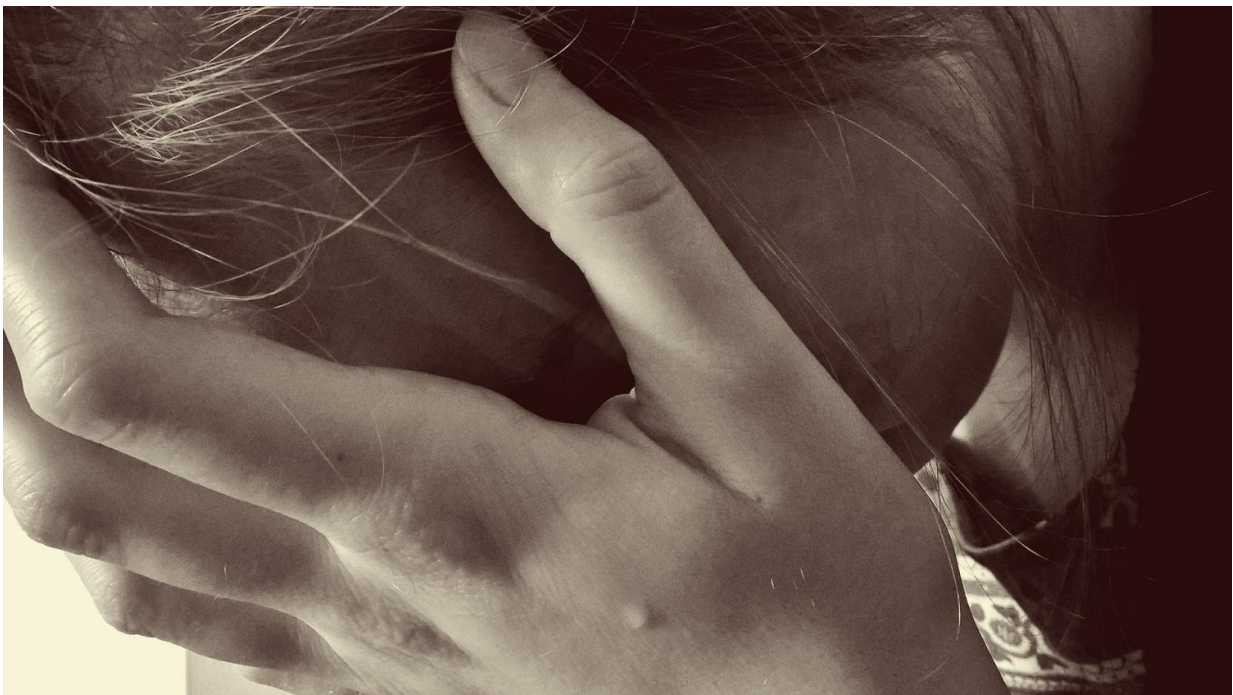# Precision medicine opens the door to scientific wellness preventive approaches to suicide

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Researchers have developed a more precise way of diagnosing suicide risk, by developing blood tests that work in everybody, as well as more personalized blood tests for different subtypes of suicidality that they have newly identified, and for different psychiatric high-risk groups.

The research team, led by scientists at the Indiana University School of Medicine, also showed how two apps, one based on a suicide risk checklist and the other on a scale for measuring feelings of anxiety and depression, work along with the blood tests to enhance the precision of tests and to suggest lifestyle, psychotherapeutic and other interventions. Lastly, they identified a series of medications and natural substances that could be developed for preventing suicide.

"Our work provides a basis for precision medicine and scientific wellness preventive approaches," said Alexander B. Niculescu III, MD, PhD, professor of psychiatry and medical neuroscience at IU School of Medicine and attending psychiatrist and research and development investigator at the Richard L. Roudebush Veterans Affairs Medical Center.

The article, "Precision medicine for suicidality: from universality to subtypes and personalization," appears in the August 15 online edition of the Nature Publishing Group's leading journal in psychiatry, *Molecular Psychiatry*.

The research builds on earlier studies from the Niculescu group.

"Suicide strikes people in all walks of life. We believe such tragedies can be averted. This landmark larger study breaks new ground, as well as reproduces in larger numbers of individuals some of our earlier findings," said Dr. Niculescu.

There were multiple steps to the research, starting with serial blood tests taken from 66 people who had been diagnosed with psychiatric disorders, followed over time, and who had at least one instance in which they reported a significant change in their level of suicidal thinking from one testing visit to the next. The candidate gene expression biomarkers that best tracked suicidality in each individual and across individuals

were then prioritized using the Niculescu group's Convergent Functional Genomics approach, based on all the prior evidence in the field.

Next, working with the Marion County (Indianapolis, Ind.) Coroner's Office, the researchers tested the validity of the biomarkers using blood samples drawn from 45 people who had committed suicide.

The biomarkers were then tested in another larger, completely independent group of individuals to determine how well they could predict which of them would report intense suicidal thoughts or would be hospitalized for suicide attempts.

The biomarkers identified by the research are RNA molecules whose levels in the blood changed in concert with changes in the levels of suicidal thoughts experienced by the patients. Among the findings reported in the current paper were:

- An algorithm that combines biomarkers with the apps that was 90 percent accurate in predicting high levels of suicidal thinking and 77 percent accurate in predicting future suicide-related hospitalizations in everybody, irrespective of gender and diagnosis.
- A refined set of biomarkers that apply universally in predicting risk of suicide among both male and female patients with a variety of psychiatric illnesses, including new biomarkers never before linked to suicidal thoughts and behavior.
- Four new subtypes of suicidality were identified (depressed, anxious, combined, and non-affective/psychotic), with different biomarkers being more effective in each subtype.
- Biomarkers that were associated with specific diagnoses and genders, such as one, known as LHFP, that appears to be a very strong predictor for depressed men.
- Two of the biomarkers, APOE and IL6, have broad evidence for

involvement in suicidality and potential clinical utility as targets for drug therapies, as well as suggest a neurodegenerative and inflammatory component to the predisposition to suicide. APOE is responsible for proteins involved with managing cholesterol and fats, and some forms of the gene have been strongly implicated as risks for Alzheimer's disease. IL6 expresses proteins involved in the body's inflammation response.

- Potential drug therapies and natural substances for preventing suicide, using the blood biomarker signatures and bioinformatics approaches. They included medications already in use to treat psychiatric illnesses and drugs approved for other uses, such as the diabetes medication metformin.