Defeating depression through early risk detection and targeted medication

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New personalized approaches to depression will either predict when a person is at risk to stop the condition in its tracks or target the illness with the optimum drug.

Depression is a chronic illness and a first episode of lingering low mood—the kind that's so severe it disrupts daily life—is often followed by relapses. Around half of sufferers experience the condition more than once.

For many, it becomes a lifelong condition. In the European Union alone, 7.2% of people suffer from chronic depression, with women four times more at risk.

As doctors and scientists work to bring this global epidemic under control, one idea gaining traction is that identifying people who are at risk before they become depressed will protect their mental health in the future.

"It's becoming increasingly clear that a first episode of depression is the trigger for a second, so scientifically there's a decent probability that preventing the first episode can stop the next," said Dr. Eiko Fried, associate professor of psychology at Leiden University in the Netherlands.

Dr. Fried is the principal investigator of WARN-D, a project that sets out to forecast who is at risk of "falling into the valley" and then generate a personalized program for preventing this from happening. The project began in 2021 and runs until 2026.

Early warnings

While preventative programs already exist—including psychological interventions that build resilience—they can work only when at-risk individuals are identified in time.

WARN-D is the first study attempting to build a reliable early-warning system.

It will take the shape of a smartphone application that can monitor the mental health of a user in real time and blend this information with what is known about the person's social, psychological and biological background. The objective is to catch people as they approach their personal tipping point: the moment when the disturbances stacking up in their life put them at risk of tumbling.

Development of the app will start within the next two years. First, the researchers must pick through reams of data, looking for common features between individuals with a susceptibility to depression.

They aim to group people according to a complex set of traits that include personality (e.g. extrovert versus introvert), factors that have catalyzed the development of their disorder (such as a traumatic childhood) and a person's innate ability to bounce back from setbacks (otherwise known as resilience).

Different groups are likely to respond to different interventions, meaning a preventative program must be tailored to be successful.

At-risk youth

The study uses a pool of 2,000 young-adult students—recruited 500 at a time—based in the Netherlands. People in this demographic are disproportionately affected by depression and, as a result, are of particular interest to the researchers.

"Early-onset depression is associated with a worse clinical outcome over a person's lifespan," said Dr. Fried. "Many young people will spend over 20% of their lives in a state of depression."

Another plus side of recruiting young students is that they are easily persuaded (with the help of a cash incentive of up to €90) to wear a

smartwatch night and day for the first three months of their two-year study. The watch tracks activity ranging from steps taken to hours slept and taps into stress levels using a heartrate sensor.

In addition, the participating students are asked questions four times a day about in-the-moment matters believed to play a role in depression. The queries can be about how well they slept, how happy they feel, how angry they are and what they happen to be doing at that moment.

Plus, every Sunday the students receive some more global questions about anxiety and depression such as: what were the best and worst events from the week?

"The holy grail is to figure out the ways in which people are different in their stress response and the ways in which they're similar," Dr. Fried said. "Once we find the communalities, we can start working on systems that will make people more resilient."

Why so sad?

Symptoms of depression range from intense sadness, tiredness and brain fog to sleep disturbance, loss of appetite and a lack of interest in previously enjoyable activities.

The causes of the condition almost certainly involve an interaction of many factors, some biological and others environmental. Genes probably play a role, with a person more likely to develop depression if someone in the family has also been affected. That said, anyone can become depressed.

Potential triggers include stress, poverty, illness, hormonal changes and traumatic life events such as childhood adversity and bereavement.

Although some research shows drugs can help, antidepressants are hit-and-miss at best, with only half of patients responding positively to their first prescription. Getting medication right from the start would have a big impact on both individual sufferers and the economy—and would ease pressure on doctors.

Dr. Talia Cohen Solal is a neuroscientist and the chief executive officer of Genetika+, an Israeli company developing tools to create personalized depression treatment.

"What we have is a trial-and-error approach to medication," said Dr. Cohen Solal. "As a result, 63% of patients try multiple medications, and a third don't respond after two rounds of treatment."

Brain in a dish

For her project, RxMine, she uses a "brain in a dish" model (where human brain stem cells and networks are generated in the lab from blood samples using stem cell technology) to identify the optimal antidepressant for each patient.

In earlier research, Dr. Cohen Solal's team discovered specific cellular changes called "biomarkers" in brain tissue that are linked to a patient's responsiveness to a given drug.

For a person to have a successful response to an antidepressant, sufficient changes in the levels of those corresponding biomarkers must be found in the generated brain models.

The researchers envision a world where all patients with depression are offered a test to determine which drug is most suited to their condition. This could reduce depression-related healthcare costs by 43%, with savings of up to €6 500 per patient a year.

The team is expanding its trials to new drugs while working on ways to making its testing procedures more efficient.

"We hope to have something to roll out within two years," said Dr. Cohen Solal. "Our ultimate hope is to fast-track the right treatment, so patients no longer have to endure the unacceptable and life-threatening process of trial-and-error medication selection."

More information:

- WARN-D
- RxMine

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