Before, Between & Beyond Pregnancy
The National Preconception Curriculum and Resources Guide for Clinicians

Guidance for Preconception Fragile X Carrier Screening

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This guidance should not substitute for clinical judgments or expert consultation

Opinions of Genetics Health Professionals

Acharya K & Friedman Ross L. Fragile X screening: Attitudes of genetic health professionals. Am J Med Genet Part A 2009;149A:626-632.

Fragile X syndrome is caused by mutations in the FMR1 gene. The technology currently exists for the population-wide identification of pre- and full mutations in individuals of both genders. Policy decisions concerning population screening must consider the social acceptability and the ethical implications of various testing and screening programs. These implications are made more complicated by the wide array of clinical symptoms associated with the spectrum of trinucleotide expansions in the FMR1 gene, including classic fragile X syndrome, fragile X associated tremor/ataxia syndrome (FXTAS) and premature ovarian failure (POF).

In the current study, the authors surveyed 273 medical geneticists and genetic counselors, described collectively as genetics health professionals (GHP), about their attitudes toward population screening for FMR1 mutations. The following factors were discussed in detail: (1) timing (preconception, prenatal, postnatal), (2) the population to be screened (targeted or universal, age), and (3) the screening methodology (gender, type of mutation identified).

The majority of respondents (72%) stated that preconception was the single best time to offer population based screening. Sixty percent (60%) also stated they supported the creation of a newborn screening (NBS) program for fragile X syndrome, though of those in favor, only 21% favored the traditional mandatory NBS offered for other conditions in the US. Despite greater preference for preconception screening, implementing preconception screening is often difficult due to lack of insurance coverage for such testing before pregnancy. Therefore, most current research is focused on NBS, perhaps

because the logistical and economic barriers to preconception screening present a greater challenge than the existing state-run NBS infrastructure.

Of those who favored preconception screening, a majority preferred targeted screening based on a positive family history of FMR1 related disorders as opposed to a general population based screening program. This is consistent with current ACOG and ACMG guidelines, which do not recommend universal preconception or prenatal screening for FMR1 mutations. Though a majority of respondents supported newborn screening, the AAP, the Advisory Committee on Heritable Disorders and Genetic Diseases (ACHDGDNC) and the ACMG do not currently endorse population wide NBS for fragile X syndrome. Additionally, over half of respondents would agree to order FMR1 testing on the typically developing child or adolescent with a positive family history (gender non-specified). This is not consistent with the AAP, which only recommends testing in childhood as part of the diagnostic evaluation of a child with cognitive impairments and/or autism.

Approximately 90% of GHP surveyed believed it was at least moderately appropriate for a newborn screening program to include male and female infants, on the basis that early developmental services could be available to all infants with a full mutation from birth. A slight majority supported the identification of full and premutations as part of a newborn screening program. As the association between FMR1 premutation status and developmental delays has not been proven, this identification is inconsistent with current professional guidelines that discourage predictive testing of children for adult onset conditions and/or knowledge of carrier status that is relevant to reproductive planning.