

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 or younger 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 aged 10 years or younger.
- 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/SitePages/Genetic-Services.aspx>.

A clinical geneticist can also be consulted via the state-wide Genetics of Learning Disability (GOLD) Service (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>).

NSW Health	FAMILY NAME	M.R.N.
	GIVEN NAME	<input type="checkbox"/> MALE <input type="checkbox"/> FEMALE
Facility:	D.O.B. / /	M.O.
	ADDRESS	
	LOCATION / WARD	
	COMPLETE ALL DETAILS OR AFFIX PATIENT LABEL HERE	
CONSENT: GENETIC TESTING (for all types of genetic and genomic testing for ADULTS, MATURE MINORS and MINORS)		
CONSENT FOR GENETIC TESTING is provided by (please tick an option below):		
<input type="checkbox"/> An adult (a patient with capacity)		
<input type="checkbox"/> A mature minor (a patient with capacity)		
<input type="checkbox"/> I (the health practitioner) have assessed this patient to be a minor with capacity to give consent as they have demonstrated sufficient maturity and intellect to fully understand what is proposed.		
<input type="checkbox"/> A parent / guardian of a minor without capacity		
PROVISION OF INFORMATION TO PATIENT / PARENT / GUARDIAN To be completed by Health Practitioner		
I _____ INSERT NAME OF HEALTH PRACTITIONER		
have discussed with this patient/ parent/ guardian the reason for conducting the proposed genetic test. I have informed this patient/ parent/ guardian of the nature, possible results, limitations and material risks of the proposed genetic test, as confirmed on this form by this patient/ parent/ guardian. This patient/ parent/ guardian has been offered additional written information and/or reference to online resources about the genetic testing.		
Genetic testing is being conducted for _____		

INSERT NAME OF CONDITION(S) OR CLINICAL INDICATIONS		
*TYPE OF GENETIC TEST (please tick an option below):		
<input type="checkbox"/> Carrier Testing: a genetic test performed on a person to identify if they carry a gene change.		
<input type="checkbox"/> Diagnostic Testing: a genetic test performed on a person to identify a specific genetic condition.		
<input type="checkbox"/> Predictive/Presymptomatic Testing: a genetic test performed on a person with a family history of a genetic condition, who does not usually have symptoms at the time of testing, to determine if they have inherited that condition or susceptibility to that condition.		
<input type="checkbox"/> Prenatal Testing: a genetic test to identify possible genetic conditions in an unborn baby.		
<input type="checkbox"/> Other (please specify): _____		
INTERPRETER PRESENT <input type="checkbox"/> Yes <input type="checkbox"/> No		
INSERT NAME OF INTERPRETER		SIGNATURE
/ /	TIME AM/PM	EMPLOYEE ID / PROVIDER NUMBER
SIGNATURE OF HEALTH PRACTITIONER		/ /
NO WRITING		DATE

- 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/>).
- Further information about consent can be found at the Centre for Genetics Education website (consent for WES: <https://www.genetics.edu.au/SitePages/Paediatric-Genetics-Video-3.aspx>; general consent resources: <https://www.genetics.edu.au/SitePages/Genomic-Testing-Consent.aspx>).

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

Impact on clinical care	<ul style="list-style-type: none"> • Onward referrals may be made for screening or management based on results.
Implications for insurance	<ul style="list-style-type: none"> • 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.
Impact on relatives	<ul style="list-style-type: none"> • Sometimes a genomic test result in one person has implications for another persons' health care. NSW Health provides guidance on this (see last page).
Unexpected family relationships	<ul style="list-style-type: none"> • Trio testing could reveal non-paternity, non-maternity or unexpected family relations.
Data	<ul style="list-style-type: none"> • Data will be stored securely in databases according to Australian standards.
Limitations of testing	<ul style="list-style-type: none"> • This is not a general health test and will not identify all gene changes that could contribute to health problems
Change of mind	<ul style="list-style-type: none"> • 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.
Sample sharing	<ul style="list-style-type: none"> • Additional testing of the sample for further research may be requested, with consent.

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
- ***It is essential that accurate and detailed clinical phenotype information is provided on the request form, to assist the laboratory with interpreting results***

