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Title **The Clinical and Cost Effectiveness of Testing For Cytochrome P450 Polymorphisms in Patients Treated with Antipsychotics: A Systematic Review and Economic Evaluation**

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Aim

To determine whether testing for cytochrome P450 (CYP) polymorphisms in adults entering antipsychotic treatment for schizophrenia leads to improved outcomes, is useful in medical, personal or public health decision making, and is a cost effective use of healthcare resources.

Conclusions and results

Tests to determine genotypes appear to be accurate, but not all aspects of analytical validity were reported. Given the absence of convincing evidence from clinical validity studies, the lack of clinical utility and economic studies, and the unsuitability of published schizophrenia models, no model was developed. Instead, key features and data requirements for economic modeling are presented. For analytical validity, 46 studies of different genotyping tests for 11 different CYP polymorphisms (most commonly CYP2D6) were included. Sensitivity and specificity were high (99%-100%). For clinical validity, 51 studies were found. In patients tested for CYP2D6, an association between genotype and tardive dyskinesia (including Abnormal Involuntary Movement Scale scores) was found. The only other significant finding linked the CYP2D6 genotype to Parkinsonism. One small unpublished study met the inclusion criteria for clinical utility.

Recommendations

See Executive Summary link www.hta.ac.uk/project/1714.asp.

Methods

See Executive Summary link www.hta.ac.uk/project/1714.asp.

Further research/reviews required

Although the evidence base does not support the use of pharmacogenetic testing in this area, it does indicate that further study in each of the key areas is needed to either demonstrate or refute the ability of pharmacogenetic testing to assist in developing individualized patient care in schizophrenia. Recommendations for future research cover both aspects of research quality and data that will be required to inform the development of future economic models. Analytical validity 1) Studies of analytical validity need to be explicit about patient selection, quality control, assay robustness, and the sensitivity and specificity of tests. Study findings should not only report on allele frequencies, but also report appropriate genotype data. Clinical validity 1) Further evidence must link phenotype to genotype. Prospective studies need to include larger numbers of patients with the UM (multiple copies of the wt allele) and poor metaboliser (mut/mut) phenotypes. 2) Studies need to consider the impact of environmental factors, eg, smoking, concomitant medicines, medication adherence, and ethnicity. In relation to medication adherence, genotypes need to be related not only to clinical parameters, but also to pharmacokinetic parameters. 3) Studies need to ensure that all currently used antipsychotics are investigated. However, given the uncertainty about the full extent of the role played by CYP2D6, further studies focusing on patients taking risperidone and olanzapine would also be useful. 4) Future research must consider a comprehensive approach that considers not only CYP isoforms involved in the metabolism of antipsychotics, but also other targets, eg, dopamine and 5-hydroxytryptamine receptors. Clinical utility 1) Prospective clinical utility studies are needed. As with clinical validity they should ensure that all currently used antipsychotics are investigated although, given their importance to the NHS (and the uncertainty about the full extent of the role played by CYP2D6), further studies focusing on patients taking risperidone and olanzapine would be particularly useful.

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