Ethnic differences in the risks of adverse reactions to drugs used in the treatment of psychoses and depression: a systematic review and meta-analysis

Ormerod S, McDowell SE, Coleman JJ, Ferner RE

CRD summary
This review concluded that there was varied and inconsistent evidence for ethnic differences in adverse drug reactions to antipsychotic and antidepressant treatments. Given some potential methodological limitations related to the under-reporting of study characteristics and quality, the extent to which the authors' conclusion is reliable is unclear.

Authors' objectives
To evaluate adverse drug reactions following treatment for psychoses and depression in relation to ethnicity.

Searching
MEDLINE, EMBASE and PsycINFO were searched for studies published from 1950 to March 2006. There were no language restrictions. Search terms were reported. Personal files and reference lists from included studies and relevant reviews were scanned to identify further studies.

Study selection
Studies of at least two different ethnic groups of adults treated with antipsychotic or antidepressant drugs listed in British National Formulary sections 4.2 and 4.3 and that measured adverse drug reactions were eligible for inclusion in the review. Case reports and cases series were excluded.

Consistent terminology was applied by the review authors to ethnic classification reported in the papers and patients were grouped by ethnic origin as Black (African ancestry), East Asian (such as China, Japan and Korea), South Asian (Indian subcontinent), Hispanic (Latin American) and White (European ancestry). Adverse drug reactions associated with antipsychotic drugs were tardive dyskinesia, extra pyramidal symptoms, hyperglycaemia, diabetes mellitus, cardiovascular events, metabolic syndrome, weight gain, blood disorders and other general drug reactions. Specific adverse drug reactions associated with antidepressant treatment included delirium, sexual dysfunction and insomnia.

Two reviewers independently selected studies for inclusion. A third reviewer examined studies identified by only one reviewer.

Assessment of study quality
Study quality was assessed using Cochrane criteria to address selection bias, performance bias, attrition bias and detection bias.

Two reviewers independently assessed study quality.

Data extraction
Data were extracted to enable calculation of relative risks (RR) and 95% confidence intervals (CI) for adverse drug reactions. Authors were contacted for missing data or for clarification of existing data.

Data extraction was performed independently by two reviewers.

Methods of synthesis
Where possible, studies were pooled by drug class and type of adverse reaction in a fixed-effect or random-effects meta-analysis, depending on the level of heterogeneity. Statistical heterogeneity was assessed using $X^2$ and $I^2$ statistics. Where meta-analysis was not possible, a narrative synthesis was presented.
Results of the review
Fifty-one studies were reported to be included in the review. It was not possible to determine the overall number of patients. Full results of the quality assessment were not presented, although the authors acknowledged that most studies had a small sample size, lack of randomisation, limited length of follow-up and small numbers of non-white patients.

In pooled analyses of antipsychotic drugs, the only statistically significant finding was that East Asian patients had a greater risk of extra pyramidal symptoms compared to non-East Asian patients (RR 1.4, 95% CI 1.1 to 1.7) in four studies that were reported to be low quality. Pooled analyses of black versus white patients and tardive dyskinesia, black versus non-black patients and hyperglycemia and white versus non-white patients and diabetes mellitus showed no significant differences in relative risk.

There were no pooled analyses of treatments with antidepressant drugs. Results were varied and inconsistent.

Authors' conclusions
There was varied and inconsistent evidence for ethnic differences in adverse drug reactions to antipsychotic and antidepressant treatments.

CRD commentary
The review question was clear and supported by broad inclusion criteria. As a result, the included studies appeared to comprise largely heterogeneous and variably-defined ethnic classification data. Full study details were not provided, which made it difficult to verify this and the generalisability of the review findings. The search strategy included some relevant sources. Language bias was minimised; publication bias was a possibility. An established validity assessment tool was applied, but the relevance of this was uncertain given that the included study designs were not reported. As full quality assessment results were not presented, the reliability of included studies could not be verified. The review process was carried out with sufficient attempts to minimise error and bias. An appropriate plan for synthesis was presented, based on levels of heterogeneity.

The authors’ conclusion reflected the evidence presented. However, the extent to which the results could be explained by confounding factors (such as differences in demographics, environmental factors, disease severity, comorbidities and medication regime) could not be determined from the information provided. Given the potential methodological limitations identified, the extent to which the authors’ conclusion is reliable is unclear.

Implications of the review for practice and research
Practice: The authors stated that the results of this review should not cause clinicians to become inappropriately cautious in prescribing certain drugs to specific ethnic groups.

Research: The authors stated that well-designed studies in multi-ethnic populations were needed and should use consistent definitions of ethnicity.

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