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Choosing Wisely Canada: The Canadian College of Medical Geneticists' (CCMG) list of five items physicians and patients should question

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Choosing Wisely Canada aims to reduce patient harm by promoting discussion and awareness of unnecessary tests, procedures and treatments. Organised by Canadian physicians and the Canadian Medical Association,¹ it is modelled after the American Choosing Wisely campaign.² The concept of 'Choosing Wisely' is now an international effort, across more than 15 countries.¹

The advances in genome sequencing technology have allowed for increased diagnostic yield while unmasking secondary findings or information of limited clinical utility.³ These findings may contribute to further unnecessary diagnostic testing, lifelong surveillance for low-risk sequelae and side effects of preventative treatment in healthy individuals, all of which may have economic consequences.³ Therefore, recommendations by genetics professionals to improve health and decrease costs are needed.

The Canadian College of Medical Geneticists (CCMG) is the national organisation that establishes Canadian professional and ethical standards for medical genetics services. The CCMG through the leadership of the Ethics, Education, and

Public Policy Committee (E2P2), undertook an iterative process to formulate five items physicians and patients should question in medical genetics as part of Choosing Wisely Canada.

The initial statements (Summer 2015) were generated by a subcommittee of E2P2. Seven statements with the option for additions were presented in a pilot survey at the 2015 CCMG annual conference. For reference, the five statements from the American Choosing Wisely campaign were also provided.⁴ After feedback, the statements from the pilot survey were modified or replaced by new ones and distributed to the entire CCMG membership (n=318) by electronic survey (SurveyMonkey, San Mateo, California, USA) in March 2016 for ranking. Answers were weighted, and the five top statements were selected. The results of statement ranking by 53/318 (17%) members responding to the electronic survey can be found in [table 1](#). The top five statements chosen for literature review are bolded.

E2P2 reviewed the literature, generated a rationale for each statement and presented these orally during the 2016 CCMG annual meeting for comment. Following revision, statements and their rationale were posted for comment online for 1 month with one reminder email sent to the membership. E2P2 reviewed comments and edited statements prior to submission to the 151 Choosing Wisely Society Leads from other specialties (Fall 2016). Comments were received and addressed, including a change from 'non-invasive prenatal testing' (NIPT) to 'non-invasive prenatal detection of fetal aneuploidies by cell-free DNA' and keeping the term 'children' rather than 'minors' despite objection, to be consistent with other society statements.^{5,6}

The final statements as below were submitted to the Choosing Wisely Canada organisation on 1 January 2017:

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 and non-invasive prenatal screening, is a method of non-invasive fetal DNA testing done through a maternal blood sample. NIPT testing for common aneuploidies, microdeletions and sex chromosome disorders⁷ is clinically available to patients in Canada. NIPT is a highly sensitive and specific screening test but is not diagnostic.⁸ 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 WITHOUT A CLEAR UNDERSTANDING OF THE LIMITATIONS AND VALIDITY OF THE TEST
Three types of potentially medically relevant direct to consumer genetic testing (DTC-GT) are available: (1) assessment of risk for common multifactorial diseases (eg, diabetes); (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.⁹ For targeted mutation analysis and sequencing, the specific test may not include all clinically relevant genes or mutations, resulting in false reassurance.¹⁰ 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 CCMG in 2012.¹¹ 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 AETIOLOGY
Microarray is the first-line test for individuals with intellectual disability/

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Table 1 Rating average following the membership survey (n=53)

Statements	Response count	Rating average*
Don't order whole exome sequencing prior to genetic counselling.	42	3.60
Don't make medical decisions based on results of direct to consumer genetic testing (DTC-GT) without having a clear understanding of the limitation and validity of the specific test used.	39	3.54
Don't order carrier testing in paediatric patients if these results will not impact their health care management in the paediatric period.	41	3.46
Don't use NIPT as a diagnostic test.	26	3.27
Don't do a karyotype in a patient presenting for developmental delay (as microarray is now the standard of care).	41	3.20
Don't order an amniocentesis for an increased maternal AFP if the 18–20 week ultrasound was normal with adequate visualisation.	22	2.77
Don't do a karyotype if a microarray has already been ordered/performed.	19	2.74
Don't order genetic testing for <i>HFE</i> -related hemochromatosis in patients who have an isolated mild elevation of ferritin.	28	2.61

*Weighted based on whether statement was chosen as first, second, third, fourth or fifth choice.

AFP, alpha feto protein; NIPT, non-invasive prenatal testing.

Bolded statements selected for literature review.

developmental delay without a recognisable syndrome.¹² Indeed, a microarray has a much higher detection rate (15%–20%) compared with a karyotype (3%–4%) in individuals presenting for this clinical indication.¹³ 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 (WES) PRIOR TO GENETIC COUNSELLING

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. Furthermore, due to methodological limitations, WES may not always be the correct test to order as WES will not detect all genetic causes of disease (eg, it will not detect chromosomal structural differences).¹⁴ Both informative and uninformative results can lead to complex patient and family psychosocial repercussions¹⁵ 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 healthcare 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.⁵ Knowing that a child is a carrier of an X-linked or autosomal recessive condition usually does not alter medical care in the paediatric years since most carriers are unaffected. Thus, in most

situations, there is not a medical indication for carrier testing in a child.⁶ Undertaking carrier testing of a child violates the right of the child to make his or her own decision about testing and could 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.

This expert CCMG consensus reflects Choosing Wisely statements covering a broad range of genetic issues relevant to Canadians. As no demographic information was collected from the membership survey, it is not known whether the responses were representative of both laboratory geneticists and clinical geneticists, but there were equal opportunities for both to provide feedback.

It is interesting that only one statement regarding WES is similar to the American recommendations.⁴ While the American version was specific about recommending informed consent, particularly around secondary findings, the Canadian version recommends genetic counselling, which is more generalised and would encompass informed consent as part of the counselling process. Three of the American statements target specific genetic tests (*APO-E*, *MTHFR* and *HFE*).⁴ In Canada, some of these tests are not routinely offered or covered by provincial healthcare. It is possible that the perspective taken in generating these recommendations in the USA versus Canada differs based on the target audience requesting the tests, the healthcare systems or the practice differences between the two countries. Regardless of the reason, this report suggests that there is value in determining country-specific recommendations. As technology and knowledge advance, these statements may need to be revised.

As the goal of the Choosing Wisely campaign is to reduce patient harm by generating greater awareness of responsible use of testing and procedures, these five recommendations represent the start of a dialogue that will hopefully optimise utilisation of resources related to medical genetics.

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