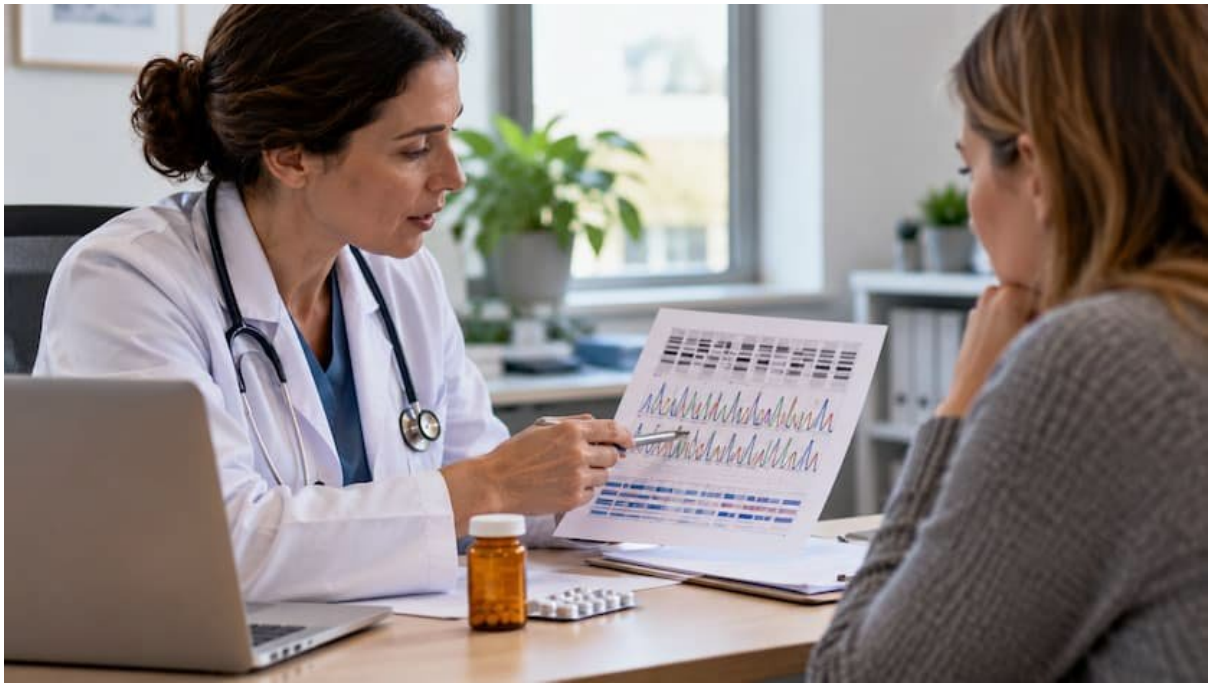
19 October 2026

Translated from Spanish

Genetic testing does not improve the effectiveness of antidepressants in a trial



A clinical study conducted in Australia with 552 adults found that selecting antidepressants based on genetic information did not produce a significant improvement in depressive symptoms compared to standard treatment recommendations.

A clinical trial conducted in Australia has tested one of the most debated proposals of personalized medicine: using genetic testing to select the most suitable antidepressant for each patient. The research, published on October 15, 2026, in the scientific journal *The Lancet Primary Care*, found that this strategy did not achieve better clinical outcomes than prescribing based on conventional medical guidelines.

The study, called PRESIDE, brought together 552 adults with moderate or severe depressive symptoms treated in 19 general medicine practices in the Australian state of Victoria.

The researchers compared two drug selection procedures. In one, physicians received recommendations based on genetic characteristics related to antidepressant metabolism. In the other, the recommendations came from Australian treatment guidelines.

After twelve weeks, both groups had experienced improvements in their depressive symptoms, but the differences between them were not statistically significant.

The work was led by Jonathan Emery, a professor at the Lee Kong Chian School of Medicine at Nanyang Technological University in Singapore, in collaboration with Australian researchers.

The results do not mean that genetics is useless in psychiatry. What they show is that systematically incorporating this type of information into the selection of antidepressants did not produce a demonstrable additional clinical benefit in the population and conditions studied.

Personalized medicine seeks to reduce trial-and-error treatments.

Depression is a mental health disorder that can affect mood, motivation, sleep, concentration, and the ability to perform daily activities.

Treatment may include psychological interventions, antidepressant medications, or a combination of both strategies, depending on the severity of symptoms, clinical history, and patient preferences.

One of the main challenges of pharmacotherapy is that not all people respond to a drug in the same way.

