

# Fragile X Testing in Obstetrics and Gynaecology in Canada

This committee opinion has been prepared by the Genetics Committee of the Society of Obstetricians and Gynaecologists of Canada (SOGC) and the Prenatal Diagnosis Committee of the Canadian College of Medical Geneticists (CCMG) and approved by the Executive of the SOGC and the Board of Directors of the CCMG.

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**Key Words:** Carrier screening, fragile X syndrome, premature ovarian failure, mental retardation

## Abstract

**Objective:** To provide Canadian family physicians, genetic counsellors, medical geneticists, midwives, and obstetrician-gynaecologists with recommendations regarding screening for fragile X in the obstetrical and gynaecological population.

**Methods:** Medline, the Cochrane Library, journals, and textbooks were searched for English-language articles, published between 1966 and March 2008, relating to fragile X testing outcomes. Search terms included fragile X, screening, prenatal testing, pregnancy outcome, premutation, trinucleotide repeats, and ovarian failure. All study types were reviewed. Randomized controlled trial results were considered evidence of the highest quality, followed by results of cohort studies. Key individual studies on which the recommendations are based are referenced. Supporting data for each recommendation are summarized with evaluative comments and references.

This document represents an abstraction of the information.

**Evidence:** The quality of evidence reported in this document has been described using the criteria outlined in the report of the Canadian Task Force on Preventive Health Care.

## Recommendations

1. Any testing for fragile X syndrome must occur only following thorough counselling and with the informed consent of the woman to be tested. (III-A)
2. Fragile X testing is indicated for a woman with a family history of fragile X syndrome, fragile X tremor/ataxia syndrome, or premature ovarian failure (in more than one family member) if the pedigree structure indicates that she is at risk of inheriting the mutated gene. Referral to a medical geneticist for counselling and assessment should be considered in these cases. (II-2A)
3. Fragile X testing is indicated for women who have a personal history of autism or mental retardation/developmental delay of an unknown etiology or who have at least one male relative with these conditions within a three-generation pedigree. (II-2A)
4. Fragile X testing is indicated for women who have reproductive or fertility problems associated with an elevated level of follicle stimulating hormone before the age of 40. (III-A)
5. Prenatal fetal testing via chorionic villus sampling or amniocentesis should be offered to women who are confirmed to be carriers of a premutation or full mutation of the fragile X gene (FMR-1). (II-2A) Pre-implantation genetic diagnosis is available as another reproductive option. (III-A)
6. Population screening for fragile X syndrome for all women in the reproductive age-range is feasible. However, it should be considered only when there is a provincial/regional program that

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**Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care**


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Quality of Evidence Assessment*	Classification of Recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

\*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.<sup>75</sup>

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can test and adequately counsel the targeted population about the meaning and implications of the results. (II-2B)

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