>
<tr>
<td>Australian Genomics patient education</td>
<td><a href="https://www.genomicsinfo.org.au">https://www.genomicsinfo.org.au</a></td>
</tr>
</tbody>
</table>

For more information about genetic conditions and Clinical Genetics services, visit the Centre for Genetics Education - www.genetics.edu.au

If your patient does not meet Medicare criteria, testing may still be appropriate. Please refer to your local genetics service

Version 6. February 2021

This resource is available at: https://www.genetics.edu.au/health-professionals/WESpaediatricresource_FINAL.pdf