Some patients experience significant improvement with the first antidepressant prescribed. Others require dose adjustments, medication changes, or additional treatments before achieving a satisfactory response.

Adverse effects may also occur that make it difficult to maintain treatment.

These differences have driven the search for tools capable of guiding medical decisions from the outset.

These include pharmacogenetic tests, which study certain DNA variants related to how the body processes medications.

The interest in finding more effective treatments has also led to research into new pharmacological options for people with treatment-resistant depression, although that line of research addresses a different clinical problem than the one examined in the Australian trial.

What information do the CYP2C19 and CYP2D6 genes provide?

Pharmacogenetics studies how certain inherited differences can modify the body's response to medications.

In the case of antidepressants, two of the most researched genes are CYP2C19 and CYP2D6.

Both participate in the production of enzymes of the cytochrome P450 system, responsible for metabolizing numerous drugs in the body.

Variations in these genes can influence the rate at which a person transforms or eliminates certain antidepressants.

Some individuals metabolize certain drugs more slowly, while others exhibit greater enzyme activity.

These differences can affect the concentration of the drug in the blood and, in certain circumstances, modify the likelihood of experiencing adverse effects or an insufficient response.

However, the relationship between metabolism and clinical efficacy is not automatic.

The improvement in depression depends on numerous factors, including the nature of the disorder, other illnesses, concomitant treatments, therapeutic adherence, and individual circumstances.

Therefore, knowing a genetic variant does not allow one to predict with certainty which medication will eliminate a person's symptoms.

The PRESIDE trial sought to determine whether using this information to guide prescriptions offered measurable benefits in routine primary care consultations.

The PRESIDE trial included 552 adults from 19 medical practices

The researchers recruited 552 people aged between 18 and 65 who had moderate or severe depressive symptoms.

The participants came from 19 general medicine practices in the state of Victoria, Australia.

The research used a randomized, double-blind design to compare two prescribing strategies.

In the intervention group, physicians received recommendations based on the patients' genetic results, specifically on variants of CYP2C19 and CYP2D6.

In the comparison group, professionals received recommendations developed from Australian therapeutic guidelines.

Random assignment sought to reduce the influence of initial differences between participants.

Furthermore, the double-blind design was intended to limit biases related to knowledge of the strategy used.

Neither the patients nor the doctors knew whether the recommendations received corresponded to the pharmacogenetic procedure or the one based on conventional guidelines.

This feature is especially important in research on depressive symptoms, where the expectations of patients and professionals can influence certain clinical assessments.

The main outcome was examined after twelve weeks.

Both groups improved, but the differences were not significant.

The researchers observed a reduction in depressive symptoms in both groups during the twelve weeks of follow-up.

However, patients whose treatment recommendations were based on genetic information did not experience significantly greater improvement than those treated using standard clinical guidelines.

The team also examined depression remission, understood as the reduction of symptoms to a previously defined clinical level.

The proportion of participants who achieved remission did not show statistically significant differences between the strategies.

Similarly, no significant difference was found in the proportion of patients who responded to treatment.

These results indicate that, under the trial conditions, having pharmacogenetic recommendations did not translate into a demonstrable clinical advantage during the evaluated period.

It is important to distinguish this finding from the claim that genetic testing can never be useful.

A trial may show that an intervention does not offer additional benefits when applied generally to a given population, without ruling out that there are subgroups of patients who may benefit.

The study also does not demonstrate that all antidepressants are equivalent or that the individual choice of medication is unimportant.

Selection continues to require a clinical evaluation of symptoms, history, contraindications, drug interactions, and patient preferences.

Why the results differ from some previous research

The authors noted that their findings contrast with certain previous studies in which prescription guided by pharmacogenomic information had been associated with more favorable outcomes.

One possible explanation lies in the differences between the populations studied.

Some previous work had been carried out with patients who had severe depression and were receiving care from specialists in psychiatry.

The PRESIDE trial, on the other hand, focused on people seen in general practices, an environment where a significant portion of depressive disorders are diagnosed and treated.

Patient characteristics, prior therapeutic experience, and the procedures used to interpret genetic results can influence the performance of these strategies.

Researchers believe that pharmacogenetic testing may be most useful in selected clinical situations, for example, when a person does not respond to an antidepressant or experiences significant adverse effects.

However, that possibility needs to be specifically evaluated and does not constitute a conclusion proven by this essay.

The complexity of treatment is also related to the diversity of biological mechanisms involved in depression. Experimental research has explored molecular alterations in brain circuits related to depressive symptoms, illustrating that the illness does not depend solely on the rate at which medications are metabolized.

