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**Prescribing antidepressants based on patients' genetic makeup does not improve the effectiveness of treatment**



Genetic testing that helps doctors select the right antidepressant for a patient did not lead to better improvements in depressive symptoms than standard prescriptions based on clinical guidelines, according to a clinical trial in Australia conducted by an international team of researchers.

Led by professor Jonathan Emery of NTU's Lee Kong Chian School of Medicine and published in The Lancet Primary Care, the study challenges previous findings that using a patient's genetic information to personalize antidepressant treatment leads to better outcomes.

According to the researchers, the trial is the first to test this approach for patients with depression in primary care.

**Putting precision medicine to the test**

Understanding how a person's unique genetic profile affects the way they respond to medications, also known as pharmacogenetics, is increasingly being explored to optimize treatments.

A test that uncovers these genetic variations may help physicians identify and prescribe drugs that are more effective for individual patients.

In the trial, 552 adults aged 18 to 65 with moderate-to-severe depressive symptoms across 19 general practices in Victoria, Australia, were randomly assigned to one of two groups.

Primary care physicians treating participants in one group received prescribing recommendations based on patients' genetic profiles, specifically variations in the CYP2C19 and CYP2D6 genes, which influence how the body metabolizes common antidepressants. Physicians caring for the other group received the report with recommended treatments based on Australian Therapeutic Guidelines.

To minimize bias, neither the participants nor the physicians knew who received the standard prescriptions or the pharmacogenetically guided treatments.

Both groups showed improvements in depressive symptoms 12 weeks after their doctor received the prescribing recommendations. However, patients who received treatment based on their genetic information did not experience significantly more improvement in their symptoms than patients whose treatment was guided by standard clinical guidelines. At 12 weeks, there was also no significant difference in the proportion of patients in remission from the two groups. Similarly, the percentage of patients in both groups who responded to the treatment at 12 weeks was not significantly different.

The findings contrast with previous studies that show that pharmacogenomic-informed prescribing led to more favorable outcomes compared with guideline-based treatments in patients with severe depression under the care of specialist psychiatrists.

The researchers say it could be that pharmacogenomic testing is only useful in selected groups such as those not responding to an antidepressant or experiencing significant side effects.

"While genetic testing may help us make more informed decisions about which treatments are most suitable for a particular patient, these results show that it may not necessarily improve outcomes in everyone. We need to better understand how pharmacogenomic results can be incorporated into clinical workflows and at what point in the treatment journey it should be used," says Dr. Sabrina Wong, senior consultant family physician at NHG Health, who was not involved in the study.

The study highlights the challenges of implementing pharmacogenomic tests in primary care and ensuring a patient's pharmacogenomic results are considered when starting a new antidepressant or if someone is not responding to an existing antidepressant. The findings also have broader implications for initiatives that are exploring precision medicine for health care, such as Singapore's National Precision Medicine strategy.

"Although studies suggest that prescribing antidepressants based on the patient's genetic makeup could lead to more effective treatments, our findings show that having more genetic information does not automatically translate into better clinical outcomes," says Emery.

"A greater understanding of which patients are most likely to benefit from pharmacogenomic-informed prescribing is required before recommending it for routine use."

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