EXOME / GENOME TEST REQUEST FORM		NSW Health Pathology	
<p><small>Send form to:</small></p> <p><small>Department of Molecular Genetics, Children's Hospital Westmead 14 Hawkesbury Rd and Hainsworth Street Westmead NSW 2145 Ph 02 98453244 Fax 02 98453204 (lab) Email ECHN_CMG_MolecularGenetics.Laboratory@health.nsw.gov.au</small></p> <p><small>NSWHP Genomics Laboratory Randwick 4th floor, Campus Centre Prince of Wales Hospital Barker Street Randwick NSW 2031 Ph 02 93829114 Fax 02 93829157 (lab) Email NSWPATH-RandwickGenomics@health.nsw.gov.au</small></p>			
PATIENT DETAILS	Surname (Print or place sticker here)	First name	<p>If the following criteria is met tests can be funded by MBS. Other referrals may be accepted if appropriately funded</p> <p>Tick at least one box (or combined box) for MBS eligibility</p> <p><input type="checkbox"/> Patient is 10yo or younger, assessed likely to have a monogenic condition, and not yet had a whole exome or genome test</p> <p>AND</p> <p><input type="checkbox"/> Dysmorphic facial appearance and one or more major structural congenital anomalies</p> <p><input type="checkbox"/> Intellectual disability or global developmental delay of at least moderate severity, as determined by a specialist paediatrician</p> <p>AND</p> <p><input type="checkbox"/> Microarray reported as non-informative</p> <p>OR</p> <p><input type="checkbox"/> Clinical Geneticist Referral</p> <p><input type="checkbox"/> Paediatrician referral in consultation with a clinical geneticist</p>
	DOB	<input type="checkbox"/> Male <input type="checkbox"/> Female <input type="checkbox"/> Other	
REQUEST	Address	Phone	<p><input type="checkbox"/> For data re-analysis previously tested patient (15 years or younger) with a suspected monogenic condition.</p> <p><input type="checkbox"/> For trio genomic tests Singleton testing inappropriate, both biological parents available.</p>
	Facility	MRN	
CLINICAL SUMMARY	Pregnant <input type="checkbox"/> N <input type="checkbox"/> Y gestation weeks	TEST: <input type="checkbox"/> Singleton - Exome <input type="checkbox"/> Trio - Exome <input type="checkbox"/> Data re-analysis <input type="checkbox"/> Bioinformatic Gene Panel <input type="checkbox"/> Known variant	<p>Family History Summary (please provide pedigree)</p> <p>If patient not index case indicate relationship within family tree</p> <p><input type="checkbox"/> = Male <input type="checkbox"/> = Female <input checked="" type="checkbox"/> = Affected Male <input checked="" type="checkbox"/> = Carrier Female</p> <p><input type="checkbox"/> = Gender unspecified</p>
	REASON: <input type="checkbox"/> Diagnostic / management <input type="checkbox"/> Reproductive management	PRIORITY: <input type="checkbox"/> Routine <input type="checkbox"/> Urgent (contact lab prior to referral - urgent turnaround time requests will incur an extra cost)	
PREVIOUS TESTS	Clinical Diagnosis <input type="checkbox"/> Certain <input type="checkbox"/> Uncertain	Clinical Features:	<p>Both parents available for testing <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>Consanguinity <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>Ancestry Maternal Paternal</p> <p>Copy of reports to <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>Consulting geneticist</p> <p>Address</p> <p>Phone Email</p> <p>MEDICARE NO <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> / <input type="checkbox"/> EXP</p> <p>At time of collection the patient</p> <p>• Is a private patient in a private hospital or approved day hospital facility <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>• a private patient in a recognised hospital <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>• a public patient in a recognised hospital <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>• an outpatient of a recognised hospital <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><input type="checkbox"/> Do NOT send my pathology report to My Health Record</p> <p>Collector ward/site</p> <p>Collection Date</p> <p>Receipt Date</p>
	Moderate Global Developmental Delay Microcephaly	Is this person affected <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Uncertain	
REQUESTING DETAILS	Index case or Relative* <input type="checkbox"/> Index case or <input type="checkbox"/> Relative*	Refer to NPAAC requirements for predictive/pre-symptomatic testing.	<p>Gene test result <input type="checkbox"/> Please include copy of previous report</p> <p>Microarray result <input type="checkbox"/> Please include copy of previous report</p> <p>WES/WGS result <input type="checkbox"/> Please include copy of previous report</p> <p>Family-specific mutation was first found in (index patient)</p> <p>Surname First name</p> <p>DOB Test lab or city</p> <p>Requesting Doctor's name Signature</p> <p>Address</p> <p>Phone Email</p> <p>Date Provider No.</p>
	Requesting Doctor's name	Signature	
MEDICARE DETAILS	Address	Signature	<p>Signature</p> <p>Date</p> <p>Practitioner use only (Reason patient cannot sign)</p> <p>Date</p>
	Phone	Email	
COLLECTION DETAILS	Date	Provider No.	<p>Collector's Name</p> <p>Collector ID</p> <p>The specimen accompanying this request was collected from the person named on this form and labelled immediately after collection</p> <p>Signature</p> <p><input type="checkbox"/> DNA <input type="checkbox"/> Blood (EDTA 2 x 2mls recommended) <input type="checkbox"/> Buccal Swab (by prior arrangement with lab) <input type="checkbox"/> Other</p>
	Requesting Doctor's name	Signature	

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

Website	Address
Medicare Benefits Scheme	http://mbsonline.gov.au/
Exome sequencing education for paediatricians / RACP module	https://www.genetics.edu.au/SitePages/Genomic-testing-Intellectual-disability-childhood-syndromes.aspx https://elearning.racp.edu.au/ (Search 'genomics') https://dontforgetthebubbles.com/?s=genomic+testing
Genomic testing consent resources for Medical Specialists	https://www.genetics.edu.au/SitePages/Genomic-Testing-Consent.aspx
NSW genomic consent	https://www.aci.health.nsw.gov.au/networks/clinical_genetics/genetic-and-genomic-testing-consent-forms
Consent video for patients	http://learn-genomics.org.au/animation-genomic-testing/
Insurance implications	https://www.genetics.edu.au/SitePages/Life-insurance-products-and-genetic-testing-in-Australia.aspx
NSW Health guidelines on the disclosure of genetic information to a patient's relatives	https://www.ipc.nsw.gov.au/sites/default/files/file_manager/N_SWUse_and_Disclosure_of_Genetic_Information_Guidelines_October_2014_ACC.pdf
Australian Genomics patient education	https://www.genomicsinfo.org.au
Genomics fact sheet for patients	https://www.genomicsinfo.org.au/wp-content/uploads/2019/03/FACTSHEET-2-V1.pdf
RACP Webinar: How genomics is changing clinical practice	https://www.genetics.edu.au/SitePages/Webinar-genomics-clinical-practice.aspx

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

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This resource is available at:
<https://www.genetics.edu.au/SitePages/Intellectual-disability-childhood-syndromes-WES-ordering-guide.aspx>