However, laboratory results on brain mechanisms cannot be used directly to decide which antidepressant a patient should receive.

Primary care presents different conditions than specialized psychiatry

One of the most relevant aspects of PRESIDE is that it evaluated pharmacogenetic prescribing in general medicine consultations.

Primary care is usually the first point of contact for people experiencing depressive symptoms.

In that environment, professionals must simultaneously address physical and mental health problems, review medications, and decide when it is necessary to request specialized support.

A genetic test can provide information about the metabolism of certain drugs, but its usefulness depends on how it is incorporated into clinical decisions.

For example, the result should be interpreted in relation to the specific drug being considered and the patient's other characteristics.

Furthermore, having a recommendation does not guarantee that the treatment will remain unchanged during the following weeks.

Symptoms may change, side effects may occur, and healthcare professionals may need to adjust dosages or substitute the medication.

The research team stressed that it is still necessary to better understand at what point in the therapeutic process it is appropriate to use pharmacogenomic tests.

It must also be determined whether certain groups of patients derive sufficient benefit to justify their systematic use.

More genetic information does not guarantee better medical outcomes.

Precision medicine seeks to adapt health interventions to the biological and clinical characteristics of each person.

In various specialties, genetic testing has made it possible to identify hereditary diseases, guide certain cancer treatments, and adjust specific medications.

However, the usefulness of a test depends on its results allowing for decisions that can improve health.

In the case of depression, drug metabolism represents only one part of the problem.

The clinical response is also influenced by psychological, social, environmental, and medical factors that cannot be summarized in two genes.

This interaction is especially evident when there are simultaneous chronic illnesses. The relationship between type 2 diabetes and depression shows how physical and mental conditions can influence each other and complicate treatment management.

Jonathan Emery, the trial's lead investigator, pointed out that having more genetic information does not automatically translate into better clinical outcomes.

His team believes it is necessary to identify more precisely which patients could benefit from this approach before recommending its routine application.

This conclusion is relevant for healthcare systems that are considering incorporating genetic testing into routine care.

Before expanding its use, it is necessary to evaluate not only its ability to identify genetic variants, but also its actual effect on symptoms, remission, adverse effects, and resources used.

The limitations of the trial require that its results be interpreted accurately.

The randomized, double-blind design is a major strength of the research.

The participation of 19 clinics also made it possible to examine the use of the recommendations in a routine clinical setting, rather than limiting the evaluation to specialized centers.

However, the trial has limitations that must be considered.

The research was conducted in a region of Australia and its results will not necessarily be reproduced to the same extent in countries with different population characteristics or health systems.

In addition, the main analysis focused on a twelve-week follow-up.

This period allows for the evaluation of initial changes in symptoms, but it does not by itself establish the consequences of using pharmacogenetic tests during prolonged treatments.

The intervention focused on variants of two genes related to the metabolism of certain medications.

Therefore, the results do not allow us to judge all possible genomic tests or all personalized medicine strategies that may be developed in the future.

Another important distinction is that the absence of a statistically significant difference does not prove that both strategies produce identical results under any circumstances.

This means that, with the data and procedures used, the trial did not find sufficient evidence of a clinical advantage of pharmacogenetic prescribing over conventional care.

What are the implications of the study for patients and professionals?

The results do not justify patients discontinuing their antidepressants or modifying the doses on their own initiative.

The research evaluated drug selection procedures, not the advisability of abandoning treatments that are working.

In clinical practice, the choice of an antidepressant continues to depend on an individual assessment.

Professionals should consider the intensity of symptoms, previous treatments, coexisting diseases, possible drug interactions, and drug tolerance.

Pharmacogenetic testing may still have specific indications, particularly when there is a clinical reason to investigate differences in the metabolism of certain drugs.

However, the Australian trial does not support the assumption that routinely performing these tests on all people with moderate or severe depressive symptoms will necessarily improve their outcome.

The research also raises a question for health policies: how to determine when a diagnostic innovation provides enough additional benefit to warrant incorporation into routine services.

In medicine, a technology can provide accurate biological information without that information significantly changing patient outcomes.

The PRESIDE study provides experimental evidence to distinguish between the two situations.

Researchers consider it a priority to develop new studies that will identify which people could benefit from genetically guided prescribing, especially those who have difficulty responding to conventional treatments or experience significant adverse effects.

Until more conclusive evidence exists for these groups, the results support maintaining an individualized selection of antidepressants based on clinical assessment and available therapeutic recommendations.

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