

Title:	Genetic test for fragile X syndrome – January 2002
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Aim

To assess the safety and effectiveness of nucleic acid amplification for fragile X testing and under what circumstances public funding should be supported for the procedure.

Conclusion and results

Safety: An extensive literature search did not identify any studies reporting adverse events associated with i) testing individuals suspected of having fragile X syndrome or ii) cascade testing of relatives of affected individuals. Similarly no adverse events specific to prenatal diagnosis of fragile X (i.e. amniocentesis or chorionic villus sampling) were identified in the literature, although the potential adverse events of these procedures are well documented.

Effectiveness: Evidence of the accuracy of the tests from the published literature indicates that cytogenetic testing is not as accurate as molecular techniques (i.e. PCR and Southern blot) in detecting the fragile X full mutation. With regards to a fragile X premutation cytogenetic testing was unable to detect such a mutation at all. The sensitivity of cytogenetic testing varied across studies, although specificity was consistently high with few false positive results reported. Studies comparing PCR to Southern blot reported high sensitivity and specificity. It should be noted however that PCR may not reliably amplify full mutations and Southern blot is usually necessary to reliably demonstrate a full mutation.

Cost-Effectiveness: A cascade testing program is estimated to cost up to 4\$ million annually, and would result in a cost per initial case detected of between \$14,000 and \$28,000.

Recommendation

Public funding should be supported for Nucleic Acid Amplification (NAA) in those with specific clinical features of Fragile X (A) syndrome, including intellectual disabilities and in first and second degree relatives of individuals with Fragile X (A) mutation; and Southern blot where the results of NAA testing are inconclusive.

Method

MSAC conducted a systematic review of the biomedical literature (Cochrane library, EBM-Reviews-ACP Journal Club, Medline, PreMedline, Current Contents, Biological abstracts and PsycINFO) from commencement to June 2001. The above sources were searched for cross sectional studies which evaluated the diagnostic characteristics of at least two test (PCR, Southern blot or cytogenetic test) for the diagnosis of fragile X (full or premutation).