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Title **Diagnostic Strategies Using DNA Testing for Hereditary Hemochromatosis in At-Risk Populations: A Systematic Review and Economic Evaluation**

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Aim

To evaluate the use of DNA tests for detecting hereditary hemochromatosis (HHC) in subgroups of patients suspected of having the disorder and in family members of those diagnosed with hemochromatosis.

Conclusions and results

Objectives: 1) determine the clinical validity of DNA tests to diagnose HHC; 2) summarize the evidence on the clinical utility of diagnostic strategies using DNA tests to detect cases for treating or monitoring in terms of clinical effectiveness and cost effectiveness; 3) compare the costs and consequences by decision analysis modeling of diagnostic algorithms for HHC and family testing strategies with and without DNA testing in terms of cost per case detected: 4) review the psychosocial literature and compare the psychosocial benefits and harms of adding DNA testing to diagnostic algorithms; and 5) identify priorities for future primary research.

We found 11 studies that could be used to estimate the clinical validity of genotyping for the C282Y mutation in diagnosing genetic hemochromatosis. Study quality varied, and different definitions had been used for the clinical phenotype. Clinical sensitivity of C282Y homozygosity for hereditary hemochromatosis ranged from 28.4% to 100% in the 11 studies; when considering only the most relevant studies, sensitivity ranged from 91.3% to 92.4%. Clinical specificity ranged from 98.8% to 100%. No clinical effectiveness studies met the inclusion criteria for the review. Two cost-effectiveness studies conducted in North America were identified, both of reasonable quality, but their generalizability to the UK is unclear.

Recommendations

Results suggest that using a diagnostic strategy that incorporates DNA testing saves costs in identifying cases and testing offspring of hemochromatosis patients. The results for siblings suggest that DNA testing is not cost saving, although cost effectiveness might be shown if the benefit of reassurance were to be incorporated in modeling. The preferred strategy is DNA testing in conjunction with testing iron parameters when clinical indications clearly raise suspicion of being at risk for hemochromatosis due to biochemical criteria or familial risk.

Methods

See Executive Summary link at www.ncchta.org/project/1502.asp.

Further research/reviews required

Epidemiological research (using national databases) is required on the environmental and other genetic factors that affect the penetrance of the genetic mutation, to identify those people homozygous for the mutation who are likely to develop iron overload.

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