狮城新闻

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Translated from Chinese

NTU clinical trial: Gene-based selection of antidepressants did not improve overall efficacy.

Can a single genetic test more accurately select the most suitable antidepressant for each patient?

This is a compelling concept in the field of precision medicine. However, a large clinical trial led by Professor Jonathan Emery of the NTU Lee Kong Chian School of Medicine showed that, at least in Australia's primary healthcare settings, prescribing based on two drug metabolism genes did not lead to better overall treatment outcomes than following existing clinical guidelines.

This study does not mean that "genetic testing is completely useless," but rather that current evidence does not support the routine use of this practice for all patients with depression in primary care settings.

How, in theory, can pharmacogenomics help with drug selection?

Drug metabolism rates vary among individuals. Pharmacogenomics aims to help doctors predict how a patient might metabolize a particular drug by analyzing genetic variations, thereby allowing them to select more appropriate drugs or dosages.

The PRESIDE trial focuses on the CYP2C19 and CYP2D6 genes. These genes influence how the body metabolizes many commonly used antidepressants and are therefore frequently used to generate pharmacogenomic recommendations.

However, the treatment response to depression is not solely determined by drug metabolism. Symptom type, disease severity, other medications, physical condition, treatment adherence, and living environment can all influence the final outcome.



How was the experiment conducted?

The research team recruited 552 adults aged 18 to 65 with moderate to severe depressive symptoms from 19 general practice clinics in Victoria, Australia, and randomly assigned them to different groups.

One group of patients received prescription recommendations from their doctors based on CYP2C19 and CYP2D6 test results; the other group received recommendations based on the Australian Treatment Guidelines. Both reports listed candidate medications and dosages, but the final medical decision was made by the doctor and the patient.

The trial employed a double-blind design, meaning neither the patients nor their doctors knew which type of prescription they received, in order to minimize the expected effect and observational bias.

After 12 weeks, both groups showed improvement.

Twelve weeks after receiving the prescription from their doctors, participants in both groups showed improvement in depressive symptoms compared to baseline. However, the gene-guided group did not show greater improvement, and there were no significant differences between the two groups in symptom relief rates and treatment response rates.

The PHQ-9 scores reported in the paper showed an average decrease of 3.45 points in the gene-guided group and an average decrease of 4.63 points in the guideline group. In other words, adding gene information did not make the treatment performance superior to standard clinical guidelines.

This study, published in *The Lancet Primary Care*, argues that it is not currently advisable to routinely implement this pharmacogenomics-guided protocol in primary healthcare in Australia.

Why is it different from some previous studies?

Previous studies in specialized psychiatric medicine have found that genome-guided prescriptions may lead to more favorable outcomes in patients with more severe conditions or more complex treatment situations.

PRESIDE is the first trial to test this approach in primary care settings for patients with depression. The patient population, stage of treatment, how physicians use reports, and actual medication changes can all influence the results.

The research team believes that this type of test may be more suitable for specific patients who have not responded to their first antidepressant treatment or have experienced significant side effects, but more research is needed to identify who may truly benefit.

A Real-World Test of Precision Medicine

The lesson from this trial is not to negate precision medicine, but rather to remind us that while testing can generate personalized data, this data must be used correctly in the right patients, at the right time of treatment, and within the right clinical process in order to improve real health outcomes.

Meanwhile, the trial was conducted in primary healthcare in Australia, with 82% of participants of European descent and approximately 10% of Asian descent. Whether the results can be fully extrapolated to other healthcare systems and ethnic groups still requires further verification.

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