

# Medical Genetics

## Five Things Physicians and Patients Should Question

by  
Canadian College of Medical Geneticists  
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### 1 **Don't use non-invasive prenatal detection of fetal aneuploidies by cell-free DNA as a diagnostic test.**

Non-invasive prenatal detection of fetal aneuploidies by cell-free DNA, also called non-invasive prenatal testing (NIPT) and non-invasive prenatal screening (NIPS), is a method of non-invasive fetal DNA testing done through a maternal blood sample. NIPT testing for common aneuploidies, microdeletions and sex chromosome disorders is clinically available to patients in Canada. NIPT is a highly sensitive and specific screening test, but is not diagnostic. Even in high-risk populations, there can be false positive NIPT results. Genetic counselling, along with confirmatory testing via amniocentesis or chorionic villus sampling, should be done prior to using the result to impact management of a pregnancy.

### 2 **Don't make medical decisions based on results of direct to consumer genetic testing (DTC-GT) without a clear understanding of the limitations and validity of the test.**

Three types of potentially medically-relevant DTC-GT are available: (1) assessment of risk for common multifactorial diseases (e.g., diabetes, etc.); (2) targeted mutation analysis for single gene disorders; and, (3) sequencing. Some DTC-GT companies state that they do not guarantee the accuracy or reliability of their tests. Many of the significant genetic risk and protective factors for multifactorial conditions have not been identified. This leads to greatly divergent risk interpretations between companies, even when performed on the same individual. For targeted mutation analysis and sequencing, the specific test may not include all clinically relevant genes or mutations; resulting in false reassurance. Genetic changes that are only weakly associated with disease may be reported, leading to anxiety or inappropriate additional testing. When making medical decisions based on results of genetic testing, the test should meet the recommendations made by the Canadian College of Medical Geneticists in 2012. Not all DTC-GT meet these recommendations.

### 3 **Don't order a chromosome analysis by doing a karyotype for individuals with intellectual disability/developmental delay of unknown etiology.**

Microarray is the first line test for individuals with intellectual disability/developmental delay without a recognizable syndrome. Indeed, a microarray has a much higher detection rate (15 - 20%) compared to a karyotype (3 - 4%) in individuals presenting for this clinical indication. A karyotype remains important in limited clinical situations where a specific numerical or structural chromosomal syndrome, such as Down syndrome, is suspected.

### 4 **Don't order whole exome sequencing prior to genetic counselling.**

Whole exome sequencing (WES) is a powerful test for individuals suspected of having an underlying genetic diagnosis. However, WES increases the likelihood of unexpected findings, which may or may not be clinically significant. Further, due to methodological limitations, WES may not always be the correct test to order as WES will not detect all genetic causes of disease (for example, it will not detect chromosomal structural differences). Both informative and uninformative results can lead to complex patient and family psychosocial repercussions, and could impair future insurability. Genetic counselling facilitates informed decision-making. Given complexity of results, WES should only be ordered after counselling by a qualified health care provider.

### 5 **Don't order carrier testing in children.**

Carrier testing is primarily useful in the reproductive period to determine the risk of an individual having a child affected by the condition for which testing is being considered. Knowing that a child is a carrier of an X-linked or autosomal recessive condition usually does not alter medical care in the pediatric years since most carriers are unaffected. Thus, in most situations, there is not a medical indication for carrier testing in a child. Undertaking carrier testing of a child violates the right of the child to make his or her own decision about testing and could potentially impair future insurability. An exception could be made for a mature adolescent who may be able to understand the reproductive implications of carrier testing after appropriate genetic counselling.

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## How the list was created

The medical genetics Choosing Wisely Canada recommendations were generated by the Ethics, Education and Public Policy (E2P2) committee of the Canadian College of Medical Geneticists (CCMG) in consultation with the entire membership of the CCMG. In the summer of 2015, the E2P2 committee generated a first list of potential statements and a pilot survey was distributed during the CCMG annual conference in September 2015. Based on the feedback received, the E2P2 committee modified the statements and generated new ones. An electronic survey (via Survey Monkey) was distributed to the entire CCMG membership in March 2016; members were asked to rank their 5 favourite statements. The answers were weighted and the 5 top statements were selected. Members of the E2P2 committee reviewed the literature and generated a rationale for each of the 5 statements. The 5 statements and their rationale were orally presented during the general assembly of the CCMG annual meeting in June 2016. Comments received at that time led to a slight revision of the wording of the rationale of some statements by the members of the E2P2 committee. The statements and their rationale were then posted online for comments in the members-only section of the CCMG website for one month during the summer of 2016. Members of the CCMG all received an email prompting them to review these statements. The E2P2 committee reviewed all comments received and slightly altered the wording of some statements. The list was then circulated to all medical professional society leads engaged in Choosing Wisely Canada for review. Comments received were considered by the E2P2 committee and the list was finalized.

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## About the Canadian College of Medical Geneticists

Medical genetics is the branch of medicine concerned with the effect of genetic variation on human development and health and also with the study, diagnosis, management, and prevention of genetic and related disorders in individuals, families, and communities. The Canadian College of Medical Geneticists is the national specialty society that represents genetic specialists (MDs and PhDs) who see patients with genetic conditions and/or direct laboratories that perform diagnostic testing for genetic conditions.



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## About Choosing Wisely Canada

Choosing Wisely Canada is the national voice for reducing unnecessary tests and treatments in health care. One of its important functions is to help clinicians and patients engage in conversations that lead to smart and effective care choices.

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