Title **Evaluation of Molecular Tests for Prenatal Diagnosis of Chromosome Abnormalities**

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Aim

To measure the technical performance of the molecular tests fluorescence in situ hybridization (FISH) and quantitative polymerase chain reaction (Q-PCR) vs. karyotyping, to estimate the relative costs of molecular tests under various conditions, to establish the value to women, clinicians, and others of more rapid molecular test results, to assess the cost effectiveness of molecular tests, and to consider changes in testing protocols.

Conclusions and results

FISH and Q-PCR are not configured to test for rarer abnormalities and do not directly replace karyotyping. Using them to replace karyotyping will leave some abnormalities undisclosed by screening. FISH and Q-PCR are as reliable and precise as karyotyping for the 5 most common chromosome abnormalities. Although 57% of obstetricians prefer molecular tests for most patients and karyotyping for a minority, only 15% would combine both tests. Midwives expressed similar views. Most women and partners expressed a pretest preference for molecular tests. Quality and anxiety measures linked faster test results to a significant increase in health status. Molecular tests cost less than karyotyping. As a replacement in larger laboratories (>1100 specimens per annum), Q-PCR is preferred; for smaller laboratories (<450), FISH is preferred.

Five testing regimes were assessed for cost effectiveness: 1. Molecular test and karyotyping for all women. 2. Molecular test as a replacement for karyotyping. 3. Molecular test for all plus karyotyping for high-risk women. 4. Karyotyping for all plus molecular test for high-risk women. 5. Parental choice plus karyotyping for high-risk women. Cost-effectiveness analysis found regimes 2, 3, and 5 to be more cost effective than karyotyping. Cost-utility analysis showed a cost per QALY gained of £23 542 to £41 939 for 1 (2–5 could not be assessed by this technique). Regimes 2, 3, and 5 do not detect some rare chromosome abnormalities. Regime 1 could increase annual UK test costs by up to £2.8 million, regimes 2 and 3 save up to £1.76 million per annum, and regime 5 two-thirds of this saving. Regime 4 is cost neutral. Prenatal testing is determined by clinicians, laboratories, and hospitals. Inequities exist, as do regional and local variations in selecting women for screening. Molecular testing without appropriate implementation protocols will result in wide variations. Inattention to patient information will create ethical problems.

Methods

Two-stage trial; assessed in a blinded comparison of molecular tests against karyotyping in a laboratory (stage 1); effectiveness and cost effectiveness measured in a service setting (stage 2). Measurement of anxiety and health status of women; willingness to pay (WTP) for 4 stakeholder groups; and survey of UK obstetricians and midwives.

Further research/reviews required

It was not possible to assess the impact on quality of life and anxiety of replacing karyotyping with molecular tests for all women or selected groups of women within this study. This could be addressed ethically as tests are introduced into service, and should form part of the implementation. Alternative mechanisms to deliver test results should be explored to optimize the advantage of faster results. There is little evidence of the potential impact of false-negative results on parents and on the healthcare system. Further research is needed if molecular tests are to replace some karyotyping tests.

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