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.

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.

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.

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.

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.

Don’t order rapid or expedited testing if the results will not change management.
Rapid genomic tests are increasingly available both pre- and postnatally and can decrease time to diagnosis compared to standard tests. Yet, there is often an added cost to their use and their utility and cost-effectiveness are not entirely
Don't automatically order metabolic testing for a child with isolated global developmental delay/intellectual disability.

Intellectual developmental disorders (IDD) affect 2.5% of the population. Inherited metabolic disorders (IMD's) may present with IDD and often other neurologic or systemic features and some IMD's are treatable. Despite years of implementing a biochemical testing algorithm on a research basis in one province, the yield of testing was not increased for IMD's. There are significant harms associated with over-investigation. Although the cost of biochemical testing is inexpensive compared to molecular or specialized tests, it is still a significant burden on the health care system. The cost of the tests is not the only consideration, since significant human resources are required for pre-test counselling, coordination of sample collection, transport and analysis, interpretation of results and follow-up. Even more importantly, there may be harm to children and families subjected to further blood draws and urine tests, extending the diagnostic odyssey as repeat testing is often required for a positive or uncertain result. There is extensive literature on the harms of false positives from newborn screening, but this is balanced against the yield of testing for treatable IMD's on the newborn screen and efficacy of early intervention. Similar data of the benefits of screening all children with IDD for IMD's does not exist. There are well-recognized red flags suggestive of an IMD in children with IDD and it would be appropriate to do targeted metabolic testing in those situations (so called “intellectual disability plus”). Consideration should also be given to patients who did not have newborn screening (NBS) for IMD. Further biochemical testing may also be a valuable tool when molecular testing is negative or
uncertain, to provide functional evidence of pathogenicity.

**Don’t proceed with genetic testing too early in a patient’s presentation.**

Watchful waiting refers to a policy of taking no immediate action with respect to a situation or course of events but of following its development intently. Different areas in medicine employ watchful waiting and have found it not to impact patient outcome in select situations. Given the increased availability, genetic testing is often requested early in a patient's presentation. However, genetic conditions and our ability to understand and diagnose them frequently evolve over time. Early investigation may result in increased cost due to repeated application of non-targeted testing, with concomitant increased likelihood of detecting variants of uncertain significance, as well as poorer result interpretation for reports reliant on complete phenotyping. When the phenotype is incomplete or unclear, and there are no red flags, such as deteriorating patient status, potential for change in management, or information necessary for timely reproductive counseling, watchful waiting may be appropriate.
How the list was created

Recommendations 1-5
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 options. 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 statements were then reviewed by the board of directors for the CCMG. They were 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.

Recommendations 6-12
The additional 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. A list of potential statements was drafted in the fall and winter of 2019 and then submitted to CCMG membership to review and complete an electronic survey. The survey was completed in spring 2020 and analyzed by the E2P2 committee leading to modifications of some of the statements. Members of the E2P2 committee reviewed the literature and generated rationales for the statements. The statements were then reviewed by the board of directors for the CCMG. They were 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.

Sources

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.

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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