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Genome-wide Sequencing (WES/WGS) as a Diagnostic Test Society Statements Table

Learn about recent society statements on genome-wide sequencing (WES/WGS)

	ACMG*	CMDA§	RACPβ	CCMG¥
Date of latest publication	July 2021[1]	June 2019[2]	February 2021[3]	May 2015[4]
Publication Type	Practice Guideline	Expert Consensus	Viewpoint	Position Statement
Sequencing Type	WES/WGS	WGS	WES/WGS	WES/WGS
Eligible Patients	Patients with one or more congenital anomalies prior to one year of age OR with intellectual disability with onset prior to age 18	Non-specific phenotype associated with intellectual disability and/or developmental delay; multiple congenital anomalies; clear clinical diagnosis associated with high level of genetic heterogeneity; previously negative WES or CMA	Any child < 10 years with: facial dysmorphism AND ≥ 1 congenital structural anomaly; OR global developmental delay/intellectual disability (moderate to severe); Test must be requested by clinical geneticist OR pediatrician following consultation with clinical geneticist	Patients with suspicion of a significant monogenic disease associated with a high degree of genetic heterogeneity; patients where specific genetic tests have failed to provide a diagnosis; when WES/WGS is a more cost-effective approach than available individual gene or gene panel testing
Tier	First or second tier test	First or second tier test	Second tier: Negative routine blood tests if indicated, negative CMA required	First or second tier test
Reporting	Not specified	Report on pathogenic, likely pathogenic, and variants of unknown clinical significance associated with the patient phenotype	Not specified	General reporting considerations discussed, including what to include on a report, managing parent sample reports and ensuring results are reviewed by certified PhD or MD

* American College of Medical Genetics and Genomics
§ Chinese Medical Doctor Association, Medical Genetics Branch
β Royal Australasian College of Physicians, Paediatric and Child Health Division
¥ Canadian College of Medical Genetics
WES = Whole-Exome Sequencing
WGS = Whole-Genome Sequencing
CMA = Chromosomal Microarray

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Informed Consent and Pretest Counseling	Set expectations, establish understanding of benefits/ limitations/potential harms of testing such as limited disease-known associations	Discuss purpose of test, test limitations, possible results, possibility of secondary findings; possibility of data reanalysis		Genetic counselling for the patient/ family should be undertaken and documented. A list of what should be discussed during the informed consent process is included in the document.
Post Test Counseling	Discuss pathogenic and likely pathogenic results, benign results, and variants of uncertain clinical significance, secondary findings, detection of nonpaternity or consanguinity, limits of testing	Counselor should explain results of test, provide information about treatment/management/risk to family members and future children, and provide patient support materials.	Results disclosure need tailored approach, should include discussion of pathogenic, likely pathogenic, and variants of uncertain significance	The patient (and family when appropriate) should receive standard-of-care genetic counselling and management regarding any new diagnosis. When a diagnosis is not identified, counseling about reanalysis/reevaluation should be discussed.
Secondary Findings	Patient can opt out with informed consent	Patient can opt out with informed consent	Referred to as Incidental Findings; Authors do not endorse the intentional clinical analysis of disease genes not related to primary indication.	Referred to as Incidental Findings; Recommend cautious approach with opt-in/opt-out. CCMG does not endorse the intentional clinical analysis of disease genes unrelated to the primary indication.
Reevaluation/Reanalysis	Value in reanalysis; frequency/strategy not specified	Not specified	In the event of a variant of uncertain significance, recommend reanalysis in 18 months, up to twice after the initial test is performed. Some situations warrant shorter reanalysis interval.	Requests for re-analysis should be initiated by a referring physician based on an established policy and may involve re-testing rather than re-analysis, at the discretion of the laboratory. Further analysis of the sequencing data through research may be an option.
WGS versus WES+CMA	WGS provides coverage of both array and exome targets with further coverage of clinically relevant regions of the genome	Not specified	Not specified	Not specified

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References

1. Manickham K, McClain MR, Demmer LA, et al. Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: an evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2021 Jul 1. Online ahead of print.
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3. Sachdev R, Field M, Baynam GS, et al. Paediatric genomic testing: Navigating medicare rebatable genomic testing. J Paediatr Child Health. 2021 Apr;57(4):477-483.
4. Boycott K, Hartley T, Adam S, et al. The clinical application of genome-wide sequencing for monogenic diseases in Canada: Position Statement of the Canadian College of Medical Geneticists. J Med Genet 2015;52: 431–437